point of 136–137° is obtained); yield, 11 g., or 50%. Warmed alone or with sodium hydroxide solution the compound evolves ammonia. When it is boiled in alcohol, hydrogen sulfide is liberated. When it is warmed with dil. nitric acid benzaldehyde is regenerated. Concd. sulfuric acid gives a vivid red solution which evolves sulfur dioxide (?) and which on addition of water slowly turns a brilliant green and deposits a green precipitate. Those of the above tests which Laurent tried with his compound gave the same results.

Anal.[13] Calcd. for $C_{21}H_{19}NS_2$: C, 72.21; H, 5.44; N, 4.01; S, 18.34. Found: C, 71.90, 71.59; H, 6.19, 5.85; N, 3.90, 3.90; S, 17.10, 18.85.

Mol. wt. (Cryoscopic method, employing naphthalene as solvent.) Calcd. for $C_{21}H_{19}NS_2$: 349. Found: 331, 338, 335.

Summary

Additional data are presented bearing on the reaction of carbon disulfide with aqueous ammonia, and on the preparation and properties of several esters of trithiocarbonic acid made from carbon disulfide-ammonia solutions. Two new compounds are described in part.

The preparation of thiobenzaldin is described.

FAYETTEVILLE, ARKANSAS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

THE COUPLING ACTION OF THE GRIGNARD REAGENT
I. THE ORTHO- AND PARA-CYANOBENZYL HALIDES

BY REYNOLD C. FUSON[1]

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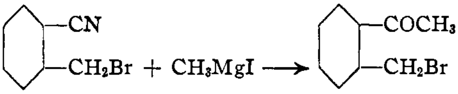
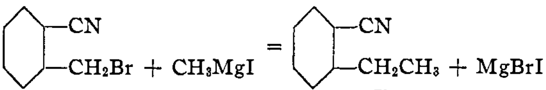
This research arose from an attempt to prepare *o*-acetylbenzyl bromide (I) by treating *o*-cyanobenzyl bromide with methylmagnesium iodide. It was expected that the following synthesis would be effected.



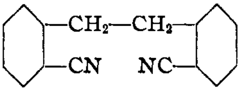
I (1)

It might have been predicted also that alkylation would result according to the equation,



II (2)

The reaction, however, took an unexpected course. Neither I nor II could be isolated but *s*-bis(*o*-cyanophenyl)ethane (III) was obtained instead:



III

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[13] Analyses for carbon, hydrogen and nitrogen were performed by Mr. John Olin.

[1] National Research Fellow in Chemistry.

The reaction of methylmagnesium iodide on *o*-cyanobenzyl bromide is, therefore, simply the removal of the bromine atoms and the coupling together of the radicals thus produced. It is analogous to the Wurtz reaction, the Grignard reagent in the present case playing the part of the metal in the Wurtz synthesis.

The coupling action of the Grignard reagent on alkyl halides has been observed by several investigators but no careful study has been made of it; it has usually been treated as an undesirable side reaction. Thus Gomberg and Kamm[2] in preparing tetraphenylmethane by treating triphenylmethyl chloride with phenylmagnesium bromide obtained a 50% yield of triphenylmethyl which they isolated in the form of triphenylmethyl peroxide. Similarly, Binaghi and Oddo[3] obtained *s*-tetraphenylethane by the action of phenylmagnesium bromide on iodoform. They explain their result by the following equations, the second of which involves the coupling reaction.

$$2\ C_6H_5MgBr + I_2CHI = 2\ MgBrI + (C_6H_5)_2CHI$$
$$2\ (C_6H_5)_2CHI + C_6H_5MgBr = (C_6H_5)_2CHCH(C_6H_5)_2 + C_6H_5Br + MgI_2$$

In the same way Binaghi[4] obtained hexaphenylethane by treating carbon tetrachloride with phenylmagnesium bromide. He postulates the intermediate formation of triphenylmethyl chloride which undergoes coupling to give hexaphenylethane.

$$CCl_4 + 3\ C_6H_5MgBr = 3\ MgBrCl + (C_6H_5)_3C{-}Cl$$
$$2\ (C_6H_5)_3C{-}Cl + C_6H_5MgBr = (C_6H_5)_3C{-}C(C_6H_5)_3 + C_6H_5Br + MgCl_2$$

Although no triphenylmethyl chloride was isolated its hydrolysis product, triphenylmethyl carbinol, was found in the reaction mixture thus giving support to the proposed mechanism.

Schmidlin and Massini[5] found that di-α-naphthylmethyl chloride when treated with phenylmagnesium iodide or with α-naphthylmagnesium bromide gave the coupling product, *s*-tetra-α-naphthylethane.

Späth,[6] in making an extensive study of the action of the Grignard reagent on alkyl halides, observed the formation of coupling products in several cases. Di-*iso*-octyl, dibenzyl, *s*-tetraphenylethane, and *s*-diphenyldiethylethane were obtained from *iso*-octyl bromide, benzyl chloride, diphenyl-bromomethane and ethylphenyl-bromomethane, respectively. Similarly, *o*-, *m*- and *p*-methoxybenzyl bromides gave the corresponding dimethoxydiphenylethanes. The yields in these cases were often considerable, being sometimes as high as 75 or 80%.

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[2] Gomberg and Kamm, This Journal, **39,** 2009 (1917). See also Gomberg and Cone, *Ber.*, **39,** 1463 (1906). Schmidlin, *Ber.*, **43,** 1141 (1910).

[3] Binaghi and Oddo, *Gazz. chim. ital.*, [II] **51,** 330 (1921).

[4] Binaghi, *ibid.*, **53,** 879 (1923).

[5] Schmidlin and Massini, *Ber.*, **42,** 2384 (1909).

[6] Späth, *Monatsh.*, **34,** 1965 (1913).

From a study now in progress it appears that the coupling reaction is of wide applicability and that under suitable conditions it often becomes the chief reaction.

The reaction of the cyanobenzyl halides with the Grignard reagent presents a peculiarly interesting case, inasmuch as these compounds would be expected to be capable of undergoing both the coupling reaction (3) and the normal addition reaction of the nitriles (1) as well as alkylation (2). The three reactions would thus be placed in competition with one another and it was to be expected that they would occur simultaneously so that from the amounts of products obtained some idea might be gained as to their relative speeds. The present paper is a report of a study of the reaction from this point of view.

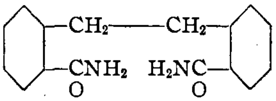
The Para-Cyanobenzyl Halides

The *p*-cyanobenzyl halides would seem to be better adapted to this study than the corresponding *ortho* compounds since in the former cases both of the reacting groups are presumably free from the hindrance effects to be expected in the latter. The results with them were, however, disappointing. Both the *p*-cyanobenzyl bromide and the corresponding iodide were treated with the Grignard reagent but in neither case was it possible to isolate either the addition product or the coupling product. The reaction product was always an amorphous solid containing halogen but no nitrogen, and it was not found possible to separate any pure substance from it.

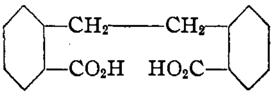
The Ortho-Cyanobenzyl Halides

Turning to the case of the *o*-cyanobenzyl halides, we should expect to find the addition reaction retarded by the hindrance offered by the halomethyl group. Moreover, the coupling reaction would probably not be hindered to the same degree by the presence of the cyano group.

The experiments with the bromide and the iodide seem to substantiate this point of view. *o*-Cyanobenzyl bromide reacts equally with methylmagnesium iodide and ethylmagnesium bromide yielding in both cases somewhat more than 40% of the calculated amount of *s*-bis(*o*-cyanophenyl)ethane (III). The structure of this compound has been established by analysis, molecular-weight determination and a study of the hydrolysis products. When boiled with alcoholic potassium hydroxide the new compound took up two molecules of water, yielding a crystalline compound melting at 241–242°; its analysis was that of the diamide, *s*-bis(*o*-amidophenyl)ethane (IV). This latter compound on long treatment with alcoholic potassium hydroxide took up two molecules of water and gave off two molecules of ammonia, yielding an acid melting at 226–228° whose composition was that of the dibasic acid, *s*-bis(*o*-carboxyphenyl)ethane (V).



IV



V

The coupling product was, however, not the sole product of the reaction. In one experiment a small amount of bromine-containing powder was obtained but the material was insufficient for satisfactory study and the compound has as yet not been identified.

The results with *o*-cyanobenzyl iodide were entirely similar to those obtained with the bromide. When treated with ethylmagnesium bromide it gave a yield of 25% of III.

The results with the *ortho* compounds although incomplete make it clear that the coupling reaction is in these cases at least as rapid as that of addition (1) or that of alkylation (2). It should be pointed out that, although it was assumed *a priori* that Reactions 1 and 2 would take place, no evidence of either was actually obtained; it may, therefore, be that there is no actual competition between these and the coupling reaction. The significant fact remains, however, that the coupling reaction does take precedence over other possible reactions.

Experimental Part

The Reaction of Ethylmagnesium Bromide on *p*-Cyanobenzyl Bromide.—*p*-Cyanobenzyl bromide was added in the course of an hour to an ether solution of four molecular equivalents of ethylmagnesium bromide at 0°. A yellow precipitate was obtained. On pouring the mixture onto cracked ice a crimson color was produced in the solution and the precipitate was transformed into brick-red clumps. Concd. hydrochloric acid was added and the mixture stirred. The solid material was slowly transformed into a greenish-yellow amorphous substance which contained halogen but no nitrogen. On being heated the substance softened at 155° but did not melt completely even at 200°. Attempts to isolate a crystalline substance from this mixture were unsuccessful. Since all of the material isolated was nitrogen-free it is evident that no *s*-bis(*p*-cyanophenyl)-ethane was present in the reaction product.

The Reaction of Ethylmagnesium Bromide on *p*-Cyanobenzyl Iodide.—*p*-Cyanobenzyl iodide, prepared by the method described below for the corresponding *ortho* compound, was treated with ethylmagnesium bromide in a manner entirely similar to that used with the corresponding bromide. Owing to the greater reactivity of the iodide it was hoped that the coupling reaction might here be sufficiently rapid to change to some extent the course of the reaction. The results, however, were in no way different from those described for the preceding case.

***o*-Cyanobenzyl Bromide.**—This compound was first prepared by Drory[7] by leading bromine vapor into boiling *o*-tolunitrile by means of a current of dry carbon dioxide. He gives the melting point as 76°. In the present work the preparation was effected by dropping liquid bromine into the nitrile in the absence of a solvent. The product obtained in this way melted at 71.5–72.5°. Repeated recrystallization from alcohol and dil. acetic acid failed to change the melting point. The procedure used was the following.

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[7] Drory, *Ber.*, **24,** 2570 (1891).

Eighty-two g. of *o*-tolunitrile was placed in a brominating flask maintained at 150° and exposed to strong sunlight; 112 g. of liquid bromine was dropped in during one and one-half hours, the flask being shaken from time to time. During the addition of the bromine the reaction mixture developed an intense purple color due probably to the presence of cresol as an impurity in the starting material. On cooling, the mixture settled to a mass of crystals. These were freed from the residual liquid by suction and were then distilled under reduced pressure. The bromide distilled at 124° (4 mm.) coming over as a clear, colorless liquid which set to a solid crystalline mass on cooling. One recrystallization from 95% alcohol gave a fairly pure product. After five such recrystallizations the melting point was 71.5–72.5°; yield, 75 g., or 57%.

Anal. Calcd. for C_8H_6BrN: Br, 40.8. Found: 40.5.

HYDROLYSIS.—Inasmuch as the compound melted several degrees lower than that reported by Drory, it seemed advisable to test it by a typical reaction. Accordingly, it was hydrolyzed, the hydrolysis product being phthalide, as was expected. Two g. of the bromide melting at 71.5–72.5° was refluxed for nine hours with 50 cc. of concd. hydrochloric acid, at the end of which time solution was complete. On cooling, the solution deposited a mass of colorless crystals which after two recrystallizations melted at 71–72.5° and were shown by the method of mixed melting points to be phthalide, m. p. 73°. The yield, which was improved by working the mother liquor, was 0.92 g., or 74%.

o-Cyanobenzyl Iodide.—This compound as well as its *para* isomer previously mentioned was prepared from the corresponding bromide by treatment with sodium iodide in acetone solution.[8] Six g. of the bromide was dissolved in 7 cc. of acetone and the solution added to 50 cc. of acetone containing 7 g. of sodium iodide. Sodium bromide formed at once and the mother liquor developed a brown color. After the mixture had stood for two hours the acetone was evaporated under diminished pressure and the residue extracted with ether. The ether was evaporated and the brown crystalline residue was twice recrystallized from dil. alcohol. The *o*-cyanobenzyl iodide thus obtained formed in colorless leaflets melting at 76.5–78.5°; yield, 7.2 g., or 97%.

Anal. Calcd. for C_7H_6NI: I, 52.19. Found: 52.47.

The Reaction of Ethylmagnesium Bromide on o-Cyanobenzyl Bromide.—A solution of ethylmagnesium bromide was prepared by dissolving 3.0 g. of magnesium in a solution of 15 g. of ethyl bromide in 100 cc. of absolute ether. To this solution was then added dropwise a mixture of 8.9 g. of *o*-cyanobenzyl bromide and 100 cc. of absolute ether, the reaction mixture being continually agitated by vigorous shaking.[9] A paste-like precipitate closely resembling the ordinary Grignard addition product was formed, the color of the mixture passing from yellow to brown as the reaction proceeded. Gas was evolved during the reaction.

The mixture was refluxed for a few minutes to make sure that the *o*-cyanobenzyl bromide which was undissolved at the beginning of the reaction might not be prevented from reacting by being enclosed in the paste. Cracked ice was then added and the mixture stirred. The pasty masses at once assumed a brick-red color (as did the ether solution) which gradually gave way as the clumps of material were disintegrated. At the end of a half hour there remained in the clear colorless liquid only a slightly colored powder. The supernatant ether when removed and evaporated left a small residue of the powder most of which had remained suspended in the water layer. The mixture

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[8] Compare Davies and Perkin, *J. Chem. Soc.*, **121,** 2208 (1922).

[9] A similar experiment was tried in which the Grignard reagent was added to the ether solution of *o*-cyanobenzyl bromide but the results were in no way different from those obtained by the method described here.

exhibited mild lachrymatory properties due to the presence of a small amount of unchanged bromide. The reaction product was *s*-bis(*o*-cyanophenyl)ethane (III). It was slightly soluble in hot alcohol from which on cooling it separated in well formed colorless plates or columnar needles depending on the conditions. The crude product was colored, usually a yellowish-green but sometimes orange, and it was necessary to recrystallize it several times to render it colorless. The mother liquor showed a marked fluorescence. The pure substance melted at 138.5–139.5°; it was soluble in benzene and hot acetone, slightly soluble in alcohol but nearly insoluble in cold ether. It was unaffected by boiling concd. hydrochloric acid and was but slowly attacked by hot alcoholic potassium hydroxide; yield, 2.2 g., or 42.5%.

Anal. Calcd. for $C_{16}H_{12}N_2$: C, 82.7; H, 5.2; N, 12.1 Found: C, 82.7; H, 5.4; N, 12.2. Mol. wt. Calcd.: 232. Found (in boiling acetone): 218.5.

The aqueous mother liquor was made strongly alkaline and boiled, but no ammonia or ethylamine was detected, indicating that the cyanide group probably had not been attacked in the usual manner. The *s*-bis(*o*-cyanophenyl)ethane (IV) was, however, not the sole product of the reaction. The alcoholic liquor used to recrystallize the crude product was evaporated on the steam-bath and the residue taken up in a minimum quantity of hot alcohol. The solution on cooling deposited a white, powdery, high-melting substance containing bromine. The amount of the material was too small to permit a further investigation.

The Reaction of Methylmagnesium Iodide on *o*-Cyanobenzyl Bromide.—Ten g. of *o*-cyanobenzyl bromide in ether was added to an excess of methylmagnesium iodide solution in a manner entirely similar to that in the case of ethylmagnesium bromide. The *s*-bis(*o*-cyanophenyl)ethane was the only product isolated; yield, 2.5 g., or 43%.

The Reaction of Ethylmagnesium Bromide on *o*-Cyanobenzyl Iodide.—Seven g. of *o*-cyanobenzyl iodide in ether was added to an ether solution of 1.2 g. of magnesium and 6.0 g. of ethyl bromide. The reaction proceeded in a manner exactly similar to that observed in the case of the bromide; 0.85 g. or a 25% yield of *s*-bis(*o*-cyanophenyl) ethane was obtained.

***s*-Bis(*o*-amidophenyl)ethane.**—To a solution of 1.5 g. of *s*-bis(*o*-cyanophenyl)ethane in 20 cc. of boiling ethyl alcohol was added 20 cc. of a 40% potassium hydroxide solution and the mixture was refluxed. At the end of five hours the odor of ammonia was very strong and a crystalline substance had separated; it remained in suspension in the upper (alcohol) layer which had become yellow. At the end of 14 hours, although a faint ammoniacal odor was still distinguishable, water was added and the crystalline material filtered off and purified by recrystallization from 95% alcohol in which it was only slightly soluble. A second recrystallization gave pure *s*-bis(*o*-amidophenyl)ethane (IV) which formed in fine, colorless needles; m. p., 241–242°; yield, 1.2 g., or 70%.

Anal. Calcd. for $C_{16}H_{16}O_2N_2$: C, 71.7; H, 6.0; N, 10.5. Found: C, 71.7; H, 6.1; N, 10.6.

The mother liquor on being acidified gave a small precipitate which was later shown to be *s*-bis(*o*-carboxyphenyl)ethane.

***s*-Bis(*o*-carboxyphenyl)ethane.**—One and one-fourth g. of *s*-bis(*o*-amidophenyl)-ethane was placed in a mixture of 20 cc. of 40% aqueous potassium hydroxide solution and 30 cc. of 95% alcohol and the whole was refluxed for 38 hours, at the end of which time most of the amide had dissolved. The alcohol was driven off and the alkaline solution was diluted with water, cooled and the unchanged material filtered off; 0.25 g. or 20% of the starting material was recovered in this way. The filtrate was then acidified; a white powder separated. This, when filtered off and recrystallized from 95% alcohol, formed flat, colorless plates; m. p., 210–222°. Under the microscope at least two types of crystals could be seen. Four successive recrystallizations from 50%

alcohol, however, gave pure *s*-bis(*o*-carboxyphenyl)ethane (V), melting at 226–228°. It formed in clusters of delicate feather-like needles. Analysis showed that the compound contained no nitrogen.

Anal. Calcd. for $C_{16}H_{14}O_4$: C, 71.7; H, 5.2. Found: C, 71.2; H, 5.5.

The other reaction product was not isolated but was presumably the intermediate compound, 1-*o*-amidophenyl-2-*o*-carboxyphenylethane.

Summary

The coupling action of the Grignard reagent on certain *o*- and *p*-cyanobenzyl halides has been studied.

The *p*-cyanobenzyl halides yielded amorphous substances which contained halogen but no nitrogen.

The *o*-cyanobenzyl halides gave approximately 40% yields of the coupling product, *s*-bis(*o*-cyanophenyl)ethane, showing that in these cases the coupling reaction takes precedence over other possible reactions.

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NOTES

Dyes from the Alkaloids of Ipecacuanha.—From the fact that the non-phenolic alkaloids of ipecacuanha couple with *p*-nitrodiazobenzene, whereas emetine does not, Palkin and Wales[1] deduce that emetamine does so, and publish curves showing the absorption spectra of the supposed *p*-nitrobenzene-azo-emetamine. Their deduction is incorrect. Experiments with the pure alkaloids show that neither emetine nor O-methylpsychotrine nor emetamine couples with *p*-nitro diazobenzene, but psychotrine does so, the dye giving a purple solution in aqueous sodium hydroxide similar to that given by the dye from cephaeline. Incidentally, I have nowhere stated that "emetamine is probably an amine," and perusal of my paper[2] will show that I regard emetamine as a ditertiary base and psychotrine as a secondary-tertiary base.

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Dyes from the Alkaloids of Ipecacuanha. A Reply.—Professor Pyman's experiments with pure emetamine prove that our assumption regarding the identity of the constituent of the non-phenolic fraction of ipecac alkaloids which forms an azo dye is untenable. It would seem, therefore, that ipecac contains a hitherto undetected alkaloid which either

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[1] Palkin and Wales, THIS JOURNAL, **47,** 2005 (1925).

[2] Pyman, *J. Chem. Soc.*, **111,** 419 (1917).