

acid, and extraction with ether yielded 10 g. of crude acid, which dissolved in hot benzene. After several crystallizations from methyl alcohol, 2 g. of an acid was obtained, melting at 213–214°, yielding finally an acid of m. p. 218–219°, which melted unchanged with 2-bromodiphenyl-4-carboxylic acid, prepared from 4-methyl-2-bromoaniline by the method of Gomberg and Pernert.¹¹

The original ether solution, after extraction with sodium hydroxide, yielded 0.6 g. of diphenyl.

The author acknowledges the assistance of Mr. Henry Sloviter in connection with a portion of the analytical work in this paper.

(11) Gomberg and Pernert, *THIS JOURNAL*, **48**, 1372 (1926).

Summary

1. A study has been made of the extent of the reaction of 3,5, 2,5, 2,4 and 3,4-dibromodiphenyls, respectively, with (a) one and two atoms of magnesium; (b) two atomic proportions of activated copper-magnesium alloy.

2. The nature of the resulting products has been determined when the Grignard reagent is (a) directly hydrolyzed; (b) first treated with carbon dioxide and then hydrolyzed.

PHILADELPHIA, PA.

RECEIVED MAY 18, 1936

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF TEMPLE UNIVERSITY]

The Preparation of 3,4-Dibromodiphenyl

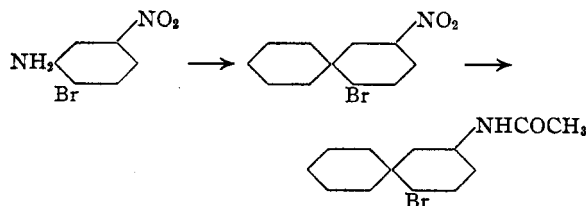
BY FRANCIS H. CASE

The preparation of 3,4-dibromodiphenyl has previously been reported by Scarborough,¹ who stated that it could be obtained by the replacement by bromine of the amino group in the bromo amine resulting from the hydrolysis of what he believed to be 4-bromo-3-acetaminodiphenyl. Scarborough's evidence for the structure of the dibromodiphenyl is based on its oxidation by chromic anhydride to 3,4-dibromobenzoic acid. Reasoning back he therefore concluded that on monobromination 3-acetaminodiphenyl is substituted in the 4-position rather than in the more to be expected 6-position.

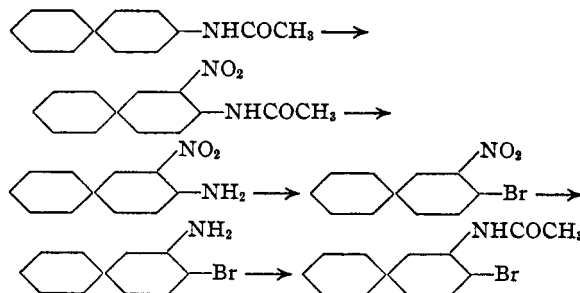
In a study of the action of magnesium on various homonuclear dibromodiphenyls,² the so-called 3,4-dibromodiphenyl of Scarborough was subjected to the action of two atoms of magnesium-copper alloy, followed by carbon dioxide. The two acids resulting were identified as 2-bromodiphenyl-5-carboxylic acid, and diphenyl-2,5-dicarboxylic acid. This suggested the possibility that Scarborough's dibromodiphenyl was derived from 2-bromo-5-acetaminodiphenyl, the normal bromination product. On repeating the oxidation of the dibromodiphenyl, however, a small amount of 3,4-dibromobenzoic acid was obtained, in addition to the expected 2,5-dibromobenzoic acid (also in small quantity). The amounts of the two dibromo acids isolated after oxidation do not, however, give a satisfactory idea of the amounts of dibromides present in the original mixture, as

experiments with the pure dibromides indicate that the 2,5-isomer is much more easily destroyed by oxidation than the 3,4.

2-Bromo-5-acetaminodiphenyl was next synthesized by the reaction of Gomberg and Pernert,³ as follows:



4-Bromo-3-acetaminodiphenyl was prepared by the following series of reactions



This latter product melted at 127°, whereas 2-bromo-5-acetaminodiphenyl prepared by Gomberg's method melts at 162–163°, and Scarborough's bromo-3-acetaminodiphenyl at 163–164°. The latter two products when mixed showed no change in melting point. Since the dibromodiphenyl obtained from Scarborough's

(1) Scarborough, *J. Chem. Soc.*, 3000 (1927).

(2) Case, *THIS JOURNAL*, **58**, 1246 (1936).

(3) Gomberg and Pernert, *ibid.*, **48**, 1372 (1926).

product by hydrolysis and use of the Gattermann reaction yields on oxidation both 3,4- and 2,5-dibromobenzoic acid, and gives with magnesium the mono and dicarboxylic acids related to 2,5-dibromodiphenyl, it seems evident that Scarborough's bromoacetaminodiphenyl is a mixture of two isomers, having a constant melting point. This type of mixture is not unfamiliar in the diphenyl series, as a similar one is obtained by brominating *p*-acetaminodiphenyl.⁴

3,4-Dibromodiphenyl was prepared in this Laboratory by hydrolyzing 4-bromo-3-acetaminodiphenyl to the free base and applying the Gattermann reaction. This product, on oxidation, yielded exclusively 3,4-dibromobenzoic acid.

In the process of identification of the acids resulting from the action of magnesium on Scarborough's dibromodiphenyl, two hitherto undescribed bromo acids were prepared: namely, 3-bromodiphenyl-4-carboxylic acid and 4-bromodiphenyl-3-carboxylic acid.

Experimental Part

3-Nitro-4-bromodiphenyl.—This was prepared in quantity by combining the reaction mixtures from unit batches of 50 g. of 3-nitro-4-aminodiphenyl and working them up together. For a unit batch 50 g. of finely powdered nitro amine was warmed on the steam-bath with 300 cc. of 40% hydrobromic acid. When the mixture had turned to a light brown color, it was cooled to 10°, and diazotized by slowly adding 23 g. of powdered sodium nitrite and shaking the stoppered flask. After standing for a half-hour the mixture was treated with 7 g. of copper powder and heated with a low flame for about half an hour after all apparent reaction had ceased. At this point all the batches were combined, the 3-nitro-4-bromodiphenyl extracted with ether, and twice distilled; yield from 294 g. of 3-nitro-4-aminodiphenyl, 249 g. of 3-nitro-4-bromodiphenyl, b. p. 210–220° (5 mm.). The pure product boils at 210–215° (6 mm.).

Anal. Calcd. for $C_{12}H_8NO_2Br$: Br, 28.75. Found: 28.86.

3-Amino-4-bromodiphenyl.—To 307 g. of $SnCl_2 \cdot 2H_2O$ dissolved in 900 cc. of absolute alcohol was added 126 g. of 3-nitro-4-bromodiphenyl, the reaction mixture being cooled at first with ice, and then refluxed overnight. After removal of the alcohol the residue was treated with concentrated sodium hydroxide to dissolve the tin salts, and the base was then extracted with ether. On removal of the ether, the 3-amino-4-bromodiphenyl was crystallized from a mixture of benzene and petroleum ether. It was found that the bromine atom was removed either by catalytic reduction or by reduction with tin and hydrochloric acid; yield 74 g.; m. p. 97–98°.

Anal. Calcd. for $C_{12}H_{10}NBr$: Br, 32.22. Found: Br, 32.44.

3-Acetamino-4-bromodiphenyl.—This was prepared by the action of acetic anhydride on the base. It crystallizes from methyl alcohol, m. p. 127°.

Anal. Calcd. for $C_{14}H_{12}NOBr$: Br, 27.56. Found: Br, 27.50.

3,4-Dibromodiphenyl.—A mixture of 37.2 g. of 3-amino-4-bromodiphenyl and 192 cc. of 40% hydrobromic acid cooled to 10° was diazotized by the slow addition of 13 g. of sodium nitrite, the flask being repeatedly stoppered and shaken. After standing a half-hour, the mixture was heated with copper powder, the heating being continued for a half hour after the reaction subsided. The dibromodiphenyl was extracted with ether and distilled *in vacuo*. The crude liquid was washed with aqueous hydrobromic acid to remove unchanged base, then dried, dissolved in absolute ether and saturated with dry hydrogen bromide. The precipitated hydrobromide was filtered off, the ether solution washed with sodium bicarbonate, dried and the process repeated. The yield of nitrogen-free base was 33 g., b. p. 192–195° (5 mm.).

Anal. Calcd. for $C_{12}H_8Br_2$: Br, 51.25. Found: Br, 51.23.

2-Bromo-5-nitroaniline.—This was prepared by the bromination of *m*-nitroaniline according to the directions of Wheeler.⁵ That it was this isomer was proven by the isolation of *p*-nitrobromobenzene from the deaminized product.

2-Bromo-5-nitrodiphenyl.—The cooled paste made by heating 90 g. of 2-bromo-5-nitroaniline with 100 cc. of concd. hydrochloric acid and 40 cc. of water was diazotized with a saturated solution of 36 g. of sodium nitrite. To the diazonium salt solution was added 300 cc. of benzene and then 128 cc. of 5 *N* sodium hydroxide, keeping the temperature below 5°. After standing overnight, the benzene was removed, yielding 36 g. of a product boiling at 190–215° (10 mm.), and solid at room temperature. On recrystallization from benzene-petroleum ether it melted at 80–81°.

Anal. Calcd. for $C_{12}H_8NO_2Br$: Br, 28.75. Found: 28.36.

2-Bromo-5-acetaminodiphenyl.—The 2-bromo-5-nitrodiphenyl was reduced by the theoretical quantity of stannous chloride in absolute alcohol to the amine, and this was acetylated by means of acetic anhydride. The 2-bromo-5-acetaminodiphenyl thus obtained was recrystallized from methyl alcohol, melting at 162–163°, and unchanged when mixed with the product resulting from the bromination of 3-acetaminodiphenyl.

Anal. Calcd. for $C_{14}H_{12}NOBr$: Br, 27.56. Found: Br, 27.51.

The 2-bromo-5-acetaminodiphenyl was converted to the corresponding dibromodiphenyl which yielded on oxidation 2,5-dibromobenzoic acid, m. p. 153–154°.

Action of Magnesium on Scarborough's Dibromodiphenyl.—The complex prepared by passing carbon dioxide into the Grignard reagent from 15.6 g. of the above dibromodiphenyl was decomposed with hydrochloric acid,³ the acid solution extracted with ether and the organic acids removed by extraction of the ether solution with sodium hydroxide solution. After reprecipitation with hydro-

(4) Kenyon and Robinson, *J. Chem. Soc.*, 3050 (1926); Scarborough, *ibid.*, 560 (1926).

(5) Wheeler, *Am. Chem. J.*, **17**, 699 (1895).

chloric acid, reextraction with ether, and removal of the ether, a gummy solid was obtained weighing 9 g. This was extracted with benzene. The benzene insoluble part, after several crystallizations from a benzene-methyl alcohol mixture, melted at 276–277°, and unchanged when mixed with a sample of diphenyl-2,5-dicarboxylic acid.² The benzene-soluble part after several crystallizations from benzene-petroleum ether, melted at 248–249°, and unchanged when mixed with a sample of 2-bromodiphenyl-5-carboxylic acid.² From the ether solution extracted by alkali, 1.1 g. of diphenyl was isolated.

4 - Bromodiphenyl - 3 - carboxylic Acid.—Seventy - one grams of 4-bromo-3-methylaniline, obtained by brominating 3-acetotoluide, was treated with 110 cc. of water and 76 cc. of concd. hydrochloric acid. The suspension was then diazotized with 27.5 g. of sodium nitrite in saturated solution, treated with 300 cc. of benzene and gradually with 110 cc. of 5 *N* sodium hydroxide keeping the temperature below 5°. After standing overnight the benzene was removed, yielding 18 g. of a liquid boiling at 165–170° (3 mm.). On oxidation with aqueous permanganate and crystallization from benzene, 4-bromodiphenyl-3-carboxylic acid was obtained, m. p. 194–195°.

Anal. Calcd. for $C_{13}H_9O_2Br$: Br, 28.85. Found: Br, 28.70.

3-Bromodiphenyl-4-carboxylic Acid.—4-Nitro-2-amino-toluene was prepared by the nitration⁶ of *o*-toluidine. It was converted to 4-nitro-2-bromotoluene by the Gattermann reaction. From this, by reduction with stannous chloride in hydrochloric acid, was prepared 2-bromo-4-aminotoluene (acetyl derivative, m. p. 111–112°. Beilstein gives 113°). Sixty-five grams of 2-bromo-4-aminotoluene was treated with 70 cc. of concd. hydrochloric acid

and 60 cc. of water, and diazotized with 26 g. of sodium nitrite in 50 cc. of water. The resulting solution was treated with 300 cc. of benzene and gradually with 100 cc. of 5 *N* sodium hydroxide solution. After standing overnight, the benzene solution was separated and the benzene removed by distillation, yielding 19.5 g. of an oil boiling at 165–170° (7 mm.). On oxidation with aqueous potassium permanganate solution and crystallization from methyl alcohol-petroleum ether, 3-bromodiphenyl-4-carboxylic acid, m. p. 179–180° was obtained.

Anal. Calcd. for $C_{13}H_9O_2Br$: Br, 28.85. Found: Br, 29.05.

The author acknowledges the assistance of Mr. Max Gabis in the preparation of certain intermediates involved in this work.

Summary

1. The "3,4-dibromodiphenyl" of Scarborough has been shown to be a mixture containing largely the 2,5-isomer, and some of the 3,4.

2. 3,4-Dibromodiphenyl has been synthesized.

3. The bromination product of 3-acetaminodiphenyl is believed to be a constant melting mixture of 4-bromo-3-acetamino- and 2-bromo-5-acetaminodiphenyls.

4. Both of these pure products have been synthesized.

5. The syntheses of 4-bromodiphenyl-3-carboxylic acid and of 3-bromo-diphenyl-4-carboxylic acid are described.

PHILADELPHIA, PENNA.

RECEIVED MAY 18, 1936

(6) Schiff and Vanni, *Ann.*, **268**, 322 (1892).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF STANFORD UNIVERSITY]

Saponins and Sapogenins. IV. The Isolation of Amolonin and Determination of the Products of Hydrolysis

BY P. C. JURIS AND C. R. NOLLER

The hydrolysis of crude methyl alcoholic extracts of the bulbs of *Chlorogalum pomeridianum*, Kunth, commonly known as California soap plant or amole, has been shown to yield two crystalline sapogenins.¹ One of these was assigned the formula $C_{26}H_{40}O_2(OH)_2$ and the name *chlorogenin*, it being isomeric with but different than gitogenin, while the other was found to be identical with tigogenin, then believed to have the formula $C_{26}H_{41}O_2(OH)$. Recent work² indicates that gitogenin and tigogenin have the formulas $C_{27}H_{42}O_2(OH)_2$ and $C_{27}H_{43}O_2(OH)$, respectively, and chlo-

rogenin is now known to have the formula $C_{27}H_{42}O_2(OH)_2$.³

The isolation of two sapogenins indicated that at least two saponins were present and early attempts by Liang to isolate the saponins proved this to be the case.⁴ On cooling hot aqueous solutions of the mixed saponins or hot methyl alcoholic extracts of the roots, a product deposited that on hydrolysis yielded pure tigogenin, while hydrolysis of the more soluble fractions in the filtrates yielded largely chlorogenin. It appeared

(1) Liang and Noller, *THIS JOURNAL*, **57**, 525 (1935).

(2) Simpson and Jacobs, *J. Biol. Chem.*, **109**, 573 (1935); Tschesche and Hagedorn, *Ber.*, **68**, 1412 (1935).

(3) Private communication from Dr. L. F. Fieser. The results of extremely accurate combustions on chlorogenin at the Chemical Laboratory of Harvard University gave C, 74.956, 74.982; H, 10.249, 10.253. Calcd. for $C_{27}H_{42}O_4$: C, 74.955; H, 10.251.

(4) Liang, Thesis, Stanford University, 1934.