TABLE I

2,5-DISUBSTITUTED BENZOXAZOLES

Compounds 1, 5 and 8 were made by refluxing the corresponding aminophenol with ethanolic carbon disulfide for 60 hours. Compounds 2, 6 and 9 were made by fusion of the corresponding aminophenol hydrochloride with urea for two hours at 140–150°. Compounds 3, 7 and 10 were made by the reaction of the corresponding aminophenol with ethanolic cyanogen bromide for 50 hours at room temperature. Compound 4 and 11 were made from the corresponding aminophenol and dicyandiamide in ethanol–HCl by the method of Smith, *et al.* (THIS JOURNAL, **51**, 2522 (1929)). The hydrochloride of butyl 4-hydroxy-3-aminobenzoate (490 mg.), refluxed for two hours with 170 mg. of dicyandiamide in 2 ml. of 90% ethanol, gave 150 mg. of a hydrochloride melting at 175–180°. The base set free from this hydrochloride, repeatedly recrystallized from ethanol and from benzene, melted at 182–183°, and gave a mixed melting point of 182–184° with a specimen of 2-amino-5-carbobutoxybenzoxazole (m.p. 186°). *Anal.* Calcd. for $C_{12}H_{14}N_2O_3$: N, 11.97. Found: N, 12.49, 12.59.

Cpd.	X	Y	Formula	Description[i]	Solvent	Solubility	Yield, %	M.p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
1	Cl	SH	C_7H_4ClNOS[a]	Needles	90% al.	V.s., Na_2CO_3	70	268 d.[b]	7.55	7.57
2	Cl	OH	$C_7H_4ClNO_2$	Fibrous needles	80% al.	V.s., al., ether, Na_2CO_3	92	189–190[c]	8.26	8.24
3	Cl	NH_2	$C_7H_5ClN_2O$[d]	Plates	50% al.	Sl.s., H_2O	88	182–183	16.62	16.55
4	Cl	$\mathrm{H_2N{-}\underset{\underset{NH}{\Vert}}{C}{-}NH{-}}$	$C_8H_7ClN_4O$[e]	Elongated plates	Benzene	I., al., acetone	40	228 d.	24.51	24.63
5	BuO_2C—	SH	$C_{12}H_{13}NO_3S$	Needles	Dil. al.	V.s., al., ether, Na_2CO_3	76	134	5.58	5.48
6	BuO_2C—	OH	$C_{12}H_{13}NO_4$	Needles	Benzene–petroleum	S., org. solvents	90	99–100	5.96	5.97
7	BuO_2C—	NH_2	$C_{12}H_{14}N_2O_3$	Prisms	Ether	I., H_2O, sl.s., C_6H_6, v.s., al.	74	186	11.97	12.01
8	HO_2C—	SH	$C_8H_5NO_3S$[f]	Prisms	Water	V.s., al.	62	282 d.[g]	7.18	7.10
9	HO_2C—	OH	$C_8H_5NO_4$	Needles	Water	S., al.	70	>300	7.82	7.88
10	HO_2C—	NH_2	$C_8H_6N_2O_3$	Needles	90% al.	I., ether, C_6H_6 Sl.s., H_2O, al.	60	275 d.	15.73	15.68
11	HO_2C—	$\mathrm{H_2N{-}\underset{\underset{NH}{\Vert}}{C}{-}NH{-}}$	$C_9H_8N_4O_3$[h]	Needles	Abs. al.	Sl.s., al., ethyl acetate	60	280 d.	25.45	25.52

[a] Na salt, colorless plates from ethanol, soluble in water. [b] Deck and Dains (THIS JOURNAL, **55**, 4989 (1933)) reported a melting point of 261–262°, and Korczynski and Obarski[3] reported a melting point of 283° for this substance. [c] Upson (*Am. Chem. J.*, **32**, 25 (1905)) reported a melting point of 184–185°, and an English patent (240,969 (1925)) reported a melting point of 189–190° for this substance. [d] Hydrochloride: needles melting at 229° with decomposition; hydrolyzed by water. *Anal.* Calcd. for $C_7H_5ClN_2O \cdot HCl \cdot H_2O$: N, 12.56. Found: N, 12.70. Hydrobromide: plates melting at 240° with decomposition. [e] Hydrochloride: needles from alcohol, melting at 273° with decomposition; slightly soluble in water. [f] Disodium salt: flat needles, hygroscopic and quite soluble in alcohol or water. Mono-sodium salt: long colorless columns from absolute alcohol, soluble in water. [g] French patent (54,436 (1933)) reported a decomposition temperature of 283–284°. [h] Hydrochloride: columns from ethanol–HCl, melting at 280° with decomposition; hydrolyzed by water. Sodium salt: plates from water, soluble in alcohol. [i] All compounds are colorless.

TABLE II

5,5′-DISUBSTITUTED-DIBENZOXAZOLE-2,2′-DISULFIDES

These compounds were made from the monosodium salts of the corresponding mercaptans by reaction with 0.1 *N* iodine–potassium iodide solution in water; the yields were practically quantitative. Compounds a and b are soluble in the usual organic solvents. Compound c is practically insoluble in organic solvents, but soluble in the calculated quantity of sodium carbonate solution.

Cpd.	X	Formula	Description	Solvent	M.p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
a	Cl	$C_{14}H_6Cl_2N_2O_2S_2$	Prisms	Benzene	141–142	7.59	7.60
b	BuO_2C-	$C_{24}H_{24}N_2O_6S_2$	Needles	Benzene	115–116	5.60	5.62
c	HO_2C-	$C_{16}H_8N_2O_6S_2$	Prisms		237–238 d.	7.22	7.11, 7.31

and was identified as 5-carboxylic-benzoxazole by mixed melting point and analysis.

Anal. Calcd. for $C_8H_5NO_3 \cdot H_2O$: N, 7.73. Found: N, 7.62.

5-Carboxylic-benzoxazole was independently synthesized by refluxing 300 mg. of 3-amino-4-hydroxybenzoic acid with an excess of formic acid for three hours, evaporating the excess formic acid, and finally heating the residue at 170° for three hours (94% yield). The product crystallized from dilute ethanol as prismatic needles melting at 249° with foaming, and gave no color with ferric chloride.

Anal. Calcd. for $C_8H_5NO_3 \cdot H_2O$: N, 7.73. Found: N, 7.72.

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4,4′,4″-Trinitrotriphenylamine[1]

BY ROBERT IRVING WALTER

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A trinitro compound prepared from triphenylamine by nitration with fuming nitric acid has been reported by Heydrich[2] and by Herz.[3] A substance having the same melting point, 280°, was subsequently described by Madelung, *et al.*,[4] who nitrated triphenylamine with nitrogen dioxide. None of these authors proposed a structure for his product, but Beilstein[5] lists the compound as 4,4′,4″-trinitrotriphenylamine on the basis of a private communication from Piccard, who also claimed that the melting point was 396°. There are no data in the literature in support of this assignment of structure.

Attempts in this Laboratory to repeat the nitration of triphenylamine using Herz's procedure[3] resulted in a yellow powder which gave yellow crystals melting at 383° from nitromethane. In no case has the nitration resulted in a substance melting at 280°, nor have the recrystallization

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(1) This work was carried out at Rutgers University in connection with contract number N7-ONR-45403 of the Office of Naval Research.

(2) C. Heydrich, *Ber.*, **18**, 2156 (1885).

(3) R. Herz, *ibid.*, **23**, 2539 (1890).

(4) W. Madelung, E. Reiss and E. Herr, *Ann.*, **454**, 36 (1927).

(5) Beilstein, "Handbuch der Organischen Chemie," Fourth Edition, Vol XII, Springer Verlag, Berlin, 1929, p. 717.

procedures in the literature given such a product.

To check the structure of the nitration product, an alternate synthesis was carried out from *p*-nitrochlorobenzene and *p*-nitroaniline in the presence of copper. (This reaction[6] occurs without rearrangement of the *p*-nitro group to give 4-nitrotriphenylamine both from diphenylamine and *p*-iodonitrobenzene[7] and from 4-nitrodiphenylamine and iodobenzene.[8]) The product was identical to the nitration product obtained by Herz's procedure, confirming the structural assignment in Beilstein.

The behavior of the substance on heating suggests the existence of more than one polymorphic form; the material reported to melt at 280° might have been an additional metastable crystal form of the same compound.

Experimental

Preparation of 4,4′,4″-Trinitrotriphenylamine.—A number of runs of the nitration procedure of Herz[3] gave 75–80% of a fine yellow powder. Analysis showed that this was contaminated with lower nitration products. These impurities are more soluble in the common solvents than the very slightly soluble trinitro compound, but in nitromethane and nitrobenzene the latter seems to be the more soluble, for fractional crystallization gave successively purer crops of diamond-shaped plates. The third crop from nitromethane was taken for analysis.

Anal. Calcd. for $C_{18}H_{12}N_4O_6$: C, 56.84; H, 3.18; N, 14.73. Found: C, 56.94; H, 3.28; N, 14.84.

Alternatively, 138 g. (1 mole) of *p*-nitroaniline, 315 g. (2 moles) of *p*-nitrochlorobenzene, 160 g. of powdered anhydrous potassium carbonate, 5 g. of copper powder (copper bronze previously washed with ether was used) and 750 ml. of nitrobenzene were refluxed with stirring for 17 hours in an all-glass apparatus designed to condense nitrobenzene but pass water through.[9] The reaction mixture was steam distilled to remove nitrobenzene, filtered, and the pasty mass washed with acetone three times by decantation. Finally, it was extracted with acetone in a Soxhlet apparatus for two hours to remove unreacted reagents and nitrobenzene. The resulting coarse yellowish powder weighed 182 g., yield 48%. Continued extraction with acetone for 72 hours gave 0.8 g. of irregular crystals in the extract. *Anal.* Calcd. values above. Found: C, 56.74; H, 3.39; N, 14.59.

Behavior on Melting.—Observation on the Kofler hot stage, for which a 500° thermometer was calibrated, showed no melting at 280° of samples previously purified by recrystallization from nitromethane, nitrobenzene–ethanol or acetone. Instead, all samples sublimed, beginning at 270–280°, to give fine needles on the cover glass. (The synthetic material can be sublimed rapidly and quantitatively at 290°, and the product is pure. The nitration product is not purified by this procedure, since the partial nitration products also sublime.) Above 375°, the needle sublimate and any unsublimed residue undergo transition to irregular crystalline plates. These melt at 382–383°. Both preparations individually, and a mixture, showed this sequence of changes.

X-Ray powder photographs were taken of the plates prepared by recrystallization from nitromethane, the needle sublimate, and these needles heated to 375° under a cover plate. The patterns were identical, indicating that if any of these samples were polymorphs, the high temperature crystal forms reverted quickly to the room temperature form on cooling.

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(6) I. Goldberg, *Ber.*, **39B**, 1691 (1906).

(7) S. Kawai, *J. Chem. Soc., Japan*, **49**, 235 (1928), in *C. A.*, **24**, 80 (1930).

(8) J. Piccard and L. M. Larsen, THIS JOURNAL, **39**, 2008 (1917).

(9) F. D. Hager in "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1932, p. 544.

A New Alkaloid from *Amianthium Muscaetoxicum* Gray

BY NORBERT NEUSS

RECEIVED FEBRUARY 23, 1953

Amianthium muscaetoxicum Gray, also called Stagger grass or Fly poison,[1] has long been known to be poisonous to cattle and sheep.[2] Over forty years ago, Alsberg[3] studied its pharmacology and found that it contained a very poisonous alkaloid which he was not able to crystallize. He claimed that the alkaloid resembled Veratrine chemically, although it did not produce a typical veratrinic response.

In view of these findings, we have undertaken a systematic investigation of Stagger grass alkaloids. The chromatographic separation of total alkaloids on acid-washed alumina, using Reichstein's technique,[4] yielded four fractions. One was readily identifiable as Jervine. Two were unidentified ester alkaloids (tentatively called Alkaloid E and F) which were shown to be responsible for the high toxicity and hypotensive action of the plant extract. The last fraction was an alkamine which has never been isolated previously. It was also isolated directly from the total alkaloids by treatment with acetone. Initial observations indicated that it might be related to steroidal alkamines. In view of recent interest in veratrum alkaloids, we would like to give our preliminary results now. The chemistry of the hypotensive principles of the plant will be published in detail later. The pharmacology of all active principles will be published elsewhere.

The new alkaloid, for which we propose the name Amianthine, is a C_{27} compound. This formulation as well as the presence of Jervine in total alkaloids and the close relationship of Stagger grass to *Veratrum* species favor the assumption that it might be a steroidal or modified steroidal alkamine.

When Amianthine is dissolved in concentrated sulfuric acid it gives a yellow color. However, it remains colorless in 84% sulfuric acid, and in this respect it is significantly different from most alkamines isolated from *Veratrum album* and *Veratrum viride*. The alkaloid has a pK_a value of *ca.* 9.7 and appears to be a tertiary base. The infrared spectrum does not show a resolved band corresponding to NH between the OH band at 2.87 μ and a very weak band at 3.14 μ. There is a very strong band corresponding to a conjugated CO at 6.06 μ and a band half as strong at 6.20 μ indicative of a carbon–carbon double bond. The ultraviolet absorption spectrum in alcohol exhibits a maximum at 250 mμ, log ϵ 4.04, which also corresponds to a conjugated CO.

It readily absorbs two moles of hydrogen in acetic acid or alcohol solution using platinum as a catalyst. The tetrahydro derivative formed is prob-

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(1) W. C. Muenscher, "Poisonous Plants of the U. S. A.," The Macmillan Co., New York, N. Y., 1951.

(2) C. D. Marsh, A. B. Clawson and H. Marsh, *U. S. Dept. Agr. Bull.*, 710 (1918).

(3) C. L. Alsberg, *Science*, **39**, 958 (1914); C. L. Alsberg, *J. Phar. Exp. Therap.*, **3**, 473 (1911–1912).

(4) T. Reichstein and C. W. Shoppee, *Discussion of the Faraday Society*, No. **7**, 305 (1949).