[Contribution from the Purdue University Department of Chemistry and the Purdue Research Foundation]

# Some Dihalo-(trifluoromethyl)-benzenes

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Nitration of 2-bromo-(trifluoromethyl)-benzene gave 2-bromo-5-nitro-(trifluoromethyl)-benzene which on reduction yielded 4-bromo-3-(trifluoromethyl)-aniline from which 2,5-dibromo-(trifluoromethyl)-benzene and 2-bromo-5-iodo-(trifluoromethyl)-benzene were synthesized. A low conversion to 4-bromo-3-(trifluoromethyl)-aniline was also obtained by bromination of 3-(trifluoromethyl)-acetanilide and subsequent hydrolysis. N,N-Diacetyl-4-bromo-3-(trifluoromethyl)-aniline was obtained on reaction of 4-bromo-3-(trifluoromethyl)-aniline with acetic anhydride. Nitration of 3-bromo-(trifluoromethyl)-benzene gives principally 2-nitro-5-bromo-(trifluoromethyl)-benzene, which, in turn, was reduced to 4-bromo-2-(trifluoromethyl)-aniline. From this amine, 2,5-dibromo-(trifluoromethyl)-benzene and 5-bromo-2-iodo-(trifluoromethyl)-benzene were prepared. Carbonation of the Grignard from 5-bromo-2-iodo-(trifluoromethyl)-benzene gave 4-bromo-2-(trifluoromethyl)-benzoic acid. Synthesis of 5,5′-dibromo-2,2′-bis-(trifluoromethyl)-1,1′-diazoaminobenzene is also reported.

## Discussion

While various dichloro- and bromochloro-(trifluoromethyl)-benzenes[1,2] have been synthesized, characterized and studied, little attention has been given to the corresponding dibromo- and bromoiodo-(trifluoromethyl)-benzenes. Synthesis of 3,4-dibromo-(trifluoromethyl)-benzene[3,4] and 2,5-dibromo-(trifluoromethyl)-benzene[4] by bromination of (trifluoromethyl)-benzene has been described. These dibromo-(trifluoromethyl)-benzenes were characterized by hydrolysis to the corresponding benzoic acids.

2-Bromo-(trifluoromethyl)-benzene, prepared by the method of Benkeser and Severson,[5] was nitrated to give 2-bromo-5-nitro-(trifluoromethyl)-benzene. The structure of this compound was determined by hydrolysis to the known 2-bromo-5-nitrobenzoic acid[6,7] and confirmation was obtained by conversion to the corresponding anilide.[7]

Reduction of 2-bromo-5-nitro-(trifluoromethyl)-benzene yielded 4-bromo-3-(trifluoromethyl)-aniline, a compound which has been reported from the bromination of 3-(trifluoromethyl)-aniline.[8] Replacement of the amino group by iodine gave 2-bromo-5-iodo-(trifluoromethyl)-benzene, while replacement by bromine yielded 2,5-dibromo-(trifluoromethyl)-benzene. Bromination of 3-(trifluoromethyl)-acetanilide in aqueous acetic acid and subsequent hydrolysis gave a low conversion to 4-bromo-3-(trifluoromethyl)-aniline. On acetylation of 4-bromo-3-(trifluoromethyl)-aniline with acetic anhydride, N,N-diacetyl-4-bromo-3-(trifluoromethyl)-aniline was formed.

The course of nitration of the four 3-halo-(trifluoromethyl)-benzenes has been studied. Several patents[9] indicate that nitration of 3-chloro-(trifluoromethyl)-benzene gives 2-nitro-5-chloro-(trifluoromethyl)-benzene. Substitution in the 6-position on nitration of 3-fluoro- or 3-iodo-(trifluoromethyl)-benzenes[10,11] has been definitely established. The structure of the liquid product obtained on nitration of 3-bromo-(trifluoromethyl)-benzene has been previously assigned only by analogy.[4] In this Laboratory it has been found that nitration of 3-bromo-(trifluoromethyl)-benzene does give an impure liquid from which crystalline 2-nitro-5-bromo-(trifluoromethyl)-benzene can be obtained. Reduction of this purified nitro compound gave 4-bromo-2-(trifluoromethyl)-aniline which has somewhat different physical properties than have previously been reported.[4]

The structure of 4-bromo-2-(trifluoromethyl)-aniline has been established by conversion to 2,5-dibromo-(trifluoromethyl)-benzene by means of the Gattermann reaction. In addition, 2-iodo-5-bromo-(trifluoromethyl)-benzene has been prepared by diazotization of 4-bromo-2-(trifluoromethyl)-aniline and treatment with potassium iodide.

2-Iodo-5-bromo-(trifluoromethyl)-benzene readily formed a Grignard reagent which on carbonation yielded 4-bromo-2-(trifluoromethyl)-benzoic acid. The ease of formation of this Grignard is in accord with the observations of McBee and Sanford,[12] who have found that the trifluoromethyl group does not retard the reaction of a para dihalo aromatic compound with magnesium.

During the course of an attempted Gattermann reaction on 4-bromo-2-(trifluoromethyl)-aniline, a vigorous gas evolution took place before diazotization was complete. A yellow solid was formed which is thought to be 5,5′-dibromo-2,2′-trifluoromethyl-1,1′-diazoaminobenzene. The material was found to be insoluble in cold and hot hydrobromic acid.

## Experimental[13,14]

**2-Bromo-5-nitro-(trifluoromethyl)-benzene.**—2-Bromo-(trifluoromethyl)-benzene[5] was nitrated in a manner similar to the procedure described for 2-chloro-(trifluoromethyl)-benzene.[15] A mixture of 75 g. of 2-bromo-(trifluoromethyl)-benzene (0.33 mole) and 37 ml. of concentrated sulfuric acid was cooled to 15°. With vigorous stirring, a mixture of 24 ml. of concentrated sulfuric acid and 15 ml. of 15% fuming nitric acid was added dropwise at such a rate as to prevent the reaction temperature from rising above 25°. At the completion of addition of mixed acids, the reactants were stirred for 1.5 hours before being poured on ice to give aqueous and organic phases.

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(1) H. S. Booth, U. S. Patent 2,063,979 (1936); L. Holt and H. Daudt, U. S. Patent 2,174,512 (1939); P. Oszwald, F. Müller and F. Steinhauser, German Patent 575,593 (1933).

(2) E. T. McBee, R. A. Sanford and P. J. Graham, This Journal, **72**, 1651 (1950).

(3) J. H. Simons and E. O. Ramler, *ibid.*, **65**, 389 (1943).

(4) G. B. Bachman and L. L. Lewis, *ibid.*, **69**, 2022 (1947).

(5) R. A. Benkeser and R. Severson, *ibid.*, **73**, 1424 (1951).

(6) A. F. Holleman and B. R. DeBruyn, *Rec. trav. chim.*, **20**, 206 (1901).

(7) A. Grohmann, *Ber.*, **24**, 3808 (1891).

(8) M. Lilyquist, J. G. Wisler and P. Tarrant, Abstracts of Papers 118th Meeting, American Chemical Society, Sept., 1950, P. 18L.

(9) H. Heyna, German Patent 637,318 (1936); British Patent 452,436 (1936); U. S. Patent 2,086 029 (1937).

(10) G. C. Finger and F. H. Reed, This Journal, **66**, 1972 (1944).

(11) R. G. Jones, *ibid.*, **69**, 2347 (1947).

(12) E. T. McBee and R. A. Sanford, *ibid.*, **72**, 4053 (1950).

(13) Carbon and hydrogen microanalyses by Dr. H. W. Galbraith.

(14) Nitrogen microanalyses by Miss H. D'Agostino.

(15) M. E. Friedrich and L. E. Schniepp, U. S. Patent 2,257,093 (1937).

The organic layer was taken up in ether and the ether solution was washed with dilute sodium carbonate solution and then with water. After drying the solution with Drierite, the ether was evaporated to leave an orange oil. Distillation of this oil at reduced pressure gave 18 g. of starting material and 67 g. (0.25 mole) of 2-bromo-5-nitro-(trifluoromethyl)-benzene (b.p. 87–88° at 2.5–3 mm.) which solidified in the receiver. Recrystallization from ethanol–water mixtures gave large white crystals melting at 46–48°. The conversion was 54.4% and the yield was 71.6%.

*Anal.* Calcd. for $C_7H_3BrF_3NO_2$: C, 31.1; H, 1.11; N, 5.19. Found: C, 31.0; H, 1.18; N, 5.21.

A sample of 2-bromo-5-nitro-(trifluoromethyl)-benzene was hydrolyzed by the method of LeFave[16] to give white needles which melted at 181–182°. This is in agreement with the reported values[6,7] for the melting point of 2-bromo-5-nitrobenzoic acid. As further confirmation, the anilide was prepared.[17] The melting point of the yellow needles thus obtained was 168–169° and is in agreement with the value found in the literature.[7]

**4-Bromo-3-(trifluoromethyl)-aniline.** A.—A solution of 19.6 g. of 2-bromo-5-nitro-(trifluoromethyl)-benzene (0.072 mole) in 40 ml. of ethanol was slowly added to a stirred solution of 45 g. of stannous chloride dihydrate (0.2 mole), 35 ml. of concentrated hydrochloric acid, and 80 ml. of ethanol which had been warmed to 40°. The reaction was exothermic and the rate of addition was adjusted to maintain the reaction temperature between 40 and 50°. After addition was complete, the reactants were allowed to stand until they had cooled to room temperature. They were then poured into excess concentrated sodium hydroxide solution.

Steam distillation of the basic solution effectively separated the desired product from the precipitated tin hydroxides. The colorless organic and aqueous layers of the steam distillate were ether extracted and the combined extracts dried with Drierite. Evaporation of the ether at reduced pressure left a light yellow solid weighing 17 g. (0.071 mole), representing a quantitative yield of 4-bromo-3-(trifluoromethyl)-aniline. Recrystallization of samples from either petroleum ether (30–60°) or ethanol–water mixtures gave large white prismatic crystals melting at 55–56°. A mixed melting point determination with a sample of the aniline prepared by bromination of 3-(trifluoromethyl)-aniline showed no depression.[18]

*Anal.* Calcd. for $C_7H_5BrF_3N$: C, 35.0; H, 2.08; N, 5.83. Found: C, 35.0; H, 2.02; N, 5.81.

B.—A solution of 115 g. of bromine (0.72 mole) in 100 ml. of glacial acetic acid was added dropwise to a solution of 140 g. (0.67 mole) of 3-(trifluoromethyl)-acetanilide,[19] 400 ml. of glacial acetic acid and 300 ml. of water which was maintained at 60°. The addition took place over a three-hour period. At the conclusion of addition, the mixture was poured on ice, decolorized with bisulfite, made slightly basic, and ether extracted. The ether was evaporated and 165 g. of the crude material was obtained.

A sample of 55 g. of this crude product was refluxed for three hours with 55 g. of concentrated hydrochloric acid and 60 ml. of ethanol. On cooling, the entire mixture solidified. Treatment with excess sodium hydroxide solution gave an organic phase which was separated, dissolved in ether, and dried with Drierite. After evaporation of the solvent the residual oil was distilled at reduced pressure and 22 g. of 3-(trifluoromethyl)-aniline (b.p. 70–71° at 7.5 mm.) was recovered. The pot residues were chilled to induce crystallization and filtered to give 6 g. of solid material. Recrystallization melting point, and mixed melting point determinations showed the material to be 4-bromo-3-(trifluoromethyl)-aniline. The conversion was 3.7%.

**N,N-Diacetyl-4-bromo-3-(trifluoromethyl)-aniline.**—A small sample of 4-bromo-3-(trifluoromethyl)-aniline was heated with excess acetic anhydride for several minutes. After trituration of the resultant oil with water, a solid was obtained which, after recrystallization from ethanol–water solution, melted at 112–113.5°. Analysis showed the material to be N,N-diacetyl-4-bromo-3-(trifluoromethyl)-aniline.

*Anal.* Calcd. for $C_{11}H_9BrF_3NO_2$: C, 40.74; H, 2.77; N, 4.32. Found: C, 40.65; H, 2.70; N, 4.40.

**2,5-Dibromo-(trifluoromethyl)-benzene.**—A solution of 4-bromo-3-(trifluoromethyl)-aniline hydrobromide was prepared by dissolution of 4.46 g. (0.019 mole) of 4-bromo-3-(trifluoromethyl)-aniline in a heated mixture of 9 ml. of 48% hydrobromic acid and 20 ml. of water. On rapid cooling to 0°, a fine white paste of the aniline hydrobromide precipitated. After 10 g. of crushed ice had been added, a solution of 1.5 g. (0.021 mole) of sodium nitrite in 10 ml. of water was introduced to the stirred reaction mixture in one portion. The reactants were then stirred at 0° for one hour before a small quantity of metallic copper was added. Stirring was continued while the reaction mixture was slowly heated to room temperature and finally to 60°. Steam distillation of the reaction mixture gave a light yellow oil which solidified on cooling. The crude 2,5-dibromo-(trifluoromethyl)-benzene weighed 4.6 g. (0.015 mole) and represented a yield of 81%. After several recrystallizations from aqueous ethanol, a sample melted at 49–50°, a value in agreement with that found in the literature.[4] The solid material is extremely volatile, even at room temperature, and considerable care must be taken in order to minimize losses due to sublimation.

*Anal.* Calcd. for $C_7H_3Br_2F_3$: C, 27.63; H, 0.99. Found: C, 27.64; H, 0.99.

**2-Bromo-5-iodo-(trifluoromethyl)-benzene.**—A solution prepared by the addition of 9.3 g. (0.041 mole) of 4-bromo-3-(trifluoromethyl)-aniline to a warmed mixture of 9.6 ml. of concentrated sulfuric acid and 43 ml. of water was cooled to 0°. A slurry of the aniline hydrogen sulfate precipitated. With vigorous stirring a solution of 2.95 g. (0.043 mole) of sodium nitrite in 20 ml. of water was added over a one-hour period. During this time the reaction temperature was maintained between 0 and 2°.

After completion of nitrite addition, the reactants were stirred for several minutes before a saturated aqueous solution of 9.3 g. of potassium iodide and a trace of copper-bronze were added. The brown reaction mixture was allowed to warm to room temperature. After stirring at room temperature for one hour, the reactants were heated at reflux over an additional hour period.

The entire reaction mixture was then steam distilled and the iodine-containing steam distillate was decolorized with bisulfite. On cooling, the organic portion of the distillate solidified. Filtration gave 10.5 g. (0.029 mole) of light tan 2-bromo-5-iodo-(trifluoromethyl)-benzene representing a yield of 70%. Recrystallization, after treatment with Norite, from an aqueous solution gave white needles, m.p. 78–80°.

*Anal.* Calcd. for $C_7H_3BrF_3I$: C, 23.93; H, 0.85. Found: C, 24.15; H, 0.87.

**5-Bromo-2-nitro-(trifluoromethyl)-benzene.**—Nitration of 120 g. (0.54 mole) of 3-bromo-(trifluoromethyl)-benzene[2] by a procedure analogous to that of Finger and Reed[10] gave 127 g. (0.47 mole, 88.2% yield) of an impure yellow oil, b.p. 99–100° (5 mm.), $n^{20}\text{D}$ 1.5202. After chilling to 0°, most of the material solidified and on filtration 55 g. of material, solid at room temperature, remained on the filter. The refractive index of the filtrate was $n^{20}\text{D}$ 1.5180. Additional solid 5-bromo-2-nitro-(trifluoromethyl)-benzene was obtained from the filtrate by further chilling and filtration. Recrystallization of a part of the solid material from aqueous ethanol or petroleum ether (30–60°) gave faintly yellow crystals of 5-bromo-2-nitro-(trifluoromethyl)-benzene, m.p. 40–44°. Several attempts to obtain material with a sharper melting point were unsuccessful.

*Anal.* Calcd. for $C_7H_3BrF_3NO_2$: C, 31.1; H, 1.11; N, 5.19. Found: C, 31.21; H, 1.11; N, 5.24.

**4-Bromo-2-(trifluoromethyl)-aniline.**—Stannous chloride reduction of a sample of crystalline 5-bromo-2-nitro-(trifluoromethyl)-benzene (m.p. 40–44°) gave an 84% yield of colorless 4-bromo-2-(trifluoromethyl)-aniline, b.p. 60.7–62° (1 mm.), $n^{20}\text{D}$ 1.5327.

*Anal.* Calcd. for $C_7H_5BrF_3N$: C, 35.0; H, 2.08; N, 5.83. Found: C, 35.09; H, 2.00; N, 5.88.

The structure of 4-bromo-2-(trifluoromethyl)-aniline, its antecedent, and the various derivatives was demonstrated by conversion to 2,5-dibromo-(trifluoromethyl)-benzene in

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[16] G. M. LeFave, THIS JOURNAL, **71**, 4148 (1949).

[17] R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," 3rd ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 158.

[18] The authors are greatly appreciative of this sample which was provided by Dr. P. Tarrant.

[19] F. Swarts, *Bull. sci. acad. roy. Belg.*, **35**, 375 (1898).

51% yield by means of a Gattermann reaction similar to that previously described.

**5-Bromo-2-iodo-(trifluoromethyl)-benzene.**—In a manner similar to that already described, 4-bromo-2-(trifluoromethyl)-aniline was converted to 5-bromo-2-iodo-(trifluoromethyl)-benzene in 41% yield. The white material after recrystallization from aqueous ethanol melted at 77–78°.

*Anal.* Calcd. for $C_7H_3BrF_3I$: C, 23.93; H, 0.85. Found: C, 23.86; H, 0.91.

**4-Bromo-2-(trifluoromethyl)-benzoic Acid.**—The Grignard reagent, readily prepared from 35 g. (0.095 mole) of 5-bromo-2-iodo-(trifluoromethyl) benzene in the usual manner, was carbonated with carbon dioxide pellets. After acidification of the complex with dilute hydrochloric acid, the ether layer was removed and extracted with sodium hydroxide solution. After decolorization of the alkaline solution with Norite, acidification gave a white precipitate of 15.6 g. (0.058 mole, 61% yield) of 4-bromo-2-(trifluoromethyl)-benzoic acid which melted at 124–125° after recrystallization from aqueous ethanol.

*Anal.* Calcd. for $C_8H_4BrF_3O_2$: C, 35.69; H, 1.49. Found: C, 35.82; H, 1.49.

**5,5′-Dibromo-2,2′-bis-(trifluoromethyl)-1,1′-diazoaminobenzene.**—During the course of an attempted Gattermann reaction on 23.5 g. (0.098 mole) of 4-bromo-2-(trifluoromethyl)-aniline, a vigorous evolution of gas, at least partly nitrogen dioxide, was observed during the addition of the sodium nitrite. A yellow solid was formed which after filtration and drying weighed 14.5 g. It darkened somewhat on exposure to air over a two-week period. A sample recrystallized from petroleum ether (90–100°) melted at 139–140°. The material does not appear to be soluble in either cold or warm hydrobromic acid. Analytical data are in good agreement with the calculated values for 5,5′-dibromo-2,2′-bis-(trifluoromethyl)-1,1′-diazoaminobenzene.

*Anal.* Calcd. for $C_{14}H_7Br_2F_6N_3$: C, 34.2; H, 1.43; N, 8.56. Found: C, 34.38; H, 1.55; N, 8.70

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF OREGON]

# Rearrangements Involving 2-Thenylmagnesium Chloride

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2-Thenylmagnesium chloride has been prepared and its reactions with carbon dioxide, ethyl chlorocarbonate, acetyl chloride, acetic anhydride, formaldehyde and ethylene oxide have been shown to give 3-substituted-2-methylthiophenes by rearrangement. Only in the case of carbon dioxide has the normal product also been isolated.

The preparation and some properties of 2-thenylmagnesium chloride were recently outlined[1]; in this report we wish to describe that work in detail and to indicate certain extensions of these rearrangements.

The production of a stable Grignard reagent indicates that 2-thenyl chloride must be considered an isoster of benzyl chloride rather than a β-halosulfide.[2] The recent development by Rowlands, Greenlee and Boord[3] of a "cyclic reactor" designed to minimize coupling made possible the preparation of 2-thenylmagnesium chloride in yields as high as 98%, whereas usual techniques gave only 7.3%. Rearrangements involving benzylmagnesium halides have been investigated extensively.[4]

Of more pertinence to this work is the literature concerning halomethyl heterocycles. In the pyridine series, Gilman and Towle[5] have shown that α-picolinyl reagents give rise only to normal products. On the other hand, both 3-thenyl[6] and 3-furfuryl[7] halides readily form reagents, which undergo rearrangement to give 2-substituted derivatives when treated with appropriate reactants.

2-Furfuryl chloride does not yield a reagent under usual conditions.[8] 2-Thenyl chloride was reported[9] previous to the present work to yield largely the dithienylethane and a small amount of a liquid, possibly the product of reaction with ethylene oxide, no other evidence being presented that a reagent was present. 5-Methyl-2-thenyl bromide was shown by Lecocq and Buü-Hoi[10] to rearrange readily to 3-bromo-2,5-dimethylthiophene and to give 2,5-dimethyl-3-thenoic acid upon reaction with magnesium followed by carbonation. Thus, 2-thenylmagnesium chloride is apparently the first example of a Grignard reagent prepared from an α-halomethyl heterocycle.

Several reactions of 2-thenylmagnesium chloride (I) are represented in Chart A. Only in the case of the reaction with carbon dioxide was a "normal" product isolated. 2-Thienylacetic acid (II) and the amide were identified by comparison with authentic samples. The minor product of carbonation, 2-methyl-3-thenoic acid (III), melted at 115–117°[11] and was oxidized with alkaline permanganate to the known thiophene-2,3-dicarboxylic acid which yielded the anhydride.[12] All products of rearrangements were characterized initially in this manner.

The same acid, III, was obtained exclusively when the thenyl reagent was added to excess ethyl chlorocarbonate and the crude ester saponified. It was possible to obtain satisfactory yields only when the mixture was cooled in an acetone–Dry Ice-bath, as was also the case in the reactions with

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[1] Gaertner, THIS JOURNAL, **72**, 4326 (1950).

[2] See Amstutz, *J. Org. Chem.*, **9**, 310 (1944), concerning cleavage of compounds of this class by active metals.

[3] Rowlands, Greenlee and Boord, Abstracts of Papers, American Chemical Society Meeting, Philadelphia, Penna., April 9 to 13, 1950, p. 8L. Dr. K. W. Greenlee kindly supplied a detailed description of the apparatus and technique.

[4] See, for example, (a) Austin and Johnson, THIS JOURNAL, **54**, 647 (1932); (b) Coleman and Forrester, *ibid.*, **58**, 27 (1936); (c) Johnson, *ibid.*, **55**, 3029 (1933); (d) Burtle and Shriner, *ibid.*, **69**, 2059 (1947); (e) Moser and Sause, *J. Org. Chem.*, **15**, 631 (1950).

[5] Gilman and Towle, *Rec. trav. chim.*, **69**, 428 (1950).

[6] Campaigne and LeSuer, THIS JOURNAL, **70**, 1555 (1948).

[7] Sherman and Amstutz, *ibid.*, **72**, 2195 (1950).

[8] Gilman and Hewlett, *Rec. trav. chim.*, [4] **51**, 93 (1932).

[9] Blicke and Burckhalter, THIS JOURNAL, **64**, 477 (1942).

[10] Lecocq and Buü-Hoi, *Compt. rend.*, **224**, 658 (1947).

[11] Steinkopf and Jacob, *Ann.*, **515**, 273 (1935).

[12] Linstead, Noble and Wright, *J. Chem. Soc.*, 911 (1937).