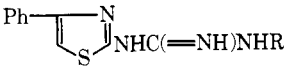
Similarly, various aryl-substituted N-aryl-N′-2-thiazolylguanidines and their hydrochlorides were prepared (see Table II).

TABLE II

N-ARYL-N′-2-(4-PHENYLTHIAZOLYL)GUANIDINES



No.	R	Mp, °C	Formula[a]	HCl Mp, °C	HCl formula[a]
1	*o*-MeC_6H_4	146	$C_{17}H_{16}N_4S$	193	$C_{17}H_{17}ClN_4S$
2	*m*-MeC_6H_4	142	$C_{17}H_{16}N_4S$	130–131	$C_{17}H_{17}ClN_4S$
3	*p*-MeC_6H_4	142	$C_{17}H_{16}N_4S$	187	$C_{17}H_{17}ClN_4S$
4	*o*-$OMeC_6H_4$	142	$C_{17}H_{16}N_4OS$	185–186	$C_{17}H_{17}ClN_4OS$
5	*m*-$OMeC_6H_4$	143	$C_{17}H_{16}N_4OS$	179–180	$C_{17}H_{17}ClN_4OS$
6	*p*-$OMeC_6H_4$	144	$C_{17}H_{16}N_4OS$	183	$C_{17}H_{17}ClN_4OS$
7	*p*-$OEtC_6H_4$	145	$C_{18}H_{18}N_4OS$	125	$C_{18}H_{19}ClN_4OS$
8	*p*-ClC_6H_4	147	$C_{16}H_{13}ClN_4S$	134–135	$C_{16}H_{14}Cl_2N_4S$

[a] See footnote *a*, Table I.

Polyiodo Derivatives of Anisidine Isomers

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Iodinated aromatic compounds are useful diagnostic agents because of their X-ray absorbtivity and their stability which minimizes generation of iodide ion.[1] We have prepared some tri- and tetraiodoanisidine derivatives for use as intermediates in the synthesis of potential radiopaque agents by treating potassium iodide with polyacetoxymercuri-N-acetylanisidines.[2] These polyiodo compounds are 70–80% in iodine, a level comparing favorably to that in currently used radiodiagnostic agents.[3]

Experimental Section[4]

Acetoxymercuration of the N-Acetylanisidines.—A ground mixture of 4.1 g (0.025 mole) N-acetyl-*p*-anisidine[5] and 32.0 g (0.100 mole) of $Hg(OAc)_2$ was heated in an open glass vessel in a 115–130° oil bath for 40 min. A shield was used. The resulting pink viscous liquid was treated at 80° with 50 ml of H_2O to yield 0.9 g (3.0%) of a white powder, mp 250–260° dec (from AcOH–H_2O). On the basis of subsequent iodination reactions, the product was tetraacetoxymercuri-N-acetyl-*p*-anisidine. Evaporation of the filtrate to 10 ml gave 3.0 g of a second white powder, mp 180–200° dec (from AcOH–H_2O). On the basis of subsequent iodination reactions, the product was a triacetoxymercuri-N-acetyl-*p*-anisidine.

It was possible to prepare the tetraacetoxymercuri derivative in 83% yield (crude) by heating for 1 hr at 130° a molar ratio of 5:1 $Hg(OAc)_2$–N-acetyl-*p*-anisidine.

The tetraacetoxymercuri derivatives of N-acetyl-*o*- and -*m*-anisidine were prepared similarly with the 5:1 molar ratio and the more severe reaction conditions. Table I (footnotes *d* and *e*) give properties.

Polyiodo-N-acetylanisidines.—Over a period of 45 min, a solution of 0.91 g (0.0040 mole) of I_2 and 1.72 g (0.012 mole) of KI in 25 ml of H_2O was added dropwise to a refluxing, stirred suspension of 0.85 g (0.00071 mole) of tetraacetoxymercuri-N-acetyl-*p*-anisidine in 100 ml of H_2O. Reaction was continued for 30 min after addition. On cooling, the product precipitated. It was filtered and washed with dilute KI solution and then H_2O to give 0.38 g (80%) of tetraiodo-N-acetyl-*p*-anisidine, mp 271° dec (from 95% EtOH). *Anal.* ($C_9H_7I_4NO_2$) I.

Tetraiodo-N-acetyl-*o*-anisidine, tetraiodo-N-acetyl-*m*-anisidine, and a triiodo-N-acetyl-*p*-anisidine were prepared essentially as above. See Table I.

Tetraiodo-*o*-anisidine and a Triiodo-*o*-anisidine.—To a solution of 4.0 g (0.0060 mole) of tetraiodo-N-acetyl-*o*-anisidine in 400 ml of 96% H_2SO_4, 164 ml of H_2O was added dropwise with stirring and cooling to keep the temperature below 60°. After addition, the solution was heated rapidly to 125° and at once was cooled to room temperature when 1.32 g (35%) of tetraiodo-*o*-anisidine separated. It was filtered on glass wool and washed (dilute $NaHCO_3$, H_2O), mp 149–151° (from MeOH). *Anal.* ($C_7H_5I_4NO$) I.

The filtrate was poured onto crushed ice and 0.38 g of a triiodo-*o*-anisidine separated, the structure of which was not determined; mp 132–133° (from MeOH). *Anal.* ($C_7H_6I_3NO$) I: calcd, 75.94; found, 76.28.

TABLE I

POLYIODO ANISIDINES

Isomer	Acetylated	Mp, °C	Yield,[a] %	Formula[g]
p	Yes	271	80	$C_9H_7I_4NO_2$
p[c]	Yes	258–259[b]	88	$C_9H_8I_3NO_2$
m[d]	Yes	266[b]	75	$C_9H_7I_4NO_2$
o[e]	Yes	278–279[b]	74	$C_9H_7I_4NO_2$
o	No	149–151	35[f]	$C_7H_5I_4NO$
o[c]	No	132–133	...	$C_7H_6I_3NO$[h]

[a] Crude yields based on acetoxymercuri precursor except where noted. [b] Melts with decomposition. [c] Particular triiodo isomer not determined. [d] Acetoxymercuri precursor obtained in 53% yield, mp 224–233° dec (from AcOH–H_2O). [e] Acetoxymercuri precursor obtained in 83% yield, mp 238–240° dec (from AcOH–H_2O). [f] Yield based on N-acetyl precusor. [g] All compounds were analyzed for I. [h] I: calcd, 75.94; found, 76.28.

Some Sulfonamide Derivatives of Cyclohexane[1]

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In continuation of our studies on reactions of N-halosulfonamides,[2] the reaction of N,N-dibromo-4-nitrobenzenesulfonamide with cyclohexene was investigated; *trans*-2-bromo-1-(4-nitrobenzenesulfonamido)cyclohexane (I) was the major product. Some compounds (III–V) having substituents other than bromine were synthesized starting from I *via* N-(4-nitrobenzenesulfonyl)-cyclohexenimine (II) and reduced catalytically to corresponding sulfanilamide derivatives (VI–IX).

Experimental Section[3]

N,N-Dibromo-4-nitrobenzenesulfonamide.—4-Nitrobenzenesulfonamide (20.2 g) was dissolved in a solution of NaOH (8 g) in H_2O (200 ml) and Br_2 (36 g) was added dropwise with stirring. The crystals that separated were filtered off, washed with H_2O, and dried, mp 163–164° dec. The yield was 34 g (94.5%). A

(1) V. H. Wallingford, *J. Am. Pharm. Assoc.*, **42**, 721 (1953).

(2) M. Ragno, *Gazz. Chim. Ital.*, **70**, 420 (1940); *Chem. Abstr.*, **35**, 3242 (1941).

(3) P. K. Knoefel in "Drill's Pharmacology in Medicine," J. R. DiPalma, Ed., 3rd ed, McGraw-Hill Book Co., Inc., New York, N. Y., 1965, p 1429.

(4) Where analyses are indicated only by symbols of elements, analytical results obtained for those elements were within ±0.4% of theoretical values. Analyses were performed by Micro Tech Laboratories, Skokie, Ill. Melting points were taken in capillary tubes and are uncorrected.

(5) N. D. Cheronis and J. B. Entriken, "Semimicro Qualitative Organic Analysis," Thomas Crowell Co., New York, N. Y., 1947, p 404.

(1) Part IX of a series entitled Reaction of N-Haloamide. Part VIII: *Chem. Pharm. Bull.* (Tokyo), in press.

(2) Y. Ueno, S. Takemura, Y. Ando, and H. Terauchi, *ibid.*, **15**, 1198, 1322, 1328 (1967).

(3) All melting points were uncorrected and determined using a W. Büchi melting point determination apparatus. Where analyses are indicated only by symbols of the elements, analytical results obtained for those elements were within ±0.4% of the theoretical values.