

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

Reaction of Phenylmagnesium Bromide and Diphenylmagnesium with 9,10-Diphenylacridyl Chloride and *p*-Dimethylaminotriphenylmethyl ChlorideBY GENNADY M. KOSOLAPOFF AND CHESTER S. SCHOEPFLE¹

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The reaction of 9,10-diphenylacridyl chloride with phenylmagnesium bromide yields the corresponding diphenylacridyl peroxide. Similar reaction with diphenylmagnesium yields a mixture of 9,10-diphenylacridane and 3,9,10-triphenylacridane. *p*-Dimethylaminotriphenylmethyl chloride and its hydrochloride failed to react with the organomagnesium reagents. A convenient laboratory procedure for dehydrative ring closures, with phosphorus pentoxide, was developed.

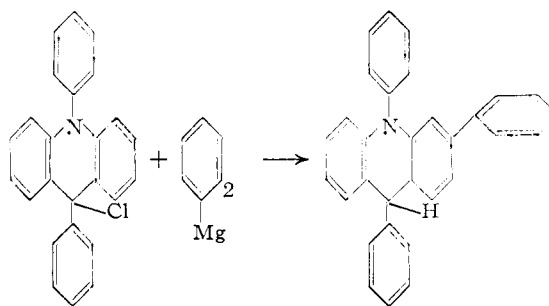
Previous work in this Laboratory has shown that Grignard reagents tend to react with derivatives of triphenylmethyl chloride either at the central carbon atom or at the conjugate position.²

It was felt that an investigation of nitrogen-bearing analogs of triphenylmethyl chloride was desirable. Accordingly, we examined this reaction with 9,10-diphenylacridyl chloride and with the hydrochlorides of *p*-dimethylaminotriphenylmethyl chloride, as well as with crude specimens of the latter chloride itself.

On the basis of the previous results with xanthane derivatives,² the reaction of 9,10-diphenylacridyl chloride with phenylmagnesium bromide could be expected to yield 9,9,10-triphenylacridane, 3,9,10-triphenylacridane and 9-biphenyl-10-phenylacridane.

In reality, this produced only 10% of 9,10-diphenylacridyl peroxide, while 80–85% of the chloride was recovered as the corresponding acridol, after the usual aqueous treatment of the reaction mixture. Thus, no attachment of the phenyl groups from the Grignard reagent took place. It was also noted that in experiments in which the diphenylacridyl chloride had not been preliminarily freed of the chloroform of crystallization, the yields of the peroxide rose to some 50–55%. Since ethereal solutions of Grignard reagents contain equilibrium amounts of magnesium halide which can alter the reaction course, experiments were run with elimination of this inorganic halide. Solutions of diphenylmagnesium in ether–dioxane mixtures were found to react with the diphenylacridyl chloride quite readily, yielding not a trace of the diphenylacridyl peroxide, while some 51–58% yields of 3,9,10-triphenylacridane and 1.5–4.0% yields of 9,10-diphenylacridane were obtained. The latter substance was apparently formed in the oxidation–reduction reaction noted previously in such interactions.² The triphenyl derivative obviously was formed as the result of reaction at the conjugate position in respect to the central carbon. The reaction can be represented by the scheme shown.

The effect of magnesium bromide on the course of the reaction may be explained by a possible formation of a complex between this salt and the acridyl chloride, a complex which is largely inert toward the organomagnesium reagent. This idea is supported by the fact that 9,10-diphenylacridyl chloride, a substance that is very sparingly soluble in dry ether or ether–benzene mixtures, displays



very much increased solubility in such solvents in the presence of anhydrous magnesium bromide. Only a qualitative visual observation of this fact was made.

The reaction of some Grignard reagents with the common dyes of the triphenylmethane series has been investigated earlier.³ These studies dealt with aliphatic Grignard reagents and there have been no data on the reaction of aromatic Grignard reagents with the prototypes of the triphenylmethane dyes. We examined the possibilities of the reaction between phenylmagnesium bromide or diphenylmagnesium, on one hand, and *p*-dimethylaminotriphenylmethyl chloride and its hydrochlorides, on the other hand. The preparation of the latter chloride proper in pure crystalline state proved to be impossible. The hydrochlorides, which were readily obtained, failed to be arylated by the organomagnesium reagents. Thus, the absence of any substantial amount of true benzenoid form of this chloride appears to have been shown.

In order to prepare, by unambiguous methods, the model substances necessary for the confirmation of structures of the products of the reaction of the organomagnesium compounds with diphenylacridyl chloride a dehydrative ring closure technique, employing phosphorus pentoxide, was developed. The procedure is described in the experimental section. It proved to be very useful for ring closures in cases other than the acridine series.⁴

Experimental Part

Reaction of 9,10-Diphenylacridyl Chloride with Phenylmagnesium Bromide.—The necessary 9,10-diphenylacridyl chloride was prepared according to Cone.⁵

This substance retains chloroform of crystallization, which can be removed readily by heating for two or three hours *in vacuo* at 100°. Slow addition of the chloride (4 g.) to a fourfold excess of phenylmagnesium bromide solution

(3) M. Freund and H. Beck, *Ber.*, **37**, 4679 (1904); M. Freund and L. Richard, *ibid.*, **42**, 1119 (1909).

(1) The material is drawn from the doctoral dissertation of G. M. K. presented to the Graduate School, University of Michigan, 1936.

(2) C. S. Schoepfle and J. H. Truesdell, *THIS JOURNAL*, **59**, 372 (1937).

(4) This procedure has been mentioned in "Organic Reactions," Vol. 2, John Wiley and Sons, New York, N. Y., 1944, p. 170, with erroneous reference.

(5) L. H. Cone, *THIS JOURNAL*, **34**, 1699 (1912); **36**, 2105 (1914).

in anhydrous ether resulted in immediate development of deep purple color, without heat evolution. After refluxing for four hours the mixture deposited a quantity of insoluble matter. The mixture was cooled and treated with ice and aqueous ammonium chloride, the organic layer was steam distilled and the residue was taken up in ether, leaving behind 7.9–11.3% of 9,10-diphenylacridyl peroxide, m.p. 206–207°. The ethereal extract and the neutralized aqueous residue yielded 80–85% of 9,10-diphenylacridol.

When the same reaction was performed with the diphenylacridyl chloride that had not been freed of chloroform by crystallization, there was obtained 49.4–55.3% yield of the above peroxide. When the chloride was held in the extraction thimble of a Soxhlet apparatus above the refluxing Grignard solution, thus permitting only the dissolved chloride to enter the reaction, the results were similar and a 52% yield of the peroxide was obtained. No other products were isolated.

Reaction of 9,10-Diphenylacridyl Chloride with Diphenylmagnesium.—The ether–dioxane solutions of diphenylmagnesium were obtained by addition of dioxane to the usual ethereal solutions of phenylmagnesium bromide, after which the precipitated magnesium bromide was removed on a centrifuge.

The diphenylacridyl chloride (2.5–3.5 g.) was added, as above, to a fourfold excess of the reagent solution. The chloride dissolved rapidly with a development of brown color and noticeable heat evolution. After a four-hour period of reflux, during which some magnesium chloride usually precipitated, the mixture was treated as described in the previous section. No peroxide was isolated in the several experiments that were tried. The residue from the steam distillation of the organic layer yielded not a trace of diphenylacridol, and its solution in ether was dried and concentrated to about 10–15 ml. On chilling this solution yielded a solid, which was recrystallized from ether, and finally from aqueous acetone; the pure substance was identified by mixed melting point as 3,9,10-triphenylacridane, m.p. 197°. In several runs the yield ranged from 50.8 to 58.4%. The mother liquor was evaporated to dryness and the residue was taken up in ether. Slow spontaneous evaporation of the solvent gave further minute amounts of the above described triphenyl derivative. The remaining solution, on further concentration and treatment with either alcohol or petroleum ether, gave 1.6–4.2% yields of 9,10-diphenylacridane, m.p. 175–175.5°, identified by mixed melting point with an authentic specimen.

***p*-Dimethylaminotriphenylmethyl Chloride and Its Hydrochlorides.**—*p*-Dimethylaminotriphenylcarbinol was obtained by conventional Grignard synthesis in 85% yield; m.p. 88–88.5°.

When the carbinol was dissolved in the least amount of concentrated hydrochloric acid and the solution was diluted with 2–3 ml. of water, there occurred, after vigorous stirring, a rapid deposition of pale yellow flat needles of the carbinol hydrochloride. After washing with cold chloroform and dry ether, the product was analytically pure and melted with decomposition at 160–161°. The yield was nearly quantitative. The same hydrochloride also was prepared by the passage of dry hydrogen chloride into a dilute solution of the carbinol in dry ether.

Anal. Calcd. for $C_{21}H_{22}NOCl$: C, 74.2; H, 6.53; Cl, 10.44. Found: C, 74.18; H, 6.55; Cl, 10.42.

When the carbinol in a solution in dry ether was treated for several hours with a stream of dry hydrogen chloride in the presence of 1–2 g. of either anhydrous calcium chloride or calcium sulfate, a dark red solution was obtained, while a small amount of dark gum deposited on the walls of the reaction flask. The clear solution was siphoned, without access of air, into a free-radical bulb and an equal volume of dry ether was added. After a few minutes there took place a rapid crystallization of *p*-dimethylaminotriphenylmethyl chloride hydrochloride. This formed long colorless needles which were extremely hygroscopic; even a brief contact with the atmospheric moisture led to bright red pigmentation and formation of a gum. The product was isolated by filtration and washing with dry ether, all operations being performed in a "dry box," provided with an air-drying system of trays with phosphorus pentoxide. The product thus obtained melted at about 108–109° with decomposition. It could not be recrystallized from any of the various solvents tried. The best specimens, which were quite

colorless, contained 19.68% chlorine, as compared with the calculated value of 19.8%.

When the carbinol hydrochloride was dissolved in a small volume of chloroform and the solution was treated with 2–3 ml. of acetyl chloride and then saturated with dry hydrogen chloride at about 0°, evidence was obtained that the solution contained higher hydrochlorides of the *p*-dimethylaminotriphenylmethyl chloride. This is shown by the fact that when this solution was diluted with an equal volume of dry ether, previously saturated with dry hydrogen chloride at 0°, and the mixture was kept for several hours in a refrigerator, there occurred a slow crystallization of large red prisms of *p*-dimethylaminotriphenylmethyl chloride dihydrochloride. After washing with dry ether and drying, again without access of air, this substance contained 26.9% chlorine, as compared with the calculated value of 26.96%.

All attempts to secure *p*-dimethylaminotriphenylmethyl chloride itself in the solid state were fruitless. When solutions of *p*-dimethylaminotriphenylmethyl chloride hydrochloride in either nitrobenzene or chloroform were slowly blown with a stream of dry nitrogen for several hours, the gas stream carried with it nearly the theoretical amount of hydrogen chloride. The residual red solution, which thus contained the desired chloride, was evaporated with most thorough protection from access of moisture, but only uncrystallizable, extremely hygroscopic gummy matter was left as the residue. Analysis of these gummy materials for labile chlorine gave results that were within a few tenths of a per cent. of the expected value, but quite obviously such characterization could not be completely satisfactory. Similar results were obtained on dehydrochlorinations with pyridine or calcium carbonate suspensions. Azeotropic removal of an equimolar amount of water from *p*-dimethylaminotriphenylcarbinol hydrochloride by distillation of its solutions in either benzene or ethylene chloride was readily accomplished, but the resulting red solutions of the desired chloride behaved precisely as did those described above.

Treatment of *p*-Dimethylaminotriphenylmethyl Chloride with Organomagnesium Compounds.—No reaction was observed when a benzene solution of the crude chloride, obtained by dehydration of the carbinol hydrochloride (see above), was treated with a threefold excess of phenylmagnesium bromide in ether; after refluxing for four hours the mixture was treated with ice and ammonium chloride and the working-up of the mixture led to nearly quantitative recovery of *p*-dimethylaminotriphenylcarbinol. The use of ether-free Grignard reagent suspended in refluxing benzene gave the same result. When *p*-dimethylaminotriphenyl chloride hydrochloride was treated with ethereal phenylmagnesium bromide (fourfold excess), a similar lack of reaction was observed.

A solution of crude *p*-dimethylaminotriphenylmethyl chloride, obtained by dehydration of 1 g. of the carbinol hydrochloride in benzene, was treated with a fourfold excess of diphenylmagnesium in ether–dioxane; even after prolonged reflux no reaction took place.

Preparation of 3,9,10-Triphenylacridane.—*p*-Phenyl-*o*-chlorobenzoic acid, m.p. 166.5–167°, was obtained in 30% yield from *p*-aminobiphenyl, following the previously described procedure.² This (5 g.) in 10 ml. of aniline and 20 ml. of amyl alcohol was refluxed with 5 g. of anhydrous potassium carbonate and a trace of copper bronze powder for 1.5 hours. After steam distillation, the hot filtrate was poured into dilute hydrochloric acid and the crude precipitate was recrystallized from alcohol, yielding 85.5% of *p*-phenyl-*o*-anilinobenzoic acid, yellowish needles, m.p. 220–221°.

Anal. Calcd. for $C_{19}H_{15}O_2N$: C, 78.86; H, 5.19; equiv. wt., 289. Found: C, 78.96; H, 5.23; equiv. wt., 286.

The above acid (5.3 g.), 5 g. of anhydrous potassium carbonate, 20 ml. of iodobenzene, 20 ml. of nitrobenzene and a trace of copper powder were refluxed for four hours. After steam distillation and acidification of the hot aqueous filtrate, there was obtained the crude product, which after crystallization from dilute acetone yielded 74.5% of *p*-phenyl-*o*-diphenylaminobenzoic acid, bright yellow plates, m.p. 222–222.5°.

Anal. Calcd. for $C_{25}H_{19}O_2N$: C, 82.16; H, 5.25; equiv. wt., 365. Found: C, 82.30; H, 5.20; equiv. wt., 363.

Attempted ring closure of the above acid with concentrated sulfuric acid led to considerable sulfonation and only grossly impure material could be isolated. Ring closure by

treatment of the acid with phosphorus pentachloride, followed by aluminum chloride was also unsuccessful in that considerable chlorination took place. However, when 4.7 g. of the above acid was refluxed with good stirring in 200 ml. of hot xylene with 5 g. of thoroughly dried filter aid and 5 g. of phosphorus pentoxide for 1.5 hours, the desired ring closure occurred very readily. The reaction mixture was steam distilled, filtered, the solid was agitated for 30 minutes with warm dilute ammonium hydroxide, filtered again and the residual solid was dried at 110°. It was then extracted in a Soxhlet apparatus with benzene and the extract was concentrated and diluted with petroleum ether; after brief standing the solution deposited nearly 100% yield of fine yellowish needles of 3,10-diphenylacridone, which melted at 217.5–218°. The product was somewhat soluble in alcohol, forming solutions with blue-violet fluorescence. Its solutions in concentrated sulfuric acid were yellow with green fluorescence.

Anal. Calcd. for $C_{23}H_{17}ON$: C, 86.42; H, 4.94; mol. wt., 347. Found: C, 86.6; H, 4.89; mol. wt., 351.

This acridone (4.25 g.) was slowly added to an excess of phenylmagnesium bromide in ether and the mixture was refluxed for two hours. After the usual treatment with ice and dilute hydrochloric acid, followed by steam distillation to remove traces of biphenyl, the residue was cooled and made alkaline with sodium hydroxide. The bulky precipitate was dried at about 100° and the residual cake was extracted with boiling benzene. Concentration of the extract and addition of petroleum ether gave a 75% yield of 3,9,10-triphenylacridol, in the form of colorless plates, m.p. 198.5–199°.

Anal. Calcd. for $C_{31}H_{23}ON$: C, 87.53; H, 5.41; mol. wt., 425. Found: C, 87.45; H, 5.39; mol. wt., 419.

The acridol (1 g.) was refluxed for four hours with 10 g. of dry sodium formate and 30 ml. of anhydrous formic acid. Dilution with two volumes of water containing a trace of hydrochloric acid, gave a 100% yield of 3,9,10-triphenylacridane, in the form of small colorless plates, m.p. 197.5–198°, after crystallization from ether or dilute acetone. The product did not give colors with mineral acids. Mixed melting point of this product with the material obtained from the reaction of diphenylacridyl chloride with diphenylmagnesium gave no depression.

Anal. Calcd. for $C_{31}H_{23}N$: C, 90.95; H, 5.62; mol. wt., 409. Found: C, 90.89; H, 5.69; mol. wt., 413.

Preparation of 9,9,10-Triphenylacridane.—*N,N*-Diphenylanthranilic acid (12 g.) was refluxed for ten hours in 200 ml. of absolute methanol with 3 ml. of concentrated sulfuric acid. The solution was concentrated to 50% of the original volume and the residue was extracted twice with 200-ml.

portions of ether. The extract was washed with dilute sodium hydroxide and with water, after which it was evaporated and the residue was taken up in boiling methanol. On cooling this deposited an 89% yield of methyl *N,N*-diphenylanthranilate, long colorless needles, m.p. 132.5–133°.

Anal. Calcd. for $C_{20}H_{17}O_2N$: C, 79.21; H, 5.61; mol. wt., 303. Found: C, 79.34; H, 5.70; mol. wt., 300.

The ester (11 g.) was slowly added to an ethereal solution of a threefold excess of phenylmagnesium bromide and the mixture was refluxed for three hours. The usual treatment gave 84% yield of *o,N,N*-diphenylaminotriphenylcarbinol, as colorless crystals (from acetone), m.p. 168–168.5°.

Anal. Calcd. for $C_{31}H_{25}ON$: C, 87.12; H, 5.86; mol. wt., 427. Found: C, 87.00; H, 5.95; mol. wt., 425.

The carbinol (9 g.) in 800 ml. of boiling ethanol was treated with 2 ml. of concentrated hydrochloric acid. Within 15 minutes the cyclization product began to crystallize and after 20 minutes the reaction was complete. There was obtained a 100% yield of 9,9,10-triphenylacridane, colorless crystals, m.p. 246.5–247°. This product gave no color with mineral acids and was quite insoluble in the usual solvents, except for warm benzene.

Anal. Calcd. for $C_{31}H_{23}N$: C, 90.95; H, 5.62; mol. wt., 409. Found: C, 91.03; H, 5.73; mol. wt., 416.

Dehydrative Ring Closure with Phosphorus Pentoxide.—Several dehydrative ring closures were successfully performed by the procedure outlined above. In many cases benzene, toluene, xylene or chlorobenzene were satisfactory reaction solvents. Celite or Filter-cel was used for the dispersion of the phosphorus pentoxide; these materials must be dried thoroughly at about 130° before use. The isolation of the final cyclization products varied according to the solubility of these in the reaction solvent. If the material was soluble, a simple filtration to remove the dispersing agent and concentration of the filtrate was sufficient. If the product was insoluble, the procedure followed that outlined above for 3,10-diphenylacridone.

The results of these experiments are summarized as follows. *N,N*-Diphenylanthranilic acid gave 100% yield of 10-phenylacridone, bright yellow plates, m.p. 276°. *o*-Phenoxybenzoic acid gave 100% yield of completely colorless xanthone, m.p. 175°. *p*-Phenyl-*o*-phenoxybenzoic acid gave a 100% yield of 3-phenylxanthone, m.p. 139–140°. *o*-Benzoylbenzoic acid gave 85–90% yields of anthraquinone when chlorobenzene was used as the reaction solvent. The use of xylene, toluene or anisole gave side reactions.⁶

(6) G. M. Kosolapoff, *THIS JOURNAL*, **69**, 1651 (1947).