NOTES

1,2-Di-(1′-isoquinolyl)-ethane

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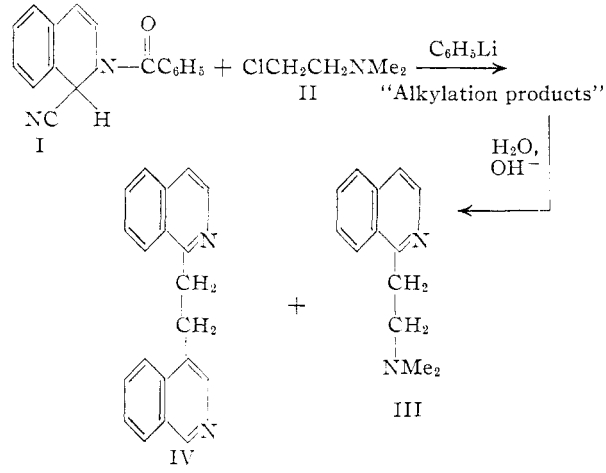
In a recent investigation of 1-vinylisoquinoline and related compounds,[2] we reported that the alkylation of 1-cyano-2-benzoyl-1,2-dihydroisoquinoline (I) with β-chloroethyldimethylamine (II) followed by alkaline hydrolysis of the crude reaction product gave 1-(β-dimethylaminoethyl)-isoquinoline (III). Further investigation of this reaction sequence now has shown that in addition to the main product (III) there can be isolated in small yield a higher boiling, basic side-product. The structural evidence to be discussed below clearly establishes this side product as 1,2-di-(1′-isoquinolyl)-ethane (IV).



The composition and molecular weight of this basic side-product IV were in agreement with the empirical formula $C_{20}H_{16}N_2$. In addition, the ultraviolet absorption spectrum of this compound showed it to be an isoquinoline derivative. Since the only logical structure to accommodate these facts was that of 1,2-di-(1′-isoquinolyl)-ethane (IV), the synthesis of IV was carried out using the procedure developed by Campbell and Teague for preparing 1,2-di-(2′-pyridyl)-ethane.[3] That the 1,2-di-(1′-isoquinolyl)-ethane obtained in this manner was identical with the basic side-product was shown through comparison of the corresponding picrates of the two samples.

Although the isolation of 1,2-di-(1′-isoquinolyl)-ethane from the alkylation of 1-cyano-2-benzoyl-1,2-dihydroisoquinoline was quite unexpected, there are several ways in which its formation can be rationalized. Of these we favor a mechanism involving conversion of III by intramolecular elimination to 1-vinylisoquinoline with subsequent addition of the 1-vinylisoquinoline to a second molecule of 1-cyano-2-benzoyl-1,2-dihydroisoquinoline. The resulting product would then by alkaline hydrolysis yield 1,2-di-(1′-isoquinolyl)-ethane as observed.

(1) Aided by a grant from the United Cerebral Palsy Association.

(2) V. Boekelheide and A. L. Sieg, *J. Org. Chem.*, **19**, 587 (1954).

(3) P. B. Campbell and P. C. Teague, This Journal, **76**, 1371 (1954).

Experimental[4]

1,2-Di-(1′-isoquinolyl)-ethane by the Alkylation of 1-Cyano-2-benzoyl-1,2-dihydroisoquinoline.—The alkylation of 1-cyano-2-benzoyl-1,2-dihydroisoquinoline with β-chloroethyldimethylamine and the alkaline hydrolysis of the resulting crude product is described for a typical experiment in our previous publication.[2] In the course of subsequent repetitions of this experiment on the same scale, it was found that a careful distillation of the final product yielded, in addition to the 7.1 g. (40%) of the main product (1-(β-dimethylaminoethyl)-isoquinoline), 1.5 g. (12%) of a light yellow oil, b.p. 160–163° at 1 mm.

Anal. Calcd. for $C_{20}H_{16}N_2$: C, 84.47; H, 5.67. Found: C, 84.30; H, 5.25.

The picrate of 1,2-di-(1′-isoquinolyl)-ethane was obtained after recrystallization from ethanol as yellow needles, m.p. 159–161°.

Anal. Calcd. for $C_{26}H_{19}N_5O_7$: C, 60.84; H, 3.73; mol. wt., 513.5. Found: C 60.54; H, 3.66; mol. wt. (by the spectrophotometric method[5]), 514.

1,2-Di-(1′-isoquinolyl)-ethane by Synthesis from 1-Methylisoquinoline.—A solution of 1-isoquinolylmethyllithium, prepared from 14.3 g. of 1-methylisoquinoline and 200 ml. of a 0.55 *M* ethereal solution of phenyllithium, was cooled to −40° and then 8.8 g. of bromine was added dropwise with stirring over a period of one hour. After the addition was complete, the reaction mixture was stirred an additional hour at −40° before it was decomposed by addition successively of 30 ml. of water and 30 ml. of 6 *N* hydrochloric acid. The aqueous layer was separated, made basic by addition of an aqueous solution of sodium hydroxide, and extracted with chloroform. When the chloroform extract was concentrated and the residual oil was distilled, there was obtained 3.6 g. (25%) of a light yellow oil, b.p. 160–165° at 1 mm.

The picrate of the 1,2-di-(1′-isoquinolyl)-ethane, obtained in this preparation, was isolated as yellow needles, m.p. 160–161°, after recrystallization from ethanol. A mixture of the picrate from this preparation and that of the preceding experiment showed no depression of melting point.

(4) Analyses by Miss Annett Smith. All melting points given are corrected.

(5) K. G. Cunningham, W. Dawson and F. S. Spring, *J. Chem. Soc.*, 2305 (1951).

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Synthesis of 2-Amino-5-dimethylaminodiphenylamine and Other Derivatives of 3,4-Dinitrodimethylaniline

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2-Amino-5-dimethylaminodiphenylamine (I) is a possible semidine rearrangement product of the hydrazo derivative of the hepatic carcinogen 4-dimethylaminoazobenzene. It is also the only rearrangement product whose formation *in vivo* is not contraindicated by the high carcinogenicities of certain polyfluoro derivatives of this dye.[1] In order to test its carcinogenicity this hitherto unknown

(1) J. A. Miller, E. C. Miller and G. C. Finger, *Cancer Research*, **13**, 93 (1953).

semidine now has been prepared from 3,4-dinitrodimethylaniline (II). This synthesis required proof of structure of II and confirmation of the reputed lability of its 3-nitro group.

Romburgh[2] first described a compound to which he assigned the structure II and later showed that one of its nitro groups was labile to attack by various aliphatic amines.[3-5] II may be prepared in three ways: (a) by nitration of dimethylaniline in a mixture of nitric and sulfuric acids[2]; (b,c) by nitration of *m*-nitrodimethylaniline with dilute nitric acid[2] or with excess sodium nitrite in dilute hydrochloric acid.[6,7] Starting from *m*-nitrodimethylaniline, four dinitro derivatives are possible and three have been described in the literature. The mobility of a nitro group is to be expected in the two isomers where the nitro groups are *ortho* to each other, *viz.*, the 2,3- and 3,4-dinitrodimethylanilines. Romburgh assumed that the attack of ammonia on II gave 3-amino-4-nitrodimethylaniline (III) but presented no evidence for this choice. We have obtained III in this way as well as by condensing 5-fluoro-2-nitroaniline or 5-bromo-2-nitroaniline with dimethylamine. This proves the structures of II and III. The isomer of III, 3-nitro-4-aminodimethylaniline, and its acetyl derivative have been described[8] and are different from the compound referred to here as III and its acetyl derivative. Thus 2,3-dinitrodimethylaniline is the remaining and unreported isomer.

In attempts to prepare II from 4-nitrodimethylaniline we found that this compound on nitration in a mixture of sulfuric and nitric acids either gave no dinitro derivative or yielded only 2,4-dinitrodimethylaniline. Similarly, the nitration of dimethylaniline in anhydrous hydrogen fluoride with sodium nitrate by the method of Finger, *et al.*,[9] gave only the 2,4-dinitro isomer. The 5-fluoro(or bromo)-2-nitroanilines were prepared by nitration of the corresponding *m*-halogenated anilines as previously described.[10,11] The 4-nitro isomers also were formed in these nitrations although in low yield. If the nitration was carried out in anhydrous hydrogen fluoride[9] the yield of each isomer was approximately 30%. The 3-fluoro-4-nitroaniline melted at 159–160° (Hodgson and Nicholson give 153°) after three successive crystallizations from water. Since the 3-hydroxy-4-nitroaniline described much earlier[12,13] also melts at 158° the structure of the 3-fluoro-4-nitroaniline was checked. On alkaline hydrolysis it gave the expected phenol melting at 158–159° (35° depression of m.p. on mixing with the starting amine). On the other hand, alkaline ethanolysis gave the known 5-amino-2-nitrophenetol.[14] The mobile nitro group in II behaves similarly since on alkaline hydrolysis it gave a phenol which is presumably 3-hydroxy-4-nitrodimethylaniline (m.p. 139–141°). Hodgson and Nicholson[10] ascribed this structure to an aminophenol of the same melting point obtained from the alkaline hydrolysis of what was stated to be 3-fluoro-4-nitrodimethylaniline. However, no proofs of structure were given. On alkaline ethanolysis II yielded what was presumably 5-dimethylamino-2-nitrophenetol (m.p. 82–84°).

Condensation of II with aniline yielded 2-nitro-5-dimethylaminodiphenylamine (IV). The same compound was obtained by phenylation of III in the presence of cuprous iodide as catalyst. This is further evidence for the correctness of the structures of II and III.

Catalytic hydrogenation of IV gave the semidine I, but it was not isolated as the free base because of its extreme sensitivity to oxidation in air. Furthermore its hydrochloride, formed in absolute ether, turned gray and resinified in a few minutes. Reductive acetylation of IV by catalytic hydrogenation in a mixture of ethyl acetate and acetic anhydride gave 2-acetylamino-5-dimethylaminodiphenylamine. This compound was relatively stable to air but assumed a violet cast on prolonged exposure.

Jacobson and Kunz[15] have claimed the isolation of a colorless salicylaldehyde derivative of I obtained from the acid rearrangement of 4-dimethylaminohydrazobenzene. This derivative was not decomposed by aqueous acid and it was assumed that the Schiff base of I had been oxidatively cyclized by air. No proofs of structure were given. We have found that I on immediate condensation with salicylaldehyde after catalytic hydrogenation of IV yielded a yellow-orange Schiff base which was not sensitive to air. This derivative gave the expected red halochromism in absolute ethanol saturated with hydrogen chloride. The color disappeared irreversibly on the addition of water. An attempt to cyclize this Schiff base by oxidation with mercuric oxide in boiling ethanol[16,17] was unsuccessful. The latter subject requires further investigation.

Experimental

Melting points are corrected and were taken with a Maquenne block.

3-Amino-4-nitrodimethylaniline (III).—Two grams of 5-fluoro-2-nitroaniline, 1.6 g. of dimethylamine hydrochloride, 2 g. of anhydrous sodium acetate and 10 ml. of absolute ethanol were heated in a sealed tube at 100° for 8 hours. For the less reactive bromo compound 18 hours of heating were required. The mixture was poured into water and the brown precipitate crystallized from ethanol; yield 2 g. (84%), m.p. 134–135° (lit.[5] 135°); no depression of m.p. when mixed with preparation obtained by treating II[2] with ammonia. The acetyl derivative of III was made with acetyl chloride and recrystallized from 50% aqueous acetic acid to give fine silky golden-yellow needles, m.p. 187.5–188.5°.

2-Nitro-5-dimethylaminodiphenylamine (IV). (a) **From III.**—Three grams of III, 2.5 g. of finely powdered potassium carbonate and 200 mg. of finely powdered cuprous iodide were refluxed in 20 ml. of bromobenzene, for 20 hours. The excess bromobenzene was steam distilled and the dark brown oily residue solidified by scratching after addition of a few drops of acetone. On crystallization from methanol

(2) V. P. Romburgh, *Rec. trav. chim.*, **6**, 251 (1887).
(3) V. P. Romburgh, *ibid.*, **14**, 65 (1895).
(4) V. P. Romburgh, *ibid.*, **42**, 804 (1923).
(5) V. P. Romburgh and C. W. Zahn, *ibid.*, **57**, 436 (1938).
(6) D. Vorländer and S. Siebert, *Ber.*, **52**, 283 (1919).
(7) W. G. Macmillan and T. H. Reade, *J. Chem. Soc.*, 2863 (1929).
(8) H. H. Hodgson and J. H. Crook, *ibid.*, 2976 (1932).
(9) G. C. Finger, F. H. Reed, E. W. Maynert and A. M. Weiner, THIS JOURNAL, **73**, 149 (1951).
(10) H. H. Hodgson and D. E. Nicholson, *J. Chem. Soc.*, 766 (1941).
(11) A. Claus and W. Scheulen, *J. prakt. Chem.*, [2] **43**, 201 (1891).
(12) R. Meldola and F. G. C. Stephens, *J. Chem. Soc.*, **89**, 923 (1906).
(13) M. A. Phillips, *ibid.*, 1910 (1930).
(14) F. Reverdin and J. Lokietek, *Bull. soc. chim.*, [4] **19**, 252 (1916).
(15) P. Jacobson and R. Kunz, *Ann.*, **303**, 353 (1898).
(16) D. R. Boyd, *J. Chem. Soc.*, **65**, 879 (1894).
(17) P. Jacobson, M. Jaenicke and F. Meyer, *Ber.*, **29**, 2680 (1896).

4 g. (94%) of yellow-brown prisms, m.p. 136.5–137.5°, were obtained; soluble in ether, ethanol, acetone, chloroform benzene and dilute aqueous acid, slightly soluble in petroleum ether, insoluble in water. After three successive crystallizations from methanol the m.p. was raised to 138.5–139.5°; formed no picrate. Wool was dyed to a beautiful lemon-yellow color in a hot solution of IV in the presence of sulfuric acid.

Anal. Calcd. for $C_{14}H_{15}N_3O_2$: C, 65.36; H, 5.88; N, 16.33. Found: C, 65.38; H, 5.91; N, 16.34.

(b) **From II.**—Fourteen grams (0.067 mole) of II was refluxed in 160 ml. (1.75 moles) of aniline for 8 hours. The excess aniline was steam distilled and the residue treated as in (a); yield 12 g. (70%); no depression of m.p. when mixed with preparation from (a).

2-Acetylamino-5-dimethylaminodiphenylamine.—Fifteen grams (0.058 mole) of IV was suspended in a mixture of 150 ml. of ethyl acetate, 25 ml. (0.264 mole) of acetic anhydride and 250 mg. of platinum oxide. The mixture was hydrogenated at room temperature at 40 lb. until the theoretical uptake of hydrogen was reached (about 4 hours). The excess hydrogen was vented, 200 ml. of petroleum ether added and the mixture allowed to stand for a half-hour. Two crystallizations from benzene–petroleum ether gave long colorless needles, m.p. 161–162°. Soluble in ether, ethanol, acetone, chloroform and benzene, slightly soluble in water, insoluble in petroleum ether.

Anal. Calcd. for $C_{16}H_{19}N_3O$: C, 71.40; H, 7.07; N, 15.61. Found: C, 71.38; H, 6.95; N, 15.47.

2-(2-Hydroxybenzal)-imino-5-dimethylaminodiphenylamine.—Two grams of IV was hydrogenated in 220 ml. of absolute ethanol over 100 mg. of platinum oxide at room temperature under 50 lb. pressure for 3 hours. The solution was filtered rapidly under nitrogen, 2.2 g. of salicylaldehyde added and the mixture refluxed for 1 hour. The yellowish-gray solution was concentrated to 10 ml. and kept in the refrigerator overnight. The crystalline mass was filtered and yielded 0.66 g. (23%) of orange-yellow rhombic platelets, soluble in ether, acetone, petroleum ether, insoluble in water; after two recrystallizations from ethanol, the m.p. was 137.5–138.5°.

Anal. Calcd. for $C_{21}H_{21}N_3O$: C, 76.10; H, 6.39; N, 12.68. Found: C, 76.15; H, 6.61; N, 13.04.

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The Decomposition of Trichloroacetic Acid Alone and in Glycerol

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Kinetic studies have been made of the decomposition of trichloroacetic acid or its salts in various solvents, *e.g.*, water and aniline,[2] dioxane–water,[3] ethanol–water[4] and formamide–water.[5] These studies have indicated that the reaction is a unimolecular decomposition of the trichloroacetate ion.

To the list of solvents already reported[2] which promote the decomposition of trichloroacetic acid may be added glycerol, ethylene glycol, propylene glycol, diethylene glycol, triethylene glycol, 1,4-butanediol, 2-methylpentanediol-2,4 and 2-ethylhexanediol-1,3. The ability of these solvents to promote the decomposition of trichloroacetic acid falls in line with the proposed mechanism of the anion decomposition, since the acid would be expected to be somewhat ionized in polyhydric alcohols.

It is also of interest, and not previously reported, that trichloroacetic acid itself decomposes at a measurable rate at about 160° when a sufficient quantity of the acid (at least one mole) is used.

The present paper describes the results of kinetic studies which have been carried out on the decomposition of trichloroacetic acid in glycerol as well as in the molten state by measuring the volume of carbon dioxide evolved with time. Further investigations in this field are in progress.

Experimental

Reagents.—Trichloroacetic acid, analytical reagent grade, and glycerol, analytical reagent grade, 95% assay, were used in these experiments.

Apparatus.—The experiments described in this paper were carried out in an apparatus similar to that used by the author in studying the decomposition of formic acid.[6]

Decomposition of Trichloroacetic Acid in Glycerol.—A 0.2916-g. sample of trichloroacetic acid (sufficient to yield 40.0 ml. of carbon dioxide at S.T.P.) was weighed into a paper-thin glass capsule. The capsule was supported in the lower neck of the reflux condenser by means of a wire which was bent into a loop at the lower end. The lower end of the condenser was attached by standard taper joint to one neck of a 2-neck 200-ml. round-bottom Pyrex brand flask immersed in the constant temperature oil-bath. The upper end of the wire projected beyond the top of the condenser after piercing a rubber policeman sealing the upper end of a small T-tube attached to the top of the condenser. The other end of the T-tube made connection with the water jacketed buret. A slight twist of the wire by the operator at the proper moment sufficed to dislodge the capsule from its resting place and permit it to drop into the reaction flask. The capsule was then immediately crushed and its contents mixed with the solvent by the mercury sealed stirrer. The course of the reaction was followed by measuring the volume of gas forced over into the buret by the evolution of carbon dioxide in the reaction flask.

In every experiment the total volume of gas collected was the stoichiometric amount within the limits of error of the measurements and the ideal gas law. At 109.0°, for example, the final observed volume of carbon dioxide, corrected to S.T.P., was 40.5 ml.; at 110.1°, 39.1 ml.; at 112.5°, 40.3 ml.; at 112.6°, 40.8 ml., and at 114.9°, 40.7 ml.

Decomposition of Trichloroacetic Acid Alone.—One mole (163.8 g.) of trichloroacetic acid was weighed into the dry reaction flask which was placed in the thermostat oil-bath at constant temperature. The acid quickly melted, and the mercury sealed stirrer was started. After temperature equilibrium was established carbon dioxide was evolved at a steady rate, and the volume of gas produced with time was carefully checked at each temperature. Determinations at each temperature were continued for periods of approximately one hour. The amount of trichloroacetic acid which decomposed during this period of time was negligible in comparison with the amount present, and hence the rate of decomposition was constant with time.

Results and Discussion

Decomposition of Trichloroacetic Acid in Glycerol.—Typical data for one run are given in Table I. The specific reaction velocity values, shown in the last column of the table, were calculated from the data on the basis of a first-order reaction.

The average value of k in sec.$^{-1}$ at 109.0° was 0.00153; at 110.1°, 0.00201; at 112.5°, 0.00271; and at 114.9°, 0.00360. For the temperature range 109.0–114.9°, E was found to be 41,700 cal.

(1) Saint Joseph College, Emmitsburg, Md.

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