chloride gives a deep orange color with this isomer but no precipitate. The **acetyl derivative**, crystallizing from benzene as white, flat needles, melts at 223–224°. Butler and Royle[2] reported the acid as melting at 240–241° and the acetyl derivative at 221–223°.

5-Amino-1-naphthonitrile.—Prepared as described for the other isomers and crystallized twice from benzene–ligroin, the yield from 30 g. of sodium salt was 4.1 g. (20%); m. p. 138.5–139.5°. After two additional crystallizations this isomer formed slender yellow prisms melting at 139.5–140°. The melting point has been reported as 137°[17] and 139°.[14]

5-Hydroxy-1-naphthoic Acid.—Following the procedure described for the 5,2-isomer, this acid was obtained in 53–57% yield. After one crystallization it formed nearly white, slender prisms of m. p. 235–238° (dec.). After further crystallization from water and finally benzene the melting point was 237–240° (dec.) (literature, 235–236°[6], 235°[18]). This isomer melts with decomposition even in an evacuated capillary. With ferric chloride it gives a cloudy violet solution which deposits a dark precipitate on standing. The **acetyl derivative** crystallizes from benzene in white iridescent leaflets with mother of pearl luster, m. p. 205–206° (literature,[6] 202°).

When hydrolysis of the 5-amino-2-naphthonitrile was carried out at 200° the product melted at 219–232°, and no pure substance could be readily isolated.

(17) Heilpern and Spielfogel, *J. Soc. Chem. Ind.*, **17**, 836 (1898).

(18) Dziewonski and Kocwa, *Bull. intern. acad. Polon.*, 405 (1928).

Summary

A convenient method has been developed for the small scale preparation of hydroxynaphthoic acids. The appropriate naphthylaminesulfonic acid is converted by distillation with potassium cyanide into the aminonitrile which is converted directly to the hydroxynaphthoic acid by heating with 10% sulfuric acid at 200° or 220°. Since the m. p. of 4-hydroxy-2-naphthoic acid prepared in this way is much higher than the previously reported value its structure has been confirmed by conversion to the known 4-hydroxy-2-methylnaphthalene.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF PENNSYLVANIA]

Some Analogs of Troeger's Base and Related Compounds[1]

BY T. R. MILLER[2] AND E. C. WAGNER

Troeger's base, obtainable in various ways by reactions involving *p*-toluidine and formaldehyde in acid media,[3] was shown by Spielman[4] to be 1,2′-methylene-3-*p*-tolyl-6-methyl-1,2,3,4-tetrahydroquinazoline. The sequence of reactions by which Troeger's base is formed was established by Wagner.[5]

Troeger's base hitherto has been the only compound of its type reported and characterized. In the study here described, the reactions known to yield Troeger's base from *p*-toluidine and from the various intermediate compounds involved were applied to four other aromatic primary amines with para-substituents. From *p*-anisidine and *p*-phenetidine, and from the corresponding trimeric methylene-arylamines, methylene-*bis*-arylamines and tetrahydroquinazolines[6] there were obtained compounds shown to be structural analogs of Troeger's base. Application of the same procedures to *p*-chloroaniline and *p*-bromoaniline, and to the corresponding trimeric Schiff bases, methylene-*bis*-arylamines, *o*-aminobenzylarylamines and tetrahydroquinazolines, yielded as products two bases eventually recognized as the 1-hydroxymethyltetrahydroquinazolines (VI in the reaction scheme).[7] Compound VI may provisionally be considered the immediate precursor of VII and convertible into VII by loss of the elements of water. Actually this relationship was not established experimentally, as the dehydration could not be effected by the means employed (heat, dehydrating agents). None the less it seems probable that in the reaction between formaldehyde and the tetrahydroquinazoline (V),

(1) This paper is constructed from the thesis submitted by T. R. Miller in partial satisfaction of the requirements for the degree of Doctor of Philosophy at the University of Pennsylvania, June, 1940.

(2) Du Pont Fellow in Chemistry, 1939-1940. Present address, Carbide and Carbon Chemicals Corporation, South Charleston, W. Va.

(3) (a) Troeger, *J. prakt. Chem.*, (2) **36**, 227 (1886); (b) Löb, *Z. Elektrochem.*, **4**, 428 (1897); (c) Goecke, *ibid.*, **9**, 470 (1903); (d) German Patent 105,797; *Friedl.*, **5**, 84; (e) Lepetit, Maffei and Maimeri, *Gazz. chim. ital.*, **57**, 867 (1927); (f) Eisner and Wagner, THIS JOURNAL, **56**, 1938 (1934).

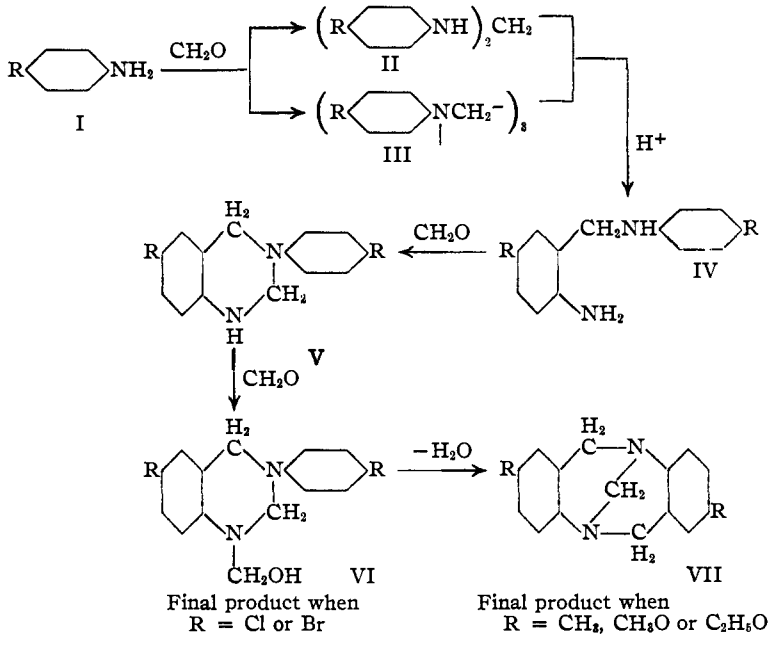
(4) Spielman, *ibid.*, **57**, 583 (1935).

(5) Wagner, *ibid.*, **57**, 1296 (1935).

(6) The *o*-aminobenzylarylamines related to *p*-anisidine and *p*-phenetidine have not proved isolable [T. R. Miller and Wagner, *ibid.*, **60**, 1738 (1938)], and were therefore not available as starting compounds.

(7) Both compounds were obtained previously [Wagner and Eisner, *ibid.*, **59**, 879 (1937)] as unidentified by-products in the preparation of the dihydroquinazolines.

yielding finally VI or VII, the initial attack is upon the nitrogen[8] (rather than at the 2′ nuclear position[9]) with formation of the N-hydroxymethyl compound (VI). The reaction scheme suggested earlier[5] may now be modified to include this step.



The structures of the Troeger base analogs were established by the methods used by Spielman[4] for Troeger's base itself. Action of nitrous acid yielded N,N′-dinitroso compounds, with elimination of the methylene bridge as carbon dioxide. Action of acetic anhydride yielded N,N′-diacetyl compounds, with liberation of formaldehyde. Cleavage by strong reduction gave as the sole isolable product 6-amino-3-hydroxytoluene.

Evidence for the structures of the bases designated by formula VI is incomplete but probably adequate. Analysis showed the molecular formula to be $C_{15}H_{14}ON_2X_2$. Reaction with phenyl isocyanate yielded in each case a urethan; Troeger's base does not react with phenyl isocyanate.[4] Cleavage by strong reduction yielded in each case only the *p*-halogeno-aniline, a result not structurally significant though consistent with structure VI. The yield of this product from each compound exceeded 50%, a result which seems to exclude the possibility that the hydroxymethyl group is attached to the 2′ carbon instead of the nitrogen. The fact that the new bases were formed directly from the corresponding tetrahydroquinazolines, and in yields in general greater than those obtained from the other starting compounds (I, II, III, IV), permits a strong presumption that the tetrahydroquinazoline is the immediate precursor of VI, in which the tetrahydroquinazoline structure is retained.

In the experiments which yielded the hydroxymethyl compounds (VI) there were isolated also relatively larger amounts of the corresponding 3,4-dihydroquinazolines. Since it has been shown that the dihydroquinazoline is formed by dehydrogenation of the tetrahydroquinazoline by compounds of types II[10] or III,[11] it may be inferred that when in the tetrahydroquinazoline the substituent para to the nitrogen atom is chlorine or bromine the reactivity of the iminohydrogen with formaldehyde is decreased. This retards the condensation of V with formaldehyde and allows dehydrogenation of V to the dihydroquinazoline to become the principal reaction.

Experimental Part

General.—Methylene-*bis*-*p*-substituted anilines (II) were prepared from the corresponding amines by the method of Bischoff and Reinfeld.[12] Trimeric methylene-*p*-substituted anilines (III) were made and purified by the procedure described by J. G. Miller and Wagner.[13] N-(*o*-aminobenzyl)-arylamines (IV) were prepared from compounds of type II or III (R = Cl or Br).[6] The corresponding compounds in which R = OCH_3 or OC_2H_5 were not available.[6] Tetrahydroquinazolines (V) in which R = Cl or Br were prepared from the corresponding aminobenzylarylamines (IV) by action of formaldehyde in alcoholic alkaline solution.[3f] Tetrahydroquinazolines in which R = OCH_3 or OC_2H_5 were obtained by reduction of the 3,4-dihydroquinazolines by sodium and alcohol.[14] The required dihydroquinazolines were prepared from the methylene-*bis*-arylamines or the trimeric Schiff bases by action of formaldehyde and formic acid.[15]

(8) Wagner, THIS JOURNAL, **55**, 724 (1933).

(9) Von Braun and Kruber, *Ber.*, **45**, 2977 (1912); v. Braun, Kruber and Aust, *ibid.*, **46**, 3056 (1913); Meldrum and Advani, *J. Ind. Chem. Soc.*, **10**, 107 (1933).

(10) Simons, THIS JOURNAL, **59**, 518 (1937).

(11) The dehydrogenation of tetrahydroquinazolines to dihydroquinazolines by trimeric methylene-*p*-toluidine has been demonstrated by J. C. Snyder and will be reported in a later paper.

(12) Bischoff and Reinfeld, *Ber.*, **36**, 41 (1903).

(13) J. G. Miller and Wagner, THIS JOURNAL, **54**, 3698 (1932).

(14) Paal and Busch, *Ber.*, **22**, 2693 (1889); v. Walther and Bamberg, *J. prakt. Chem.*, (2) **73**, 209 (1906).

(15) Wagner, *J. Org. Chem.*, **2**, 157 (1937).

For the analyses reported below, samples were dried at 80°. Carbon and hydrogen were determined by a semi-micro procedure. Nitrogen was determined by the semi-micro Kjeldahl method, with boric acid absorption of ammonia. Nitroso compounds were submitted to preliminary reduction by zinc dust and salicylic–sulfuric acid mixture. Halogen was determined gravimetrically after decomposition in a Parr sodium peroxide bomb. Molecular weights were determined in benzene by semi-micro ebullioscopic or macro cryoscopic methods.

General Procedures: Conversion of II, III, IV, V to products VI or VII.—A general procedure similar to that of Goecke[3c] and Spielman[4] was used. Into a mixture of 100 cc. of 95% alcohol, 20 cc. of 39% formalin and 20 cc. of concentrated hydrochloric acid, chilled in an ice-bath, 10 g. of the selected starting compound[16] was sifted during one-half to one hour, more alcohol being added if needed to effect complete solution. After an hour or two the mixture was removed from the ice-bath and was allowed to stand twenty-four to forty-eight hours. The red liquid was diluted with 300 cc. of water, and the crude product was precipitated by excess ammonium hydroxide. It was generally yellowish and more or less oily or resinous, in most cases becoming solid after a time. The procedure for purification of the Troeger base analogs through the hydrochloride was essentially as follows. The crude base was dissolved in 6 *N* hydrochloric acid, and the solution treated with charcoal and filtered hot. Addition of about one-fifth volume of concentrated hydrochloric acid precipitated the hydrochloride, which was removed and dissolved in hot water. The base was precipitated by ammonium hydroxide, removed by filtration, washed with water, and air-dried. It was recrystallized from alcohol or dilute alcohol. In some cases the presence of resinous impurities made necessary the repetition of one or more of these operations.

This procedure gave satisfactory yields (up to 70%) when the tetrahydroquinazolines were the starting compounds. The other substances (II, III, IV) gave smaller yields and considerable resinous material.

The isolation procedures used for the hydroxymethyl bases (VII) and the accompanying dihydroquinazolines are outlined later in appropriate places.

Preparation of Troeger Base Analogs

1,2′ - Methylene - 3 - (*p* - anisyl) - 6 - methoxy - 1,2,3,4-tetrahydroquinazoline. (1) **From *p*-anisidine.**[3c]—A solution of 24.6 g. (0.2 mole) of *p*-anisidine in 200 cc. of alcohol was added to a mixture of 70 cc. of concentrated hydrochloric acid and 70 cc. of 39% formalin, and the liquid was allowed to stand for twenty-four hours at room temperature. Excess formaldehyde and alcohol were removed by evaporation under reduced pressure, and the residual liquid was diluted with 800 cc. of water. The crude base was precipitated as a resinous mass by ammonium hydroxide, and was purified by crystallization from alcohol with the aid of decolorizing charcoal. The yield was 7.0 g. and the m. p. 160° obsd. After recrystallization from dilute alcohol the yield was 5.5 g. (19.5%) of colorless crystals of m. p. 169–169.5° obsd., or 172–172.5° cor.

Anal. Calcd. for $C_{17}H_{18}O_2N_2$: C, 72.4; H, 6.38; N, 9.93; mol. wt., 282. Found: C, 72.76, 72.0; H, 6.58, 6.49; N, 9.7, 9.8; mol. wt., 271, 276.

The **hydrochloride,** made from an ether–alcohol solution of the base with hydrogen chloride, melted at 213–215° obsd.

Anal. Calcd. for $C_{17}H_{18}O_2N_2 \cdot HCl$: N, 8.79. Found: N, 8.64, 8.40.

The hydrochloride prepared from aqueous solution appears to be the dihydrate of the monohydrochloride. It melted at 115–120° obsd. to a viscous mass which liquefied slowly, becoming fluid near the melting point of the anhydrous salt.

Anal. Calcd. for $C_{17}H_{18}O_2N_2 \cdot HCl \cdot 2H_2O$: N, 7.90. Found: N, 7.85, 7.67.

The **picrate,** made in alcohol from 0.25 g. of base with one equivalent of picric acid, weighed 0.41 g. (90.5%), and melted at 202° obsd. With two equivalents of picric acid the yield was 88.6% and the m. p. 203° obsd. A mixture melted at 202–203° obsd., or 207.5–208.5° cor. (1:1 picrate).

The **dinitrosamine,** made as described by Spielman,[4] was obtained in a yield of 0.35 g. from 0.5 g. of the hydrochloride. Crystallized from toluene, it melted at 225–226° obsd. (decompn.).

Anal. Calcd. for $C_{16}H_{16}O_4N_4$: N, 17.1. Found: N, 16.8, 16.9.

The **diacetyl derivative** was obtained[4] by heating 0.4 g. of the base with 6 cc. of acetic anhydride as long as formaldehyde was evolved. The product, precipitated by water and crystallized from glacial acetic acid, weighed 0.3 g., and melted at 298–300° (decompn.).

Anal. Calcd. for $C_{20}H_{22}O_4N_2$: N, 7.91. Found: N, 7.83, 7.68.

(2) **Preparation from Methylene-*bis*-*p*-anisidine.**—Ten grams (0.039 mole) of II gave 2.1 g. (19.2%) of a yellowish product of m. p. 164–167° obsd. Recrystallization from dilute alcohol yielded colorless needles of m. p. 169–169.5° obsd. A mixture with the base made by the preceding method melted at 169–169.5° obsd.

(3) **Preparation from Trimeric Methylene-*p*-anisidine.**—Twenty grams (0.049 mole) of III gave 5.1 g. (20.8%) of yellowish crystals of m. p. 162–166°. A mixture with an analyzed specimen of VII melted at 169–169.5° obsd.

(4) **Preparation from 3-(*p*-Anisyl)-6-methoxy-1,2,3,4-tetrahydroquinazoline.**—From 1.0 g. (0.0037 mole) of V there was obtained 0.5 g. (47.9%) of a product melting at 168–169° obsd., and shown by mixed melting point test to be identical with the above.

1,2′ - Methylene - 3 - (*p* - phenetyl) - 6 - ethoxy - 1,2,3,4-tetrahydroquinazoline. (1) **From *p*-phenetidine.**—Condensation of 27.4 g. (0.2 mole) of *p*-phenetidine with formaldehyde,[3c] with isolation of the product through the hydrochloride and crystallization from dilute alcohol, gave 6.0 g. (19.4%) of base VII, melting at 129–129.5° obsd., or 131.5–132° cor.

Anal. Calcd. for $C_{19}H_{22}O_2N_2$: C, 73.55; H, 7.10; N, 9.03; mol. wt., 310. Found: C, 73.29, 73.03; H, 6.98, 7.02; N, 9.01, 8.97; mol. wt., 294, 298.

(16) Quantities other than 10 g. were used in individual cases, the proportions being kept the same. The gram basis is chosen because there is no molar basis common to the various starting compounds used in the procedure.

The **hydrochloride,** prepared from ether–alcohol solution of the base with hydrogen chloride, melted at 230–232°, obsd.

Anal. Calcd. for $C_{19}H_{22}O_2N_2 \cdot HCl$: N, 8.08. Found: N, 7.89, 7.69.

The hydrochloride obtained from aqueous hydrochloric acid melted at 135–137° obsd., and quickly solidified, melting again at 228–232° obsd., or 236–240° cor., the m. p. of the anhydrous hydrochloride.

Anal. Calcd. for $C_{19}H_{22}O_2N_2 \cdot HCl \cdot 2H_2O$: N, 7.30. Found: N, 7.30, 7.24.

The **picrate,** made in alcohol with one equivalent of picric acid, was obtained in 87.6% yield; with two equivalents of picric acid the yield was 92.3%. Both picrates, and a mixture of the two, melted at 192–193° obsd., or 196.5–197.5° cor. (1:1 picrate).

The **dinitrosamine** from 0.5 g. of base weighed 0.3 g. It was colorless, and melted at 181–183° obsd., or 184–186° cor.

Anal. Calcd. for $C_{18}H_{20}O_4N_4$: N, 15.7. Found: N, 15.6, 15.6.

The **diacetyl derivative,** made from 0.5 g. of base by the procedure used for the anisidine analog, weighed 0.4 g., and melted at 225–226° obsd., or 232.5–233.5° cor.

Anal. Calcd. for $C_{22}H_{26}O_4N_2$: N, 7.34. Found: N, 7.25, 7.17.

(2) **Preparation from Methylene-*bis*-*p*-phenetidine.**—Ten grams (0.035 mole) of II yielded, by the general procedure, 1.6 g. (14.5%) of a base of m. p. 128–129° obsd. A mixture with a specimen made by the preceding method melted at 128.5–129° obsd.

(3) **Preparation from Trimeric Methylene-*p*-phenetidine.**—Ten grams (0.022 mole) of III gave 2.3 g. (24.6%) of VII after crystallization from alcohol. A mixed melting point test with the preceding gave the result 129–129.5° obsd.

(4) **Preparation from 3-(*p*-Phenetyl)-6-ethoxy-1,2,3,4-tetrahydroquinazoline.**—One gram (0.0034 mole) of V yielded 0.7 g. (67.2%) of product melting at 128–129° obsd.; a mixed melting point with an identified specimen showed no depression.

Cleavage of Troeger Base Analogs by Reduction.—A mixture of 1.0 g. of the base with 1.0 g. of red phosphorus and 15 cc. of 57% hydriodic acid was heated for ten to twelve hours at 200° in a sealed glass tube.[4] The contents of the tube were neutralized with sodium hydroxide, then acidified slightly with acetic acid. Sodium acetate and freshly distilled benzaldehyde were added, and the liquid boiled several minutes. After steam distillation to remove excess benzaldehyde the residual liquid deposited the benzal derivative of 6-amino-3-hydroxytoluene: from the anisidine analog 0.7 g. (43.7%), m. p. 130.5–132° obsd., and from the phenetidine analog 0.5 g. (34.2%), m. p. 131–132° obsd. An authentic specimen of 6-benzalamino-3-hydroxytoluene,[17] mixed with each of these products, showed no m. p. depression.

Preparation of Hydroxymethyl Tetrahydroquinazolines (VI)

1 - Hydroxymethyl - 3 - (*p* - chlorophenyl) - 6 - chloro-1,2,3,4-tetrahydroquinazoline. (1) **From *p*-Chloroaniline.**—The procedure outlined for *p*-anisidine was used with modifications. The crude product from 25.5 g. (0.2 mole) of *p*-chloroaniline, as precipitated by ammonium hydroxide, was partially purified by separation as hydrochloride. The recovered mixed bases were dissolved in hot 95% alcohol. The filtered solution, on chilling, yielded a less soluble base of m. p. 187–188° obsd., identified as the 3,4-dihydroquinazoline (m. p. 192° obsd.[7]) by mixed melting point test (188–189° obsd.). Dilution of the mother liquor and chilling yielded 3.0 g. (9.7%) of the more soluble base VI, m. p. 133–134° obsd., raised to 135–136° obsd. after crystallization from dilute alcohol.

Anal. Calcd. for $C_{15}H_{14}ON_2Cl_2$: C, 58.3; H, 4.53; N, 9.06; Cl, 22.98; mol. wt., 309. Found: C, 58.5, 58.6; H, 4.55, 4.62; N, 9.15, 9.21; Cl, 22.9, 23.0; mol. wt., 300, 307, 308.

The **hydrochloride,** made in ether–alcohol with hydrogen chloride, melted at 273–274° obsd. (decompn.).

Anal. Calcd. for $C_{15}H_{14}ON_2Cl_2 \cdot HCl$: N, 8.12. Found: N, 8.07, 7.90.

The **picrate,** made in alcohol with one equivalent of picric acid, separated in 89.5% yield; using two equivalents of picric acid the yield was 95.0%. The melting points were 184–185° obsd., or 188–189° cor., and 183–185° obsd. A mixture of the two samples melted at 184–185° obsd. (1:1 picrate).

The **urethan,** made by heating the base with a slight excess of phenyl isocyanate,[18] and crystallized from dilute alcohol, melted at 139–140° obsd., or 141–142° cor.

Anal. Calcd. for $C_{22}H_{19}N_3O_2Cl_2$: N, 9.81. Found: N, 9.55, 9.45.

(2) **Preparation from Methylene-*bis*-*p*-chloroaniline.**—Ten grams (0.0375 mole) of II was treated by the general procedure. The product precipitated by ammonium hydroxide did not solidify. It was extracted with cold ether, leaving undissolved most of the dihydroquinazoline,[7] which was washed with ether and identified. Evaporation of the ether filtrate left a yellow resinous mass. This was worked up through the hydrochloride, which was dissolved in 500 cc. of hot water. The solution was made alkaline with ammonium hydroxide, and the precipitated bases were dissolved in the least hot 95% alcohol. Upon chilling the solution there separated a little more of the dihydroquinazoline. By dilution of the filtrate and chilling, base VI separated. It melted at 134–135° obsd.; a mixture with the base made by the preceding method showed the same m. p. Final yields were 2.3 g. of the dihydroquinazoline and 0.75 g. (6.25%) of base VI.

(3) **Preparation from Trimeric Methylene-*p*-chloroaniline.**—The crude mixed bases obtained from 40 g. (0.096 mole) of III were treated as outlined above. There were isolated 10.5 g. of the dihydroquinazoline (m. p. 187–188° obsd.) and 2.4 g. (5.4%) of base VI, m. p. 133–134° obsd., identified by mixed m. p. test (134–135° obsd.).

(4) **Preparation from N-(*o*-Amino-*m*-chlorobenzyl)-*p*-chloroaniline.**—The crude product from 5.0 g. (0.0186 mole) of IV, as precipitated by ammonium hydroxide, was viscous but quickly solidified. Isolation through the hydrochloride, and crystallization from alcohol, yielded

(17) Ger. Pat. 213,592; *Chem. Zentr.*, **80**, II, 1097 (1909).

(18) Shriner and Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 2d ed., 1940, p. 136.

2.3 g. (39.6%) of VI, m. p. 133–134° obsd.; identified by mixed melting point test (134–135° obsd.).

(5) **Preparation from 3-(*p*-Chlorophenyl)-6-chloro-1,2,-3,4-tetrahydroquinazoline.**—Two grams (0.0072 mole) of V, treated as outlined in (4), yielded by fractional crystallization of the mixed bases from alcohol, 0.5 g. of the dihydroquinazoline, and 0.5 g. (22.6%) of base VI, m. p. 134–135° obsd., identified by mixed melting point test.

1 - Hydroxymethyl - 3 - (*p* - bromophenyl) - 6 - bromo-1,2,3,4-tetrahydroquinazoline. (1) **From *p*-bromoaniline.**—By the procedure outlined for *p*-chloroaniline 34.4 g. of *p*-bromoaniline (0.2 mole) yielded after twenty-four hours a red precipitate, increased by evaporation to one-half volume under reduced pressure. The precipitate (21.0 g.) was dissolved in much hot water (*ca.* 200 cc. per g.), and the bases were precipitated by ammonium hydroxide and dissolved in hot 95% alcohol. On chilling the solution there separated 9.0 g. of the dihydroquinazoline, m. p. 202–204° obsd. Dilution and chilling of the filtrate yielded 3.0 g. of colorless crystals which melted badly (120–150°). Repeated recrystallizations raised the m. p. to 200°, indicating removal of the more soluble base, which was obtained from the combined mother liquors by evaporation, dilution with water, and chilling. The product (VI) weighed 1.5 g. (3.77%) and melted at 138.5–139.5° obsd., or 139.5–140.5° cor.[19]

Anal. Calcd. for $C_{15}H_{14}ON_2Br_2$: C, 45.2; H, 3.52; N, 7.03; Br, 40.2; mol. wt., 398. Found: C, 45.0, 45.3; H, 3.57, 3.71; N, 6.81, 6.72; Br, 40.7, 40.2; mol. wt., 379, 385.

The **hydrochloride,** made in ether–alcohol with hydrogen chloride, melted at 276–278° obsd. (decompn.).

Anal. Calcd. for $C_{15}H_{14}ON_2Br_2 \cdot HCl$: N, 6.45. Found: N, 6.37, 6.44.

The **picrate,** made in alcohol with one equivalent of picric acid, separated in a yield of 95.0%; with two equivalents of picric acid the yield was 90.0%. The melting points were 198–199° obsd., or 203.5–204.5° cor., and 198–199° obsd. A mixture of the two picrates showed the same melting point.

The **urethan** melted at 157–158° obsd., or 159.5–160.5° cor.

Anal. Calcd. for $C_{22}H_{19}O_2N_3Br_2$: N, 8.12. Found: N, 8.11, 8.18.

(2) **Preparation from Methylene-*bis*-*p*-bromoaniline.**—Twenty grams (0.056 mole) of II gave final yields of 6.0 g. of the dihydroquinazoline (m. p. 199–201° obsd.), and 0.9 g. (4.01%) of the more soluble base VI, melting at 135–136° obsd. A mixture of the latter with material made by method I melted at 135–136° obsd.

(3) **Preparation from Trimeric Methylene-*p*-bromoaniline.**—Twenty grams (0.044 mole) of III gave final yields of 4.0 g. of the dihydroquinazoline (m. p. 190–192° obsd.), and 0.85 g. (4.84%) of base VI, melting at 133–134° obsd., raised to 135–136° obsd. by several recrystallizations. Mixed melting point test gave the result 136–137° obsd.

(4) **Preparation from N-(*o*-Amino-*m*-bromobenzyl)-*p*-bromoaniline.**—Five grams (0.014 mole) of IV yielded 1.2 g. of dihydroquinazoline (m. p. 200–202° obsd.), and 0.7 g. (12.5%) of base VI, m. p. 134–135° obsd., raised to 138.5–139.5° obsd. by recrystallization. A mixture with base VI made by method 1 showed the same m. p.

(5) **Preparation from 3-(*p*-Bromophenyl)-6-bromo-1,-2,3,4-tetrahydroquinazoline.**—Using the same procedure, 3.0 g. (0.0008 mole) of V yielded 0.5 g. of the dihydroquinazoline (m. p. 202–203° obsd.), and 1.0 g. (30.8%) of base VI, melting at 130–131°, raised to 135–136° obsd. by recrystallization. The m. p. was not changed by admixture with a specimen made by method 1.

Cleavage of N-Hydroxymethyltetrahydroquinazolines by Reduction.—A mixture of each base (1.0 g.) with red phosphorus (1 g.) and 57% hydriodic acid (15 cc.) was refluxed for ten hours. More acid (50 cc.) was added, and granulated tin was introduced in portions until about 40 g. had been added. The tin was either removed as sulfide or was converted to sodium stannite with concentrated sodium hydroxide. The liquid (made alkaline if necessary) was subjected to steam distillation, and the steam-volatile oil was benzoylated by the Schotten–Baumann method. The product was extracted in ether and, after evaporation of the ether, was crystallized from dilute alcohol. There were obtained: (a) from the chlorine compound 0.4 g. (54%) of N-*p*-chlorophenylbenzamide, m. p. 188° obsd., which, mixed with an authentic specimen, melted at 188–189° obsd., and (b) from the bromine compound 0.40 g. (57.5%) of N-*p*-bromophenylbenzamide, m. p. 195–197° obsd., which, mixed with an authentic specimen (m. p. 204°) melted at 196–197° obsd.

(19) In two experiments this base was not obtained, the product being a compound of m. p. 121° obsd. The low nitrogen content (4.6%) showed it to be neither the Troeger base nor the hydroxymethyl compound. It was not examined further.

Summary

1. *p*-Anisidine and *p*-phenetidine were found to condense with formaldehyde in acidified alcoholic solution to yield products shown to be analogs of Troeger's base.

2. These compounds were obtained under similar conditions also by condensation of formaldehyde with compounds derived from *p*-anisidine and *p*-phenetidine, *viz.*, methylene-*bis*-*p*-alkoxyanilines, trimeric methylene-*p*-alkoxyanilines, and substituted tetrahydroquinazolines. This indicates that the sequence of the reactions which led to the formation of Troeger base analogs is the same as that demonstrated previously in the case of Troeger's base itself.

3. Under the same experimental conditions *p*-chloroaniline and *p*-bromoaniline and the corresponding methylene-*bis*-arylamines, trimeric methylene arylamines, *o*-aminobenzylarylamines, and tetrahydroquinazolines were found to form final products shown to be 1-(hydroxymethyl)-tetrahydroquinazolines. They appear to represent a previously unrecognized step intermediate in the elaboration of compounds having the essential structure of Troeger's base.

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