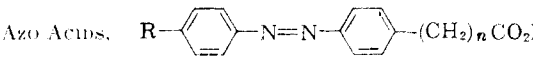
TABLE I

AZO ACIDS, 

Compound R	n	Reagents: p-H2NC6H4-	Reagents: p-NOC6H4-	M.p., °C.	Formula	Analyses, %: Calcd. C	Calcd. H	Found C	Found H	Ultraviolet absorption: λmax, mμ (ε × 10⁻³)		
H	0	CO_2H	H	247–249	$C_{13}H_{10}N_2O_2$[a]	. . .	. . .	. . .	. . .	228 (112)	320 (21.2)	434 (1.0)
H	1	CH_2CO_2H	H	193–195	$C_{14}H_{12}N_2O_2$	69.99	5.03	70.30	5.22	230 (123)	320 (20.2)	434 (5.9)
CH_3	0	CO_2H	CH_3	280–282	$C_{14}H_{12}N_2O_2$	69.99	5.03	70.13	5.25	231 (117)	331 (25.8)	440 (8.8)
CH_3	1	CH_2CO_2H	CH_3	217–219	$C_{15}H_{14}N_2O_2$	70.85	5.55	70.60	5.35	234 (139)	327 (23.8)	434 (8.3)
C_2H_5	0	C_2H_5	CO_2H	245–247	$C_{15}H_{14}N_2O_2$	70.85	5.55	70.97	5.74	229 (114)	330 (24.7)	441 (8.9)
C_2H_5	1	CH_2CO_2H	C_2H_5	193–195	$C_{16}H_{16}N_2O_2$	71.62	6.01	71.83	6.43	234 (127)	327 (19.4)	435 (10.)
n-C_3H_7	0	n-C_3H_7	CO_2H	232–234	$C_{16}H_{16}N_2O_2$	71.62	6.01	71.64	6.18	231 (113)	330 (26.4)	443 (8.4)

[a] Spectra measured in 95% ethanol on a Beckman DB spectrophotometer. [b] H. D. Anspon, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, New York, N. Y., 1955, p. 711.

of reactions was used to transform *n*-propylbenzene to *n*-propylaniline.[14]

***p*-Phenylazophenylacetic Acid.**—The following procedure is representative of those used to synthesize the azo acids recorded in Table I.

To a hot solution of 25 g. (0.17 mole) of *p*-aminophenylacetic acid in 165 ml. of glacial acetic acid was added 17.8 g. (0.17 mole) of nitrosobenzene. The reaction mixture was allowed to stand at room temperature for 20 hr. and the precipitate which had formed was collected by filtration, washed with acetic acid, and then with water. After two recrystallizations from 95% ethanol (400 ml.), there was obtained 20.6 g. (52%) of product, m.p. 193–195°.

(14) Ng. Phi. Buu-Hoï, Ng. D. Xuong, and Ng. H. Nam, *J. Chem. Soc.*, 1573 (1955).

Some Derivatives of 2,2′-(Phenylimino)diethanol

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Because N,N-bis(2-chloroethyl)aniline (I) and 1,4-butanediol dimethanesulfonate (II) are carcinostats,[1,2] it was deemed desirable to prepare and study a new compound possessing structural features of both I and II, namely, the dimethanesulfonate (III) of 2,2′-(phenylimino)diethanol (IV). Compound III might be expected to exhibit behavior somewhat analogous to that of I, because a methylsulfonyloxy group resembles a halogen atom in some of its chemical properties.[3] Indeed, its carcinostatic activity might even prove higher than that of I because, whereas the *p*-aldehyde derived from I is inactive, that related to III is active.[4]

Interestingly, although the dibenzenesulfonate (V),[5,6] di-*p*-toluenesulfonate (VI),[5,6] and bis-*p*-nitrobenzenesulfonate[7] of IV have been prepared, III does not appear to have been described, despite the preparation[5] of the dimethanesulfonate of 2,2′-(2,4-dinitrophenylimino)-diethanol.

In 1951, IV (in pyridine) was treated with benzenesulfonyl chloride, and a 26% yield of recrystallized V was isolated[5]; similarly, a 35% yield of pure VI was obtained.[5] In the following year, an "improvement" was patented,[6] in which IV was converted to its disodium derivative and this, in xylene, was treated with *p*-toluenesulfonyl chloride to afford pure VI in an even poorer yield (16.3%). Consequently, we first attempted the preparation of III by a route different from either of these, namely, by the reaction of I with two molecular proportions of silver methanesulfonate in acetonitrile. Compound III was isolated, in quantitative yield, as a sirup which was readily converted into its crystalline hydrochloride. For the preparation of I from IV, an improved method, based on that devised[3] for the direct synthesis of N-(2-chloroethyl)aniline hydrochloride from 2-anilinoethanol, was developed; this gave the crystalline hydrochloride of I directly. The preparation and properties of this salt are described here because, although it has been used in pharmacological and hydrolysis studies,[3] its properties have never, so far as can be ascertained, been reported in the literature.

Although III was successfully prepared in this way, the method is slow and tedious; moreover, it involves the prior preparation of both I and silver methanesulfonate. We therefore attempted the synthesis of III directly from IV, by rapid sulfonylation[10]; this gave a quantitative yield of III, isolated as its crystalline hydrochloride. A modification of the procedure afforded pure V and VI in yields of 87 and 90%, respectively, as compared with reported yields[5] of 26 and 35%.

Such compounds as III can undergo intramolecular transformation. Hence, in order to verify the structure of III, the compound was converted into the corresponding *p*-aldehyde (VII). This was identical with a specimen of *p*-{bis[2-(methylsulfonyl)-oxyethyl]-amino}benzaldehyde prepared[4] from *p*-[bis(2-chloroethyl)amino]benzaldehyde (VIII), showing that III had the proposed structure.

(1) A. Haddow, G. A. R. Kon, and W. C. J. Ross, *Nature*, **162**, 824 (1948); A. Haddow and G. M. Timmis, *Acta Unio Intern. Contra Cancrum*, **7**, 469 (1951).

(2) A. Loveless and W. C. J. Ross, *Nature*, **166**, 1113 (1950).

(3) R. S. Tipson, *Advan. Carbohydrate Chem.*, **8**, 107 (1953).

(4) R. C. Elderfield, R. N. Prasad, and T.-K. Liao, *J. Org. Chem.*, **27**, 573 (1962).

(5) G. M. Timmis, British Patent 662,645 (1951).

(6) G. M. Timmis, British Patent 672,691 (1952).

(7) M. Ishidate, Y. Sakurai, and S. Owari, *Pharm. Bull.* (Tokyo), **5**, 203 (1957).

(8) R. S. Tipson, *J. Org. Chem.*, **27**, 1449 (1962).

(9) C. C. Hunt, *J. Pharmacol. Expl. Therap.*, **95**, 177 (1949); L. F. Lacionov, *Brit. J. Cancer*, **10**, 26 (1956); V. M. Rakova, A. D. Chinaeva, and A. Y. Berlin, *J. Gen. Chem. USSR*, **29**, 3922 (1959); compare, "The Merck Index," 7th Ed., P. G. Stecher, Ed., Merck & Co., Inc., Rahway, N. J., 1960, p. 622.

(10) R. S. Tipson, *J. Org. Chem.*, **9**, 235 (1944).

As additional evidence regarding the structure of III, its treatment with sodium iodide in acetone at room temperature[11] gave crystalline N,N-bis(2-iodoethyl)aniline (IX)[12]; the same product was obtained by similar treatment of VI.

Finally, VII was treated with sodium iodide in acetone, giving the corresponding *p*-aldehyde (X), which was identical with *p*-[bis(2-iodoethyl)amino]benzaldehyde, previously prepared[13] by the action of sodium iodide on VIII; this confirmed the structure assigned to VII and, therefore, to III.

Occasion was taken to prepare *p*-[bis(2-*p*-tolylsulfonyloxyethyl)amino]benzaldehyde (XI) by two methods, namely, from VI and from VIII.

Screening data[14] revealed that III is inactive *vs.* Walker carcinoma 256 implanted in rats, whereas I is active.[1] In the Dunning IRC-741 leukemia in rats, III produced 30-day survivors at the maximum tolerated dose of 5 mg./kg./day, negative results being obtained at lower dosage levels; I produced 30-day survivors at a dose of 12.5 mg./kg./day. Compound IX is inactive, at dosage levels covering the range of 200–25 mg./kg./day, *vs.* Walker carcinoma 256 implanted in rats.

Experimental[15]

2,2′-(Phenylimino)diethanol (IV).—Compound IV (practical grade) was recrystallized from dry ether (10 ml./g.) by adding pentane (2 ml./g.), giving colorless crystals (64%); m.p. 58° (lit.[16] m.p. 58°). A second crop (28%) had m.p. 55–57°.

(a) N,N-Bis(2-chloroethyl)aniline (I) and (b) its Hydrochloride.—An improvement on an earlier method[17] was used. A solution of IV (18.1 g., 0.1 mole) in 50 ml. of chloroform was saturated with dry hydrogen chloride (4 g.) and cooled to −5°. Phosphoryl chloride (36 ml., 0.4 mole) was added in one portion, and the mixture was refluxed in the dark, with stirring, for 1.5 hr., cooled, and evaporated under diminished pressure (bath temp., 65°). The resulting sirup was dissolved in 50 ml. of chloroform, absolute ethanol (50 ml.) was added in portions[8] with cooling, and the solution was evaporated to a sirup (A).

(a) Base I.—Sirup A was stirred with 250 ml. of water, giving light gray crystals which were washed with water and dried; wt., 20.4 g. (94%); m.p. 42–45°. It was recrystallized from methanol (1 ml./g.) and washed with cold methanol[18]; wt., 17.8 g.; m.p. 45–46°. A second crop (1.6 g.) gave, on recrystallization, 1.3 g.; m.p. 45–46°. Total yield, 19.1 g. (88%) (lit.[19] m.p. 45–47°; lit.[17] yield, 82%).

(b) Hydrochloride.—Sirup A was re-evaporated several times with absolute ethanol,[8] giving a crystalline mass which was stirred with cold absolute ethanol[18] and filtered; colorless crystals; wt., 16.6 g. (65%); m.p. 89–94°. It was recrystallized from absolute ethanol (1 ml./g.) or from acetone (1.7 ml./g.); m.p. 93–95°.

Anal. Calcd. for $C_{10}H_{14}Cl_3N$: C, 47.2; H, 5.5; Cl, 41.8; N, 5.5. Found: C, 47.1; H, 5.8; Cl, 41.2; N, 5.3.

Protected from moisture, the compound can be kept at room temperature for several years without appreciable decomposition; such a sample, slightly darkened in color, was readily purified by conversion into the free base and reconversion into the hydrochloride.

2,2′-(Phenylimino)diethyl Dimethanesulfonate (III) Hydrochloride. (a) From I.—The procedure was based on an improved method[20] for the synthesis of sulfonic esters. A solution of 10.9 g. (0.05 mole) of I and 30.5 g. (0.15 mole) of silver methanesulfonate in 275 ml. of acetonitrile was refluxed in the dark, with stirring, for 9.5 hr., the suspension was filtered, and the precipitate was washed with acetonitrile. The combined filtrate and washings were evaporated to a sirup which was mixed with 25 ml. of dichloromethane; unreacted silver salt was removed and washed with dichloromethane, and the combined filtrate and washings were evaporated to dryness, giving 16.9 g. (100%) of III as a red sirup. This was dissolved in chloroform (4 ml./g.), dry hydrogen chloride was passed in to saturation, and the solution was refrigerated overnight. The suspension was filtered with suction, and the crystals were washed with cold chloroform[18] (without exposure to the air) until practically colorless and pressed dry. The crystals were then suspended in cold acetone,[18] refiltered, and dried; colorless crystals; wt., 13.7 g. (73%). Recrystallization from hot acetone (7 ml./g.) did not change the infrared spectrum; m.p. 98–105° (sealed tube; bath preheated to 95°; heating at 2°/min.).

Anal. Calcd. for $C_{12}H_{20}ClNO_6S_2$: C, 38.6; H, 5.4; Cl, 9.5; N, 3.8; S, 17.2. Found: C, 38.7; H, 5.5; Cl, 9.6; N, 3.6; S, 17.2.

(b) From IV.—Methanesulfonyl chloride (19.2 ml., 0.252 mole) was added in one portion, with stirring, to a solution of 19.0 g. (0.105 mole) of IV in 120 ml. of dry pyridine at −5°, and the mixture was stirred at −5° for 30 min. Water (10 ml.) was added in portions,[10] with stirring and cooling below 5°, the stirred mixture was quickly diluted with ice-cold sulfuric acid (70 ml. of concentrated acid added to 215 ml. of water), the mixture was immediately extracted with chloroform, and the extract was processed in the usual way,[10] to give a quantitative yield of sirupy III having the same infrared spectrum as that of the specimen prepared by method a. It was converted into the hydrochloride; colorless crystals, having the same melting point and infrared spectrum as the previous specimen.

2,2′-(Phenylimino)diethyl Di-*p*-toluenesulfonate (VI) from IV.—A solution of IV (9.5 g., 0.053 mole) in 88 ml. of dry pyridine was cooled to −5°, and 22 g. (0.115 mole) of *p*-toluenesulfonyl chloride was added in one portion. The mixture was stirred at −5° for 30 min. and kept overnight in a refrigerator. Water (10 ml.) was added in portions,[10] whereupon VI crystallized. A further 250 ml. of water was added with stirring and the crystals were filtered off, washed with water, and dried; wt., 24.5 g. (96%); m.p. 87–89° (lit.[5] yield of crude material, 72%). A solution of the crude product in chloroform was washed in the usual way,[10] and the dried solution was evaporated to dryness. The product was dissolved in acetone, the solution re-evaporated to dryness, the residue dissolved in 200 ml. of acetone, the solution treated with decolorizing carbon, the filtrate evaporated to 150 ml., and pentane (250 ml.) gradually added; colorless crystals; wt., 19.8 g.; m.p. 90–91°. A second crop (3.9 g.) gave, on recrystallization, 3.2 g.; m.p. 90–91°. Total yield of recrystallized VI, 23.0 g. (90%) (after recrystallization from methanol, lit.[5] yield, 35%; lit.[5] m.p. 91°).

2,2′-(Phenylimino)diethyl Dibenzenesulfonate (V) from IV.—This was prepared as for VI, except that 14.7 ml. (0.115 mole) of benzenesulfonyl chloride was used. After portionwise addition of 10 ml. of water,[10] the solution remained clear, but gradual addition of 250 ml. of water gave pale tan crystals; wt., 22.9 g. (95%); m.p. 68–73° (lit.[5] yield of crude material, 63%). This was purified as for VI and recrystallized from acetone (1 ml./g.) by adding absolute ethanol (4 ml./g.) and refrigerating; colorless crystals; wt., 18.1 g.; m.p. 72–74°. A second crop (2.8 g.) had m.p. 72–73°. Total yield of recrystallized V, 20.9 g. (87%) (after recrystallization from methanol, lit.[5] yield, 26%; lit.[5] m.p. 64–65°). Because of the higher melting point of our material, the compound was analyzed.

Anal. Calcd. for $C_{22}H_{23}NO_6S_2$: C, 57.3; H, 5.0; N, 3.0; S, 13.9. Found: C, 57.3; H, 5.1; N, 2.9; S, 14.1.

***p*-{Bis[2-(methylsulfonyl)-oxyethyl]amino}benzaldehyde (VII) from III.**—A solution of 16.9 g. (0.05 mole) of III in 30 ml. of N,N-dimethylformamide was added dropwise during 1 hr., with

(11) R. S. Tipson, M. A. Clapp, and L. H. Cretcher, *J. Org. Chem.*, **12**, 133 (1947).

(12) Compound IX had only been known, hitherto, as an oil: J. L. Everett and W. C. J. Ross, *J. Chem. Soc.*, 1972 (1949).

(13) R. H. Wiley and G. Irick, *J. Org. Chem.*, **26**, 593 (1961).

(14) The compounds were evaluated by the Cancer Chemotherapy National Service Center. Details of the testing procedures employed are given in *Cancer Chemotherapy Rept.*, **25**, 1 (1962).

(15) For recrystallization of alkylating agents, use of hot hydroxylic solvents was avoided where possible. Melting points were determined in a modified Hershberg apparatus and were corrected.

(16) G. O. Gabel, *Ber.*, **58**, 577 (1925).

(17) R. C. Elderfield, I. S. Covey, J. B. Geiduschek, W. L. Meyer, A. B. Ross, and J. H. Ross, *J. Org. Chem.*, **23**, 1749 (1958).

(18) Precooled in Dry Ice–chloroform.

(19) M. H. Benn, L. N. Owen, and A. M. Creighton, *J. Chem. Soc.*, 2800 (1958).

(20) (a) W. D. Emmons and A. F. Ferris, *J. Am. Chem. Soc.*, **75**, 2257 (1953); (b) see also, J. M. Sprague and E. L. Engelhardt, U. S. Patent 2,671,105 (1954).

stirring, to a solution of 10.0 ml. (0.11 mole) of phosphoryl chloride in 30 ml. of N,N-dimethylformamide at −5°. The cooling bath was then removed, stirring was continued for 1.75 hr., and the mixture was poured onto 1500 g. of ice, giving a clear solution which was made basic by the addition of sodium bicarbonate. The blue, crystalline product was washed with water and dried; wt., 15.2 g. (83%); m.p. 108–111°. For purification, a solution in cold acetone (25 ml./g.) was stirred with activated carbon, filtered, and evaporated to dryness; the residue was recrystallized from acetone (8.7 ml./g.) by adding pentane (6.6 ml./g.); colorless crystals; m.p. 114–115° (lit.[4] m.p. 122.5–123.5°). Because the melting point was lower than that recorded[4] for VII prepared from VIII, the preparation of VIII and, thence, of VII was repeated.

p-[Bis(2-p-tolylsulfonyloxyethyl)amino]benzaldehyde (XI) from VI.—Compound VI (6.12 g., 0.0125 mole) was treated with the same proportions of reactants as in the preceding section. After completion of the reaction, the mixture was poured onto 375 g. of ice, with the precipitation of a sirup; the mixture was made basic with sodium bicarbonate and extracted with chloroform. The extract was dried and evaporated to dryness, the residue was mixed with acetone and filtered, and the filtrate was evaporated to dryness. The resulting sirup was dissolved in 1 ml. of acetone and 10 ml. of absolute ethanol was added, giving 3.61 g. (56%) of crystals; m.p. 109–113°. On recrystallization from acetone–pentane, it had m.p. 112–115° (bath preheated to 106°; heating at 2°/min.).

Anal. Calcd. for $C_{25}H_{27}NO_7S_2$: C, 58.0; H, 5.3; N, 2.7; S, 12.4. Found: C, 58.0; H, 5.3; N, 2.7; S, 12.5.

p-[Bis(2-chloroethyl)amino]benzaldehyde (VIII) from IV.—The following is an improvement on an earlier procedure.[13] Phosphoryl chloride (45.9 ml., 0.5 mole) was added in one portion to 77.4 ml. of N,N-dimethylformamide cooled to −5°; the temperature rose to 60°. The solution was cooled to 5° and a solution of 30.25 g. (0.167 mole) of IV in 75 ml. of N,N-dimethylformamide was rapidly added with stirring, the temperature again rising to 60°. The solution was heated (bath temp. 100–106°) while stirring for 90 min., cooled, and processed as usual.[13] The product was triturated twice with water and dissolved in chloroform, and the solution was washed successively with aqueous potassium hydrogen sulfate and water, dried, and evaporated to dryness. It was crystallized from absolute methanol (1 ml./g.); cream-colored crystals; wt., 32.4 g.; m.p. 86–88°. The mother liquor afforded a second crop; wt., 1.7 g.; m.p. 85–87°. Total yield, 34.1 g. (83%); lit.[13] yield, 58%. On recrystallization from methanol, it had m.p. 87–88° (lit. m.p. 85–88°[13,17]; 86–87°[21]; 88.5°[22,23]).

VII from VIII.—A mixture of 6.15 g. (0.025 mole) of VIII, 15.5 g. (0.076 mole) of silver methanesulfonate, and 150 ml. of acetonitrile was refluxed in the dark, with stirring, for 67 hr. It was then processed as in the preparation of III from I, except that N,N-dimethylformamide was used for removal of unreacted silver salt; the combined filtrate and washings (65 ml.) were diluted with 100 ml. of water, and nucleated with VII. After some crystal growth (10 min.), the suspension was diluted with 500 ml. of water and stirred; purple crystals; wt., 7.3 g. (80%); m.p. 107–112° [lit.[4] yield (crude), 79%; lit.[4] m.p. (crude) 118–122°]. On recrystallization from cold acetone–pentane (see VII from III), it had m.p. 114–115°, unchanged by a second recrystallization. Its infrared spectrum was identical with that of VII prepared from III, and a mixture melting point showed no depression. A specimen of VII, kindly supplied by Dr. R. C. Elderfield, had an infrared spectrum identical with those of our two specimens; it had m.p. 114–116°, and the mixture melting point with either of our specimens showed no depression.

An over-all yield of 47% of VII from IV (*via* I and VIII) had earlier been obtained.[4,17] However, for our preparation of VII from IV (*via* III), which took only 1 day, the over-all yield was 83%.

The **2,4-dinitrophenylhydrazone** of VII was prepared in the usual way,[24] except that a solution of VII in N,N-dimethylformamide (7 ml./g.) was used; yield, 100%; m.p. 180–182°. It was recrystallized from N,N-dimethylformamide (55 ml./g.) by adding absolute ethanol (214 ml./g.); dark red crystals; m.p. 183–184°.

Anal. Calcd. for $C_{19}H_{20}N_4O_6S_2$: C, 41.8; H, 4.3; N, 12.8; S, 11.8. Found: C, 41.8; H, 4.4; N, 12.7; S, 11.6.

p-[Bis(2-p-tolylsulfonyloxyethyl)amino]benzaldehyde (XI) from VIII.—Silver *p*-toluenesulfonate was prepared as previously described,[26a] except that for its isolation the final concentrate was mixed with acetone and filtered. Compound VIII (2.46 g., 0.01 mole) was treated for 3 days with 8.37 g. (0.03 mole) of silver *p*-toluenesulfonate in 60 ml. of acetonitrile (see VII from VIII). Water (20 ml.) was added to the cooled filtrate to give 4.2 g. (dry) of crystals which were dissolved in acetone. The solution was filtered and evaporated to dryness, the sirup was dissolved in 1 ml. of acetone, and the solution was diluted with 6 ml. of absolute ethanol and refrigerated; 3.21 g. (62%) of crystals; m.p. 109–113°. After a second recrystallization (acetone–ethanol), it had m.p. 110–113°; mixed with the product prepared from VI, there was no depression in melting point. Its infrared spectrum was identical with that of the previous specimen.

The **2,4-dinitrophenylhydrazone** was prepared and recrystallized as for that of VII; red crystals; m.p. 153–156° (bath preheated to 150°; heating at 4°/min.).

Anal. Calcd. for $C_{34}H_{34}N_8O_{16}S_2$: C, 53.4; H, 4.5; N, 10.0; S, 9.2. Found: C, 53.5; H, 4.6; N, 9.9; S, 9.2.

N,N-Bis(2-iodoethyl)aniline (IX) and its Hydrochloride. (a) From III.—A solution of 6.75 g. (0.02 mole) of III and 12.0 g. (0.08 mole) of anhydrous sodium iodide in 120 ml. of acetone was kept in a stoppered flask at room temperature for 72 hr. The resulting, colorless precipitate (containing sodium methanesulfonate[25]) was filtered, washed with acetone, and dried; wt., 5.9 g. (125% of the theoretical yield[25]). The combined filtrate and washings were evaporated to dryness at room temperature, the residue was dissolved in chloroform and water, and the chloroform layer was dried and evaporated to dryness, giving 8.0 g. of an amber sirup which crystallized at 0° and which was recrystallized from 8 ml. of acetone plus 160 ml. of absolute ethanol at −70°; m.p. 30–31°.

Anal. Calcd. for $C_{10}H_{13}I_2N$: C, 30.0; H, 3.3; I, 63.3; N, 3.5. Found: C, 30.1; H, 3.5; I, 63.2; N, 3.5.

A solution of IX (8 g.) in 32 ml. of acetone was saturated with dry hydrogen chloride and cooled, giving yellow crystals which were filtered, washed with cold acetone,[18] and dried; wt., 4.41 g.; m.p.[26] 118–120° dec. A second crop (4.12 g.) had m.p.[26] 118–121° dec.; total yield, 8.53 g. (98%). It was recrystallized from cold chloroform (4 ml./g.) by adding acetone (2 ml./g.) and refrigerating; colorless crystals; m.p. 120–121°.

Anal. Calcd. for $C_9H_{14}ClI_2N$: C, 27.5; H, 3.2; Cl, 8.0; I, 58.0; N, 3.2. Found: C, 27.7; H, 3.3; Cl, 8.0; I, 57.2; N, 3.2.

(b) From VI.—A solution of 9.80 g. (0.02 mole) of VI and 12.0 g. (0.08 mole) of sodium iodide in 120 ml. of acetone was treated as in a, giving 7.7 g. (100%) of sodium *p*-toluenesulfonate. The combined filtrate and washings were processed as in a, giving colorless crystals; wt., 8.0 g. (100%); m.p. 30–31°. The infrared spectrum was identical with that of IX prepared from III. The compound was converted into its crystalline hydrochloride as in a (yield, 93%). After recrystallization, it had m.p. 120–121°. Its infrared spectrum was identical with that of the previous specimen.

p-[Bis(2-iodoethyl)amino]benzaldehyde (X) from VII.—A solution of 1.83 g. (0.005 mole) of VII and 3.0 g. (0.02 mole) of sodium iodide in 30 ml. of acetone was kept at room temperature for 6 days, giving 1.55 g. (131%) of crystals containing sodium methanesulfonate.[25] The filtrate and washings were processed as for IX, giving 2.15 g. (100%) of crystals. It was recrystallized from chloroform (2.5 ml./g.) by dropwise addition of pentane (2.5 ml./g.), giving, in three crops, 1.96 g. (91%); m.p., 99–106°. After a second such recrystallization, it had m.p. 107–108° (lit.[13] yield, 59% after one recrystallization; lit.[13] m.p. 105–107° after three recrystallizations). As the material described in the literature[13] had a poor analysis, the compound was analyzed.

Anal. Calcd. for $C_9H_{11}I_2NO$: C, 30.8; H, 3.1; I, 59.2; N, 3.3. Found: C, 30.9; H, 3.0; I, 59.1; N, 3.3.

(21) A. K. Sen, T. Okada, C. C. Price, and R. Ratoosh, *Acta Unio Intern. Contra Cancrum*, **26**, 774 (1960).

(22) R. M. Anker and A. H. Cook, *J. Chem. Soc.*, 489 (1944).

(23) I. G. Farbenindustrie A.-G., British Patent 456,534 (1936).

(24) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 219.

(25) This compound apparently crystallizes as a double salt with sodium iodide.

(26) This melting point was determined by placing the tube containing the sample in a bath preheated to 115° and continuing the heating at the rate of 2°/min.