B. **Hydrolysis with Water.**—Three grams of base and 3 g. of water was heated in a test-tube. Boiling began at 94° and continued, after removing the flame, for five minutes, while the temperature rose to 108°. The colorless liquid, which still smelled of oxazoline, was heated for thirty minutes more in the boiling water-bath and then dried *in vacuo* at 100°. A colorless, odorless oil remained which contained 14.9% nitrogen as compared with 15.7% calculated for ethanol formamide. A part of the oil was heated to 100° in oxalic acid solution for one hour; ethanol now precipitated the characteristic alcohol-insoluble ethanolamine oxalate.

C. **Reaction with Hydrogen Chloride.**—To 3 g. of oxazoline dissolved in 10 g. of ether, 15 g. of a 10% ethereal solution of hydrogen chloride was added with ice cooling. A white crystalline powder separated at once which at room temperature soon melted to a clear colorless liquid. After removing the ether and excess of hydrogen chloride *in vacuo* at 100°, the product contained 32.1% of chlorine; calculated for β-chloroethyl formamide, 32.8%.

D. **Reaction with Sodium.**—A piece of sodium in 1 g. of oxazoline caused a violent reaction with evolution of gas. The residue, a yellow amorphous mass, gave a precipitate of prussian blue by the usual test for cyanides.

E. **Picrate.**—The alcoholic solution of the base remained clear with picric acid. Ether precipitated an oil which did not crystallize.

s-β,β-Dichlorodiethyl Oxamide.—Twenty grams of s-diethanol oxamide,[4] 100 g. of toluene and 42 g. of thionyl chloride was heated for thirty minutes to 60°, then for ninety minutes in a boiling water-bath. Without first dissolving, the diethanol oxamide changed to a thick white crystal sludge. After cooling, the crystals were filtered, washed subsequently with ethanol, boiling water, ethanol, and crystallized from 200 g. of boiling "cellosolve" (ethylene glycol monoethyl ether). The yield was 19 g. or 78%. The product forms white needles, insoluble in water, sparingly in hot ethanol, which melt at 203°.

Anal. Calcd. for $C_6H_{10}N_2O_2Cl_2$: Cl, 33.3. Found: Cl, 33.1.

2,2'-Δ^2-Dioxazoline.—Ten and six-tenths grams of the preceding compound in 100 cc. of *N* methyl alcoholic potassium hydroxide was boiled for one hour, the clear solution filtered from potassium chloride, evaporated on the water-bath and the crystalline residue recrystallized from 100 g. of toluene. The yield was 5.9 g. or 84%. 2,2'-Δ^2-Dioxazoline crystallizes from toluene in white, fern-like aggregates which melt at 213°. It is very soluble in water and in ethanol, almost insoluble in ether and in cold toluene.

Anal. Calcd. for $C_6H_8N_2O_2$: N, 20.0. Found: N, 19.9.

Reaction with Hydrogen Chloride.—One and four-tenths grams of dioxazoline was dissolved in methanol and 10 g. of a 10% solution of hydrogen chloride in ether was added. White crystals separated and were identified, after crystallization from "cellosolve," by melting point and mixed melting point (203°) as s-β,β-dichlorodiethyl oxamide.

Picrate.—Thirty-five hundredths of a gram of dioxazoline and 1.3 g. of picric acid both dissolved in hot ethanol gave a sparingly soluble picrate which crystallized in long needles and melted at 182°.

Summary

Thionyl chloride reacts with ethanol formamide and with s-diethanol oxamide with formation of β-chloroethyl formamide and of s-β,β-dichlorodiethyl oxamide. With alkali, the latter two compounds yield Δ^2-oxazoline and 2,2'-Δ^2-dioxazoline, respectively. Some characteristic reactions of the two oxazolines are described.

ELIZABETH, N. J. RECEIVED JUNE 20, 1938

---

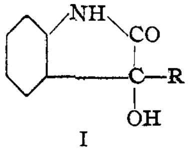
[4] Knorr, *Ber.*, **36**, 1278 (1903).

[CONTRIBUTION FROM THE NICHOLS LABORATORY OF NEW YORK UNIVERSITY]

Reactions of Grignard Reagents with Isatin and N-Alkyl Isatins[1]

BY FREDERICK J. MYERS[2] AND H. G. LINDWALL

The reactions of several Grignard reagents with isatin and N-methylisatin have been reported by Kohn.[3] With isatin the Grignard reagents yield the respective 3-alkyl(or aryl)-3-hydroxy-oxindoles, as would be anticipated. These products have the general formula



I

Kohn prepared the 3-methyl, 3-phenyl and 3-benzyl derivatives of I, but did not investigate the chemical characteristics of these compounds.

Structure I suggested the possibility of the preparation of 3-alkylidene oxindoles through the action of dehydrating agents; using 3-benzyl-3-hydroxyoxindole as the representative of the group, various methods of dehydration were attempted, but without success. In most cases, the compound was recovered unchanged, or, under extremely strenuous conditions, suffered changes more complex than the simple splitting off of a molecule of water.

Kohn[4] also studied the action of phenylmagne-

---

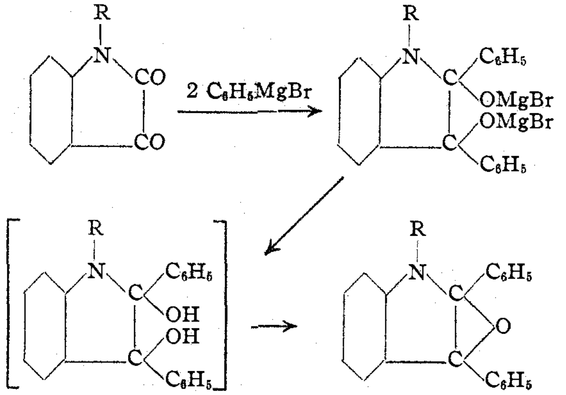
[1] Presented in part at the Rochester meeting of the American Chemical Society, September, 1937.

[2] Present address: c/o Röhm and Haas Co., Bridesburg, Penna.

[3] Kohn and Ostersetzer, *Monatsh.*, **32**, 905 (1911); Kohn, *ibid.*, **31**, 747 (1910).

[4] Kohn and Ostersetzer, *ibid.*, **34**, 789 (1913).

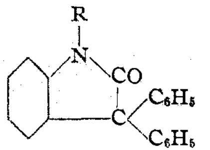
sium bromide upon N-methylisatin, and reported a single compound, 2,3-diphenyl-1-methylindole-oxide-2,3 (II), as the product. He postulated the mechanism



II

The reaction has been repeated; the product isolated was found to melt at 140–143°, which was in close agreement with the melting point (145°) reported for II by Kohn. However, upon repeated recrystallization of the product from dilute ethyl alcohol, it soon became apparent that two compounds were present; one (II) melting at 137.5–138.5°, was yellow and, as reported by Kohn for II, gave a marked fluorescence in solution, and the other (III) was almost white, melted at 171–171.5°, and gave no fluorescent effect in solution. Compound II was obtained as plates, while III was in the form of needles. The longer the period of time of exposure of the original Grignard complex to the hydrolytic agent (sulfuric acid), the larger was the relative amount of III obtained. Analyses showed II and III to be isomeric.

The oxide ring structure assigned by Kohn to II suggested that III might be a rearrangement product of II, and that III was possibly N-methyl-3,3-diphenyloxindole. Synthesis proved this structure for III to be correct. Inagaki's[5] method of preparation of 3,3-diphenyloxindole by the action of benzene upon 3,3-dichlorooöxindole in the presence of aluminum chloride was applied, substituting N-methyl-3,3-dichlorooöxindole. This Friedel–Crafts reaction proceeded smoothly, and yielded III.



III

Furthermore, phenylmagnesium bromide and N-ethylisatin were found to yield two products (IV and V) paralleling II and III. The higher melting compound (V) was shown, by synthesis as above, to be N-ethyl-3,3-diphenyloxindole, and compound IV was similar to II in general characteristics.

Experimental Part

2,3-Diphenyl-1-methylindole-oxide-2,3 (II).—Powdered N-methylisatin (0.05 mole) was added slowly, over the period of one hour, to a boiling solution of phenylmagnesium bromide (0.25 mole) in 150 cc. of ether and 150 cc. of benzene. After addition the mixture was kept at its boiling point with vigorous stirring for one-half hour, and then was poured into an ice and concd. sulfuric acid mixture. After standing overnight, 52% of crude product had separated; the residual liquid mixture was set aside for one week, in the course of which time further solid product appeared (see below).

The crude product, which had separated after overnight standing of the hydrolytic mixture, was obtained as a crystalline mass, green in tint, soluble in dilute ethyl alcohol, dilute methyl alcohol, and dilute acetic acid; thin plates from dilute ethyl alcohol, m. p. 140–143° (Kohn and Ostersetzer report 145°).

Repeated recrystallizations finally yielded II in purer form as thin plates, m. p. 137.5–138.5°, and showing a marked fluorescence in solution. Also (see below), another product (III) was isolated which differed from II in crystal form and did not show fluorescence in solution.

Anal. Calcd. for $C_{21}H_{17}ON$: N, 4.68. Found: N, 4.71, 4.80.

3,3-Diphenyl-1-methyloxindole (III). By the Action of Phenylmagnesium Bromide upon N-Methylisatin.—Repeated recrystallization of II (above) yielded small amounts of III, though not in very pure form (m. p. 167–168°). The residual hydrolytic mixture (see above for II), after removal of crude II and after one week of standing at room temperature, yielded a sample of III, which was easily purified by crystallization from aqueous alcohol; m. p. 171–171.5°; short stubby needles, showing no fluorescence in solution.

Anal. Calcd. for $C_{21}H_{17}ON$: N, 4.68. Found: N, 4.92, 4.52.

Compound III. By the Friedel–Crafts Reaction.—Powdered anhydrous aluminum chloride (0.0125 mole) was added slowly to 3,3-dichloro-1-methyloxindole (0.005 mole) in 20 cc. of absolute benzene, and the mixture was then heated at 50° for four hours. After removing the benzene by distillation under diminished pressure, the residue was treated with ice and dilute hydrochloric acid. A gummy mass resulted which was extracted with dilute methyl alcohol; the extract was decolorized with charcoal and cooled and the product (III) separated as white needles from methyl alcohol, m. p. 171–171.5°. Melting point methods showed samples of III to be identical with that obtained from the Grignard reaction.

2,3-Diphenyl-1-ethylindole-oxide-2,3 (IV).—N-Ethylisatin and phenylmagnesium bromide were allowed to react

---

[5] Inagaki, *J. Pharm. Soc. Japan*, **53**, 686 (1933).

following a procedure similar to that shown above for II. After hydrolytic treatment in the usual manner, the crystalline material that had formed in two hours was removed and purified by recrystallization from dilute methyl alcohol to which a little acetic acid had been added. Compound IV was thus obtained as short diamond-shaped crystals, greenish-yellow in color, and showing greenish fluorescence in solution; m. p. 116–117°; yield, 56%. The residual benzene–ether solution, from which the crude IV was obtained originally after the hydrolysis of the Grignard complex, was set aside for ten days, after which time compound V was isolated (see below).

Anal. Calcd. for $C_{22}H_{19}ON$: N, 4.47. Found: N, 4.29.

3,3-Diphenyl-1-ethyloxindole (V). By the Action of Phenylmagnesium Bromide upon N-Ethylisatin.—The residual benzene–ether solution, from which IV had separated (see above), was allowed to stand for ten days and then was concentrated by distillation. Compound V, yield 16%, separated and was purified by crystallization from dilute methyl alcohol; long white needles, m. p. 156–157°, giving no fluorescence in solution.

Anal. Calcd. for $C_{22}H_{19}ON$: N, 4.47. Found: N, 4.40.

Compound V. By the Friedel–Crafts Reaction.—Compound V was prepared by the reaction of benzene with 3,3-dichloro-1-ethyloxindole, as for III. The product was identical with the V obtained from the Grignard reaction in melting point and physical characteristics. A mixture of samples from the two sources showed no depression of the melting point.

Summary

3,3-Diphenyl-1-methyloxindole and 3,3-diphenyl-1-ethyloxindole accompany the respective 2,3-diphenyl-1-alkylindole-oxide-2,3 as products of the reaction of phenylmagnesium bromide with N-methylisatin and N-ethylisatin.

UNIVERSITY HEIGHTS
NEW YORK, N. Y.

RECEIVED JUNE 28, 1938

[CONTRIBUTION NO. 364 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

Friedel–Crafts Reactions on *m*-Diphenylbenzene[1]

BY H. GAINES GOODMAN, JR., AND ALEXANDER LOWY

In the process for the preparation of biphenyl from benzene, considerable amounts of high boiling products are produced. *m*-Diphenylbenzene is one of the constituents of this high boiling material. Wardner and Lowy[2] have reported references to the literature concerned with the preparation of this hydrocarbon and its derivatives up to 1932. Since then the additional articles[3] listed have dealt with the subject.

Because a search of the literature has revealed that no attempt has been made previously to apply the Friedel–Crafts type of reaction to *m*-diphenylbenzene, a study was undertaken, with the object of synthesizing and identifying several new compounds of the ketonic types, prepared by the action of acyl halides and anhydrides on *m*-diphenylbenzene in the presence of anhydrous aluminum chloride.

The Friedel–Crafts reaction needs no discussion here since it is covered admirably by several comprehensive reviews.[4]

The structure of the *m*-diphenylbenzene molecule is such that six theoretical monosubstitution products are possible. It was desirable, therefore, to determine the position of attack in the case of each reactant, and, in order to accomplish this, an oxidation of each acylation product was carried out and a study of the oxidation products made. The oxidation products isolated indicated that, in each reaction, the para position of an end ring had been attacked, except in the case of *m*-diphenylbenzene-phthaloylic acid,[5] the exact structure of which was not determined. This was in agreement with numerous examples contained in the literature, which indicated the para position of a substituted benzene ring to be the one generally attacked in the Friedel–Crafts syntheses.

Experimental

The writers are indebted to Mr. R. E. Bowman, of Wilmington, Delaware, who is investigating the high boiling material furnished by the Monsanto Chemical Co., for a generous supply of *m*-diphenylbenzene. The *m*-diphenylbenzene thus obtained was recrystallized twice from ethyl alcohol, producing white needle-shaped crystals, m. p. 85°. Redissolving these crystals in boiling ethanol, and filtering after cooling to 70°, resulted in the

---

(1) Abstracted from a thesis presented by H. Gaines Goodman, Jr., to the Graduate School in partial fulfilment of the requirements for the Ph.D. degree.

(2) Wardner and Lowy, THIS JOURNAL, **54**, 2510 (1932).

(3) Cook and Cook, *ibid.*, **55**, 1212 (1933); Wulff and Roell, U. S. Patent 2,004,546; Busch and Weber, *J. prakt. Chem.*, **146**, 1 (1936).

(4) Kränzlein, "Aluminiumchlorid in der organischen Chemie," Verlag Chemie, G. m. b. H., Berlin, 1932; Calloway, *Chem. Rev.*, **17**, 327 (1935); Groggins, "Unit Processes in Organic Syntheses," McGraw-Hill Book Co., Inc., New York, N. Y., 1935.

(5) *m*-Diphenylbenzene-phthaloylic acid is the term selected for use here, in order to embrace all of the six monosubstitution products which might be obtained theoretically by the action of phthalic anhydride on *m*-diphenylbenzene. Groggins, *Ind. Eng. Chem.*, **22**, 620 (1930), has suggested a better nomenclature in the event that the structures of the acids are definitely known.