[Contribution from the Chemistry Laboratory of the
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PREPARATION AND REACTIONS OF 9-ANTHRYLMAGNESIUM BROMIDE

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Investigations in the field of carcinogenic compounds have stimulated renewed interest in meso-substituted anthracene derivatives and methods for their synthesis. The development of 9-anthrylmagnesium bromide as a synthetic reagent is therefore of considerable import, particularly in view of the wide applicability of the Grignard reaction and the ready availability of 9-bromoanthracene from the bromination of anthracene.[1] Miller and G. B. Bachman[2] have reported that 9-bromoanthracene does not react appreciably with magnesium and ether even in a sealed tube at 200°. Dufraisse, Velluz, and Velluz[3] however obtained a Grignard reagent from 9-phenyl-10-bromoanthracene by reaction with a large quantity of ethyl bromide and excess magnesium in anhydrous ether. We have now prepared 9-anthrylmagnesium bromide in several different solvents and have investigated its reactions with a number of reagents.

When 9-bromoanthracene was heated in a benzene-butyl ether mixture with a slight excess of pure, pulverized magnesium, and iodine was employed to activate the magnesium, a 73 per cent. yield of the Grignard reagent was obtained in twelve hours. Further heating did not materially increase the yield. When ethyl bromide was used to activate the magnesium a clear, red-brown solution of the Grignard reagent was obtained; when iodine was employed the solutions were always dark brown and the reaction products were more difficult to isolate. Ordinary magnesium turnings reacted to the extent of only 55 per cent. in twenty-four hours, and solutions prepared from impure magnesium were found to contain a large quantity of dark by-products. When 9-bromoanthracene was allowed to react with magnesium in boiling *n*-butyl ether the production of the Grignard reagent was found to be 71 per cent., complete in thirty minutes, but the resulting solutions were again very dark. The by-products in this reaction were dark tars, for the most part, although one crystalline product was obtained whose nature was not determined.

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[1] Barnett and Cook, *J. Chem. Soc.*, **125**, 1086 (1924).

[2] Miller and G. B. Bachman, *J. Am. Chem. Soc.*, **57**, 767 (1935).

[3] Dufraisse, Velluz, and Velluz, *Bull. soc. chim.*, [5], **4**, 1260 (1937).

9-Anthrylmagnesium bromide was also prepared in anhydrous ethyl ether, the magnesium being activated with ethyl bromide. Under these conditions the mixture must be shaken frequently during the first few hours of reaction in order to prevent coating of the magnesium, and the reagent is obtained as a dense, cream-colored precipitate. This method of preparation produces the reagent in purest condition and in superior yields (86–87 per cent.). For some reactions however it is advisable to dissolve the solid Grignard reagent in benzene.

The Grignard reaction offers a convenient method for preparing 9-anthroic acid. This acid has been previously prepared by the action of aluminum chloride on a mixture of anthracene and oxalyl chloride,[4] by the hydrolysis of 9-cyanoanthracene,[5] and by the action of phosgene on anthracene at 200° in a sealed tube.[6] We have now prepared the acid in 72 per cent. yield by passing carbon dioxide into a hot suspension of 9-anthrylmagnesium bromide in ether-benzene.

9-Benzoylanthracene can also be prepared in good yields by interaction of 9-anthrylmagnesium bromide and benzonitrile or from 9-cyanoanthracene and phenylmagnesium bromide, followed by hydrolysis of the ketimine obtained. It was found that 9-cyanoanthracene was readily produced when 9-bromoanthracene and cuprous cyanide were heated together in a small volume of dry pyridine at 220°. This method offers another convenient route to 9-anthroic acid.[5] As in the case of the β-methylnaphthylphenanthrylketimines,[7] diortho-substitution in the ring attached to the ketimino group appears to introduce considerable steric hindrance, for 9-anthrylphenylketimine hydrochloride must be heated to 145° for several days in a sealed tube with dilute hydrochloric acid in order to effect complete hydrolysis to the ketone.

The Grignard reagent reacts with alkyl halides to give 9-alkylanthracenes. Methyl iodide and diphenylbromomethane give 9-methylanthracene and 9-anthryldiphenylmethane (I) respectively. The yields of the products actually isolated in pure condition were, however, low due to the fact that the products had to be separated mechanically from accompanying anthracene.

Reaction of 9-anthrylmagnesium bromide with ketones gives the expected tertiary carbinols. Thus, 9-anthryldiphenylcarbinol (II) is obtained from reaction with benzophenone, and 9-anthrylbiphenylenecarbinol (III) from fluorenone. The ketones were always allowed to react

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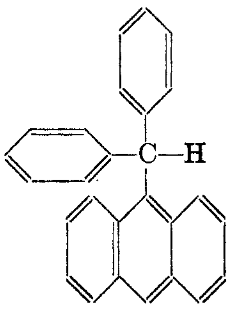
[4] LIEBERMANN AND ZSUFFA, *Ber.*, **44**, 208 (1911).

[5] KARRER AND ZELLER, *Helv. Chim. Acta*, **2**, 486 (1919).

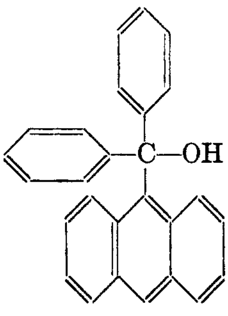
[6] GRAEBE AND LIEBERMANN, *Ber.* **2**, 678 (1869).

[7] BACHMANN AND PENCE, *J. Am. Chem. Soc.*, **57**, 1131 (1935).

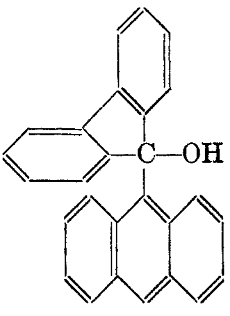
with the Grignard reagent in the cold, for when the mixture was refluxed after addition of benzophenone the yield of carbinol was considerably reduced, and no 9-anthrylbiphenylenecarbinol was ever isolated when the reaction mixture of 9-anthrylmagnesium bromide and fluorenone was refluxed. In these instances also, the reduced yields of pure product were caused by the necessary mechanical separation from accompanying anthracene in the hydrolysis mixture.



I



II



III

Finally, the reaction of 9-anthrylmagnesium bromide with iodine offers a convenient method for the preparation of 9-iodoanthracene. This new halide was obtained in 53 per cent. yield when an ethereal solution of excess iodine was added to the cold, solid Grignard reagent.

9-Bromoanthracene was found to react readily with maleic anhydride in boiling xylene solution to give 9-bromoanthracene-9,10-*endo*-α,β-succinic anhydride (IV). The addition reaction of anthracene derivatives with maleic anhydride has been found to be reversible, and both the rate and the extent of reaction are influenced by meso-substitution.[8] Thus, 9-methylanthracene reacts with maleic anhydride more rapidly than does anthracene, while 9-phenylanthracene reacts much slower than anthracene. In the case of both anthracene and 9-methylanthracene, however, the equilibrium in boiling xylene is 99 per cent. toward adduct formation, while with 9-phenylanthracene reaction proceeds only 75 per cent. to completion. We have now found that the addition of 9-bromoanthracene to maleic anhydride is somewhat slower than the addition of anthracene itself, but the equilibrium in boiling xylene is very favorable to adduct formation (at least 94 per cent.). Barnett[9] has recently observed the reaction of 9-bromoanthracene with maleic anhydride in *o*-dichlorobenzene but the yield of adduct was not reported.

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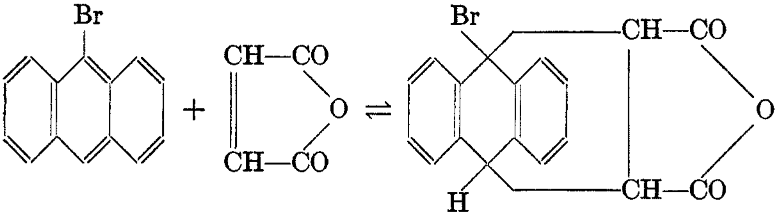
[8] Bachmann and Kloetzel, *ibid.*, **60**, 481 (1938).

[9] Barnett, *J. Chem. Soc.*, 1225 (1934).



IV

We have found that 9-bromoanthracene also reacts readily with lithium in anhydrous ether, and this preliminary survey is being extended to include reactions of 9-anthryllithium as well as an investigation of the Grignard reaction involving meso-halides of polycyclic anthracene derivatives.

EXPERIMENTAL

9-Bromoanthracene.—Technical (80–85%) anthracene was crystallized twice from toluene and then brominated according to the method of Barnett and Cook.[1] The crude product was distilled *in vacuo*, fractionally crystallized from petroleum ether (90–100°) five times to remove anthracene and finally fractionally crystallized from a large volume of ethanol to remove dibromoanthracene. The product melted at 100–101°; yield, 55%.

*9-Bromoanthracene-9-10-*endo-*α,β-succinic anhydride* (IV).—When a solution of 1.0 g. of 9-bromoanthracene and 0.40 g. of sublimed maleic anhydride in 5 cc. of dry xylene was heated, a deep-yellow color was produced which gradually faded on further heating. The solution was refluxed for two hours and cooled, whereupon 1.30 g. (94% yield) of colorless crystals separated. The adduct crystallizes from acetic anhydride in nacreous plates, m.p. 253–254° (dec.), which sublime unchanged *in vacuo* (225°/0.5 mm.).

In another experiment a mixture of 100 mg. of 9-bromoanthracene, 39 mg. of maleic anhydride and 2 cc. of xylene was refluxed for thirty minutes. After evaporation of the xylene by a current of air the residue was heated for a few minutes on the steam bath with 5 cc. of 40% potassium hydroxide solution to hydrolyze the adduct to the dicarboxylic acid. The potassium salt of the acid was then dissolved in hot water, and benzene was added. The layers were separated, and evaporation of the benzene yielded 29 mg. of unreacted 9-bromoanthracene, indicating 71% reaction.

9-Cyanoanthracene.—To 2.0 cc. of dry pyridine was added 1.0 g. of dry cuprous cyanide, and after the vigorous reaction had subsided 2.57 g. of 9-bromoanthracene was added. The mixture, protected from moisture by a mercury trap, was heated in a metal bath at 220° for nine hours, cooled, and then shaken with dilute ammonium hydroxide and ether. The ethereal layer was washed with water, dilute hydrochloric acid, again with water, and dried. The residue, after evaporation of the ether, crystallized from ethanol in yellow needles; yield, 1.76 g. (87%); m.p. 174–175°. The nitrile prepared by Karrer and Zeller[5] melted at 170–172°.

9-Anthrylmagnesium bromide.—For use in the preparation of the Grignard reagents, pure (99.7%; from the Aluminum Company of America), cleaned magnesium ribbon was pulverized in a Wiley mill, washed twice with acetone and dried. The *n*-butyl ether was distilled (139.5–140.5°/745 mm.) and stored over lithium wire; anhydrous ethyl ether and thiophene-free benzene were stored over sodium wire.

Method A.—9-Bromoanthracene melting below 100° is not satisfactory for the preparation of the Grignard reagent by this method. For each experiment a mixture of 2.57 g. (0.01 mole) of 9-bromoanthracene, 0.26 g. of pulverized magnesium, 5 cc. of butyl ether, 15 cc. of benzene and 0.10 g. of iodine was refluxed on the steam bath for twelve hours, and was constantly protected from air and moisture by a mercury trap. A vigorous reaction began in less than one-half hour and a deep-brown solution of the Grignard reagent was finally obtained. The reagent crystallizes readily from the butyl ether-benzene mixture in colorless needles when the solution is cooled.

To determine the extent of the reaction, the hot solution of Grignard reagent was filtered through cotton into standard normal hydrochloric acid and after complete reaction the excess acid was titrated with standard alkali. The anthracene obtained from hydrolysis checked the titration within 2%. In a number of experiments where heating was continued for varying periods of time the yields were as follows: six hours, 67%; twelve hours, 73%; twenty-four hours, 73%; forty-eight hours, 74%. The by-products in this reaction were mostly dark tars, although one product sublimed *in vacuo* (250°/0.5 mm.) and crystallized from toluene in long, yellow needles; m.p. 313–315°.

Method B.—A mixture of 2.57 g. of 9-bromoanthracene, 0.26 g. of pulverized magnesium, 5 cc. of butyl ether, 15 cc. of benzene and five drops (approximately 80 mg.) of ethyl bromide was refluxed on the steam bath for twelve hours. Reaction began immediately, and a clear, red-brown solution of the Grignard reagent was obtained.

Method C.—A mixture of 2.57 g. of 9-bromoanthracene, 0.26 g. of pulverized magnesium and 20 cc. of butyl ether was refluxed on the sand bath. After one hour reaction was found by titration to have gone 69% toward completion; after one and one-quarter hours, 70%. When 0.05 g. of iodine was used to activate the magnesium, 66% reaction took place within fifteen minutes and 71% in thirty minutes. The solution obtained was dark-brown.

Method D.—A mixture of 2.57 g. of 9-bromoanthracene, 0.50 g. of pulverized magnesium, 20 cc. of ethyl ether and five drops of ethyl bromide was refluxed on the steam bath for twenty-four hours. The solution, which becomes cloudy within fifteen minutes, must be shaken frequently during the first few hours to prevent coating of the magnesium. The Grignard reagent is finally obtained as a dense, cream-colored precipitate and may be used as such, or the ether may be boiled off and the solid dissolved in 60 cc. of anhydrous benzene by boiling for approximately ten hours. Hydrolysis of a sample of Grignard reagent prepared in this way yielded 1.53 g. (86%) of pure anthracene; m.p. 212–213°.

9-Iodoanthracene.—To the cold suspension of solid Grignard reagent prepared by method D was added a solution of 3.0 g. of iodine in 50 cc. of anhydrous ether. The iodine color quickly disappeared and a clear yellow solution was formed. This was washed with water and with aqueous sodium bisulfite, dried and evaporated. The residue crystallized from ethanol in broad, yellow needles; m.p. 82–83°; yield, 1.61 g. (53%).

Anal. Calc'd for $C_{14}H_9I$: I, 41.8. Found: I, 42.4.

9-Methylanthracene.—To a cold suspension of solid Grignard reagent in ether prepared by method D was added 7.5 g. of methyl iodide and 25 cc. of anhydrous benzene. The excess magnesium quickly disappeared and after refluxing for forty-eight hours the solution became clear yellow. The product was hydrolyzed with dilute acetic acid, and the organic layer was washed, dried, and evaporated. When the residue was crystallized slowly from ethanol, large yellow tablets of 9-methylanthracene were obtained which could be separated mechanically from accompanying anthracene; yield, 0.80 g. (41%). The hydrocarbon crystallized from ethanol in long, yellow blades; m.p. 78–79°.

9-Anthroic Acid.—To a suspension of 9-anthrylmagnesium bromide prepared by method D was added 25 cc. of anhydrous benzene, and dry carbon dioxide was passed into the boiling mixture for one and one-half hours. The solution became clear yellow while a gummy deposit formed on the surface. After adding water the mixture was heated, the layers were separated and the organic layer was extracted with dilute ammonium hydroxide. Acidification of the combined aqueous extracts with dilute hydrochloric acid precipitated 1.6 g. (72%) of 9-anthroic acid which crystallized from dilute ethanol in yellow needles; m.p. 215–216° dec.

9-Anthrylphenylketimine.—(*a*) *From 9-anthrylmagnesium bromide and benzonitrile.*—A solution of 1.25 g. of benzonitrile in 20 cc. of anhydrous benzene was added to a suspension of solid 9-anthrylmagnesium bromide in ether prepared according to method D. The mixture was refluxed for six hours, hydrolyzed with dilute acetic acid, and the organic layer was shaken for five minutes with 10 cc. of 36% hydrochloric acid, whereupon the ketimine hydrochloride separated in crystalline form. The salt crystallizes from ethanol-ethyl acetate in orange leaflets; m.p. 272–274°.

Anal. Calc'd for $C_{21}H_{15}N \cdot HCl$: Cl, 11.2. Found: Cl, 11.2.

The ketimine hydrochloride is very soluble in hot ethanol, slightly soluble in chloroform or acetone and nearly insoluble in hot ethyl acetate or hot carbon tetrachloride.

Warming for a few minutes on the steam bath with benzene and dilute ammonium hydroxide converted the hydrochloride to 9-anthrylphenylketimine. The product obtained by evaporation of the benzene crystallized from ethanol or acetone in pale yellow, diamond-shaped plates m.p. 152–153°; yield, 2.45 g. (87%). The ketimine sublimes *in vacuo* (195°/0.5 mm.) in tablets. It gives a red-orange color with concentrated sulfuric acid.

Anal. Calc'd for $C_{21}H_{15}N$: C, 89.6; H, 5.4. Found: C, 89.0; H, 5.3.

(*b*) *From 9-cyanoanthracene and phenylmagnesium bromide.*—To the Grignard reagent prepared from 1.5 g. of bromobenzene in 5 cc. of anhydrous ether was added 1.0 g. of 9-cyanoanthracene and 15 cc. of anhydrous benzene, and the mixture was refluxed for six hours. The ketimine was isolated as previously described; yield, 1.26 g. (92%); m.p. 152–153°. No depression of the melting point was produced when a sample was mixed with ketimine prepared from 9-anthrylmagnesium bromide and benzonitrile.

9-Benzoylanthracene.—9-Anthrylphenylketimine hydrochloride is not readily hydrolyzed to the ketone. A sample heated with dilute hydrochloric acid in a sealed tube for six hours at 180° was hydrolyzed only to the extent of 20%, and considerable decomposition appeared to have taken place. The hydrolysis was finally effected in 93% yield by heating 0.8 g. of the hydrochloride, 50 cc. of water and 1 cc. of 36% hydrochloric acid for eighty hours at 145° in a sealed tube. The ketone crystallized from ethanol in broad, yellow needles; m.p. 145–146°.

9-Anthryldiphenylmethane (*I*).—To the slightly cooled solution of the Grignard reagent prepared by method B was added 2.6 g. of diphenylbromomethane in 20 cc. of anhydrous benzene. The solution became much lighter in color and solidified. The mixture was refluxed for ten hours, hydrolyzed with dilute acetic acid, and the organic layer was evaporated. The residue crystallized from benzene in nodules; yield, 0.34 g. (10%). 9-Anthryldiphenylmethane crystallizes from benzene in practically colorless prisms; m.p. 204–205°.

Anal. Calc'd for $C_{27}H_{20}$: C, 94.1; H, 5.9. Found: C, 93.7; H, 5.8.

9-Anthryldiphenylcarbinol (II).—To the slightly cooled solution of 9-anthrylmagnesium bromide prepared according to method A was added 1.82 g. of benzophenone. The mixture was shaken and allowed to stand at 25° for twenty hours, and then at 0° for forty-eight hours. The yellow addition product was filtered and hydrolyzed with cold aqueous ammonium chloride. By allowing an ethereal solution of the product to evaporate slowly, large transparent tablets of the carbinol were obtained which could easily be separated mechanically from anthracene; yield, 1.20 g. An additional 0.14 g. of carbinol was obtained when the filtrate from the addition compound was hydrolyzed; total yield, 37%.

A 36% yield of the same carbinol was obtained when 2.0 g. of benzophenone was added to a benzene solution of 9-anthrylmagnesium bromide prepared according to method D, and the solution was refluxed for five hours.

9-Anthryldiphenylcarbinol crystallizes from ether or benzene-petroleum ether in colorless, hexagonal prisms; m.p. 191–192°. With concentrated sulfuric acid the carbinol gives an intense yellow color.

Anal. Calc'd for $C_{27}H_{20}O$: C, 90.0; H, 5.6. Found: C, 89.7; H, 5.4.

9-Anthrylbiphenylenecarbinol (III).—To a slightly cooled solution of the Grignard reagent prepared by method A was added 1.35 g. (75% theoretical) of fluorenone. The mixture was shaken and allowed to stand at 25° for sixteen hours and at 0° for five hours. The brown-yellow addition compound was filtered and hydrolyzed with cold, aqueous ammonium chloride. When an ethereal solution of the product was allowed to evaporate slowly, the carbinol was obtained in long prisms which could be conveniently separated mechanically from anthracene; yield, 0.90 g. An additional 0.19 g. of carbinol was obtained when the filtrate from the addition compound was hydrolyzed; total yield, 1.09 g. (30%). 9-Anthrylbiphenylenecarbinol crystallizes from benzene-petroleum ether in long, colorless needles; m.p. 205–206°. It gives an intense brown-red color with concentrated sulfuric acid.

Anal. Calc'd for $C_{27}H_{18}O$: C, 90.5; H, 5.1. Found: C, 90.3; H, 5.0.

9-Anthryllithium.—A mixture of 2.57 g. of 9-bromoanthracene, 20 cc. of anhydrous ether and 0.20 g. of lithium wire was refluxed for twenty-four hours. Reaction began immediately, the lithium became coated with a yellow precipitate and a yellow-brown solution was obtained. Excess lithium was decomposed with methanol, the ether was boiled off and a large volume of water containing a little hydrochloric acid was added. The precipitated anthracene was filtered and recrystallized from benzene; yield, 0.85 g. (48%); m.p. 211–213°.

SUMMARY

9-Anthrylmagnesium bromide has been prepared and a study has been made of its reaction with a number of reagents.