the evolution of hydrogen chloride commenced and proceeded vigorously for several minutes. After cooling, the mixture was poured into a large volume of water and the solid collected. The acidic material was dissolved in sodium carbonate, treated with charcoal, filtered and reprecipitated by addition of concentrated hydrochloric acid. After drying at 120° the white powder melted at 279–280° (lit.[10] 278°). Neutral equivalent calcd. for $C_8H_5O_4Cl$: 100.3. Found: 105, 104.

The dimethyl ester was obtained as white needles, m. p. 79–80°.

Anal. Calcd. for $C_{10}H_9O_4Cl$: Cl, 15.51. Found: Cl, 15.59.

The ethyl ester melted at 50–51° (lit.[10] 45°).

Dichlorination of 1,3-*bis*-(Trichloromethyl)-benzene.—The chlorination was carried out essentially as described above for the preparation of the 5-chloro-1,3-*bis*-(trichloromethyl)-benzene except that chlorination was continued for ten hours, and the temperature was allowed to go as high as 145°. From 204 g. of *bis*-(trichloromethyl)-benzene, 138 g. of a very viscous liquid was obtained b. p. 184–189° (9 mm.). Essentially the same result was obtained by starting with 5-chloro-1,3-bis-(trichloromethyl)-benzene.

Anal. Calcd. for $C_6H_2Cl_2(CCl_3)_2$: active Cl,[13] 55.9. Found: active Cl, 55.4.

In the dichlorination of *bis*-(trichloromethyl)-benzene prepared from research grade *m*-xylene (E. K. 275), a small quantity of a high melting isomer, m. p. 191–192°, was obtained. This was shown to be **2,5-dichloro-1,4-*bis*-(trichloromethyl)-benzene** (lit.[9] 193°).

Anal. Calcd. for $C_8H_2Cl_8$: Cl, 74.3. Found: Cl, 74.8.

2-Chloro-1,3-*bis*-(trichloromethyl)-benzene (V).—The chlorination of 179 g. of 2-chloro-1,3-dimethylbenzene[14] (b. p. 181.5–183°; $n^{25}D$ 1.5241) was carried out at 120–130° in a glass reactor and in the presence of a mercury arc. After the theoretical quantity of chlorine had been absorbed (fifteen hours), the mixture was cooled and the crude crystals collected, m. p. 115–125°; yield 130 g. (30%). On recrystallization from ethanol, white prisms were obtained, m. p. 136–137°.[15]

Anal. Calcd. for $C_8H_3Cl_7$: Cl, 71.5. Found: Cl, 71.5.

4-Chloro-1,3-*bis*-(trichloromethyl)-benzene (VI).[6b,6c]—The chlorination of 166 g. of 4-chloro-1,3-dimethylbenzene (b. p. 181–184°, $n^{17}D$ 1.5269) under similar conditions to those used in the preparation of the 2-isomer yielded 177.5 g. (50%) of 4-chloro-1,3-*bis*-(trichloromethyl)-benzene as a viscous liquid, b. p. 180–185° (8.5 mm.).

Anal. Calcd. for $C_8H_3Cl_7$: Cl, 71.5. Found: Cl, 71.0, 71.5.

The residue from the distillation of 4-chloro-1,3-*bis*-(trichloromethyl)-benzene yielded a small quantity of solid which was identical with the 2-chloro-1,3-bis-(trichloromethyl)-benzene (VI) described above and gave no depression of melting point when mixed with it.

4-Fluoro-1,3-*bis*-(trichloromethyl)-benzene.—The chlorination of 4-fluoro-1,3-*bis*-(trichloromethyl)-benzene[16] was carried out essentially as described for the chloro compounds above, twenty-eight hours being required. Vacuum distillation gave an 82% yield of a colorless oil, b. p. 157.5–159.5° (11 mm.).

Anal. Calcd. for $C_8H_3Cl_6F$: Cl, 64.3. Found: Cl, 64.4, 64.5.

2-Chloro-1,4-*bis*-(trichloromethyl)-benzene[5] was prepared in 79% yield by side-chain chlorination of 2-chloro-*p*-xylene in the manner described above, the crude chlorination product being purified by recrystallization from ethanol, m. p. 78–80°.

Anal. Calcd. for $C_8H_3Cl_7$: Cl, 71.5. Found: Cl, 71.4.

Summary

Some bis-(trichloromethyl)-benzenes containing nuclear halogen have been prepared, and some evidence has been obtained in support of the assigned structures.

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(13) The compound was refluxed for eighteen hours with a mixture of 10 ml. of 15% potassium hydroxide solution and 20 ml. of ethanol. After acidification, the chloride ion was determined by the Volhard method.

(14) U. S. Patent 1,796,108; *C. A.*, **25**, 2441 (1931).

(15) This compound has been prepared previously (ref. 6a) but no constants were given.

(16) Balz and Schiemann, *Ber.*, **60**, 1186 (1927).

DURHAM, N. C. RECEIVED MARCH 31, 1947

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF DUKE UNIVERSITY]

Chlorination of 1,3-bis-(Trifluoromethyl)-benzenes[1a,b]

BY CHARLES K. BRADSHER AND RICHARD S. KITTILA

In an investigation of methods for the preparation of *bis*-(trifluoromethyl)-benzenes containing nuclear chlorine,[2] the direct chlorination of *bis*-(trifluoromethyl)-benzenes was studied. Recently McBee, Hass, Weimer, Burt, Welch, Robb and Speyer[3] have reported that chlorination in the presence of conventional catalysts, and at temperatures approaching the boiling point of *bis*-(trifluoromethyl)-benzenes is without effect, and this is confirmed by our observations. While it was stated that chloro-*bis*-(trifluoromethyl)-benzenes could be obtained by reaction in the vapor phase at 500°, it was added that "at this high temperature there was extensive chlorinolysis."[4]

We have found that chlorination of *bis*-(trifluoromethyl)-benzenes may be effected readily by carrying out this reaction in an iron reactor at 150–170° and under a chlorine gage pressure of 300 lb./sq. in.

The material used in the majority of our chlorination experiments was a mixture containing both

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(1a) This work was sponsored by the Naval Research Laboratory.

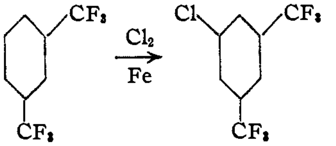
(1b) With the exception of the experiment noted, the material contained in this communication is drawn from a thesis submitted to the faculty of the Graduate School of Arts and Sciences for the degree of Master of Arts, November, 1943.

(2) *Cf.* Bradsher, Gross, Hobbs, Saylor, Tarrant and West, Abstracts of Papers Presented Before the Division of Organic Chemistry at the 111th Meeting of the American Chemical Society, April, 1947.

(3) McBee, Hass, Weimer, Burt, Welch, Robb and Speyer, *Ind. Eng. Chem.*, **39**, 387 (1947).

(4) No yields have been mentioned, and it is clear from the text that this process was abandoned as unworkable.

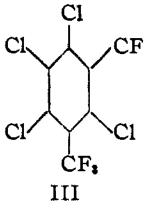
1,3- (I) and 1,4-*bis*-(trifluoromethyl)-benzenes,[5a] but the principal product isolated was 5-chloro-1,3-*bis*-(trifluoromethyl)-benzene[5b] (II), the best yield being 57% (42% conversion).



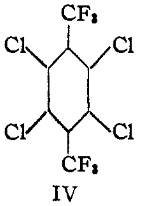
I II

In each case some material boiling at 170–175° was obtained, and though no chemical individual was isolated with certainty, analysis showed this to consist of dichloro-*bis*-(trifluoromethyl)-benzenes. Similar material could be obtained by the chlorination of either "technical" 4-chloro-[6] or crude 5-chloro-1,3-*bis*-(trifluoromethyl)-benzenes.

Fractionation of the higher boiling material yielded fractions which may have contained trichloro-*bis*-(trifluoromethyl)-benzenes, but no chemical individual other than a crystalline tetrachloro derivative was isolated. The low melting point (47–48°) of the tetrachloro-*bis*-(trifluoromethyl)-benzene suggests that it is 2,4,5,6-tetrachloro-1,3-*bis*-(trifluoromethyl)-benzene (III) rather than the symmetrical 2,3,5,6-tetrachloro-1,-4-*bis*-(trifluoromethyl)-benzene (IV).



III



IV

The authors are indebted to Dr. Paul M. Gross for his encouragement and many helpful suggestions, to Drs. Marcus E. Hobbs and John H. Saylor for direction of the physical measurements, and to Dr. Carl H. Deal and Miss Virginia Goodbody for most of the physical constants reported.

Experimental

Apparatus.—The reactor used in most of the experiments reported here was made from a 39 in. length of 2.5-in. black iron pipe closed at the bottom by a plate welded on, and at the top by a leaded pipe cap to which was attached a short length of 0.5-in. copper tubing. The copper tubing was connected by flare fittings to a "T" which was provided with a 0–300 lb./sq. in. compressed air gage and a stainless steel exit valve. The gage was protected from the action of the corrosive gas by a coil of 0.25-in. copper tubing, connection being made to the "T" and gage by short lengths of 0.125-in. copper tubing.

General Procedure.—The gage and valve assembly was removed while the reactor was charged through the copper tube at the top with the material to be chlorinated and the apparatus assembled. The end of the tube leading from the exit valve of the reactor was secured to a tank of liquid chlorine and the reactor cooled for one-half to one hour while chlorine distilled into the reactor.

The lower twelve inches of the reactor was next immersed in an oil-bath[7] and the temperature raised. Excess chlorine was valved off until the gage pressure wa 300 lb./sq. in. at the desired bath temperature (usually 150–175°). After heating for a number of hours, the reactor was cooled and the hydrogen chloride and excess chlorine valved off. The gage and valve assembly was removed and the product poured out of the reactor, filtered, washed with dilute acid, dried and distilled.

The reactor was cleaned after each reaction by filling with dilute hydrochloric acid and allowing it to stand for one to three hours. It was rinsed with water and then acetone, and finally dried by evacuation.

5-Chloro-1,3-*bis*-(trifluoromethyl)-benzene.—Using charges of 100–150 ml. of *bis*-(trifluoromethyl)-benzene[5a] and chlorinating for three hours at 150–170°, the best yield of monochloro-*bis*-(trifluoromethyl)-benzene (b. p. 135–145°) obtained under these conditions was 57%, representing a conversion of 42%. Refractionation showed that nearly all of this material boiled at 139–140°, n^{30}D 1.4023, ϵ 3.08. (A sample prepared by the indirect fluorination of 5-chloro-1,3-*bis*-(trichloromethyl)-benzene by the technique of German Patent 575,593 gave: b. p. 138.2–138.3°, n^{25}D 1.4027, ϵ^{23} 3.04.)

Anal. Calcd. for $C_8H_3ClF_6$: Cl, 14.28. Found: Cl, 14.26.

Chlorination of a relatively pure sample of 1,3-*bis*-(trifluoromethyl)-benzene yielded a product boiling at 137.5–138.5°.

Dichloro-*bis*-(trifluoromethyl)-benzene.—(a) By chlorination of *bis*-(trifluoromethyl)-benzene: The chlorination was carried out as in the preparation above except that the reaction was allowed to run longer at slightly higher temperatures. In some cases, the reactor was cooled, the gas pressure released, additional chlorine distilled in, and heating continued for a further period. For example, the chlorination of 280 g. of *bis*-(trifluoromethyl)-benzene for three hours at 175°, recharging with chlorine and heating for an additional four and one-half hours yielded 42% of the dichloro-*bis*-(trifluoromethyl)-benzene (b. p. 167–177°) or a conversion of 39%. This material was refluxed with 6 *M* sulfuric acid to remove hydrolyzable material, washed, dried and redistilled. Most of the material boiled at 173–175°.

(b) By chlorination of "technical" 4-chloro-1,3-*bis*-(trifluoromethyl)-benzene[6]: A small reactor was charged with 67 g. of the 4-chloro-*bis*-(trifluoromethyl)-benzene and chlorinated for two hours at 160–170° to give a 58% yield (45% conversion) of product, b. p. 169–174°.

(c) By chlorination of 5-chloro-1,3-*bis*-(trifluoromethyl)-benzene: Crude 5-chloro-1,3-*bis*-(trifluoromethyl)-benzene (b. p. 135–145°) obtained by chlorination of *bis*-(trifluoromethyl)-benzene was chlorinated for one and one-half hours at 170–185°. The reactor recharged with chlorine and chlorination continued for an additional three hours. An 83% yield (49% conversion) of product (b. p. 168–177°) was obtained.

The material obtained by procedure (a) (b. p. 173–175°) had the properties: n^{25}D 1.4389, ϵ^{27} 2.97, and appeared to be a mixture of isomers.

Anal.[8] Calcd. for $C_8H_2Cl_2F_6$: Cl, 25.06. Found: Cl, 24.75.

(5a) We are indebted to the Hooker Electrochemical Company for this material which is now being manufactured by them on a commercial scale; *cf.* Murray, Beanblossom and Wojcik, *Ind. Eng. Chem.*, **39**, 302 (1947).

(5b) Since this manuscript was submitted but before it was accepted for publication, McBee, Bolt, Graham and Tebbe, THIS JOURNAL, **69**, 947 (1947), have reported some physical properties of 5-chloro-1,3-*bis*-(trifluoromethyl)-benzene; the constants reported are in fairly good agreement with ours. The article referred to indicates that the method of syntheses will be published at a later date.

(6) This material was prepared from monochlorinated technical *meta*-xylene. The low dielectric constant (4.92) suggests that it contains some 2-chloro-1,4-*bis*-(trifluoromethyl)-benzene.

(7) The bath used was made from a larger pipe and was electrically heated by a length of nichrome ribbon insulated with asbestos.

(8) Analysis by Miss Louise Gurney (1947).

Tetrachloro-*bis*-(trifluoromethyl)-benzene.[9]—Chlorination of 238 g. of the dichloro-*bis*-(trifluoromethyl)-benzene obtained above for three hours at 165–215° in the presence of 0.05 g. of aluminum chloride yielded 76 g. of starting material, 55 g. of intermediate fractions (b. p. 180–241°), and finally 31 g. (b. p. 241–244°) which solidified on cooling. Crystallized from ethyl alcohol, it gave colorless crystals, m. p. 47–48°.

Anal. Calcd. for $C_8Cl_4F_6$: Cl, 40.04. Found: Cl, 40.09.

Summary

It has been demonstrated that chlorination of bis-(trifluoromethyl)-benzenes may be effected at elevated temperatures and pressures.

DURHAM, N. C.

RECEIVED APRIL 2, 1947

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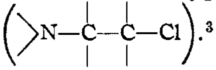
[9] Experiment by Jean B. Bond.

[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

α-Chloro-β-amino Ketones

BY NORMAN H. CROMWELL AND RONALD A. WANKEL

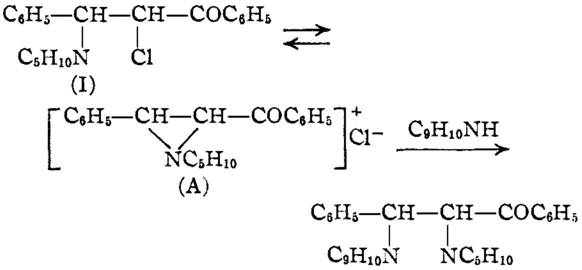
In a previous communication[1] a study was reported concerning the rate of iodine release from acidified potassium iodide solution by α-bromo β-amino ketones prepared from α-bromobenzalacetophenone. These results were compared with those obtained from similar studies with bromobenzylaminobenzylacetophenone hydrobromides prepared by the reactions of 1-benzyl-2-phenyl-3-benzoylethylenimine with wet and dry hydrogen bromide.[1,2] Also recorded was the fact that at room temperature the chlorobenzylaminobenzylacetophenone hydrochlorides, produced by the action of wet or dry hydrogen chloride, gave a slow iodine release. In this latter case no authentic α-halogenated β-amino ketones were available for comparison as had been the case with the bromo series.

Recently considerable interest has been shown in various types of β-chloroethylamines, .[3] β-Halogenated ethylamines seem to owe some of their unusual chemical and physiological properties to the ability of their solutions to form the very reactive quaternary ethyleneimmonium ions.[4]

In the present investigation certain α-chloro β-amino ketones have been prepared for iodine release studies and for pharmacological investigation.

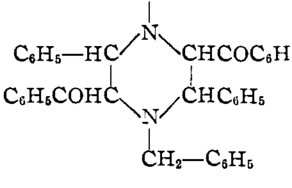
Piperidine, morpholine and tetrahydroisoquinoline each added readily to both α-chlorobenzalacetophenone and α-chlorobenzalacetone to give the desired α-chloro β-amino ketones. Attempts to add benzylamine or dibenzylamine or tetrahydroquinoline to α-chlorobenzalacetophenone were not successful. These α-chloro β-amino ketones, especially the α-chloro-β-aminobenzylacetophenones, proved to be considerably more stable than the corresponding bromo compounds reported in the previous studies.[4]

α-Chloro-β-piperidinobenzylacetophenone (I) was quite stable in absolute alcohol solutions at room temperature, showing little tendency to form the quaternary ethyleneimmonium ion (A), as indicated by the slight reaction of such solutions with silver nitrate after standing fifteen hours. However, this α-chloro β-amino ketone reacted readily with tetrahydroquinoline, as did the analogous bromo ketone,[5] to give a good yield of α-piperidino-β-tetrahydroquinolinobenzylacetophenone.



The hydrochlorides of the α-chloro-β-aminobenzylacetophenones were readily prepared and found to be quite stable in alcohol solution, showing no tendency to rearrange to the β-chloro α-amino ketone hydrochlorides. The hydrochlorides of the α-chloro-β-aminobenzylacetones proved to be too unstable to isolate.

For comparative purposes the reactivity of α,β-dichlorobenzylacetophenone with benzylamine was checked and it was found that the yield of the ethyleneimine ketone was about the same as with dibromo ketones.[6] The molecular weight of this product was determined to eliminate the possibility that this compound might be a piperazine such as



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[1] Cromwell and Caughlan, THIS JOURNAL, **67**, 2235 (1945).

[2] Cromwell, Babson and Harris, *ibid.*, **65**, 312 (1943).

[3] For example, the nitrogen mustards, Gilman and Philips, *Science*, **103**, 409 (1946); N,N-dibenzyl-β-chloroethylamine, Nickerson and Goodman, *Federation Proc.*, Feb., 1946, p. 195; N-benzohydryl-β-chloroethylamines, Cromwell and Fitzgibbon, THIS JOURNAL, **70**, 387 (1948).

[4] Cromwell and Cram, *ibid.*, **65**, 301 (1943); Cromwell, *Chem. Rev.*, **38**, 118 (1946).

[5] Cromwell, THIS JOURNAL, **63**, 2984 (1941).

[6] Cromwell, *ibid.*, **69**, 258 (1947).