(3) **With Benzaldehyde and Piperidine.**—The solution was refluxed for two hours. The 2-phenylphenanthroxazole, obtained after cooling the solution, was recrystallized from absolute alcohol; yield 97%; m. p. 204.5–205.5°.

Anal. Calcd. for $C_{21}H_{13}NO$: N, 4.74. Found: N, 4.58.

(4) **With Benzaldehyde and Triethylamine.**—In this reaction the solution was refluxed for only thirty minutes. The 2-phenylphenanthroxazole, obtained after cooling the solution, was recrystallized from absolute alcohol; yield 77%; m. p. 204–205.5°.

Anal. Calcd. for $C_{21}H_{13}NO$: N, 4.74. Found: N, 4.69.

(5) **With *n*-Butyraldehyde and Aniline.**—No oxazole was formed in this reaction even after long refluxing.

(6) **With *n*-Butyraldehyde and Two Equivalents of Triethylamine.**—After refluxing the solution for sixteen hours, it was evaporated and the gummy residue taken up in 10 cc. of methyl alcohol. On the addition of 2 cc. of water, a dark, viscous oil slowly separated. After four hours the supernatant liquid was decanted and let stand in the ice-box overnight. On standing, a small amount of 2-propylphenanthroxazole separated. The dark, viscous oil was stirred with 50% methyl alcohol and a few pellets of sodium hydroxide until it had entirely solidified. The combined solids were recrystallized from 80% alcohol, with the aid of decolorizing carbon, until colorless crystals were obtained; yield 50%; m. p. 84–86°. This compound has not been reported previously.

Anal. Calcd. for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.67; H, 5.74; N, 5.38.

Summary

1. Retenequinonimine and phenanthraquinonimine have been shown to react with aldehydes, in the presence of amines, to form 2-substituted retenoxazoles or phenanthroxazoles.

2. The first step in the reaction has been shown to consist of an aldol-type of condensation, with the quinonimine supplying the labile hydrogen.

3. The base-catalyzed reaction is a new and useful method of synthesis for 2-substituted retenoxazoles and phenanthroxazoles, giving high yields and products of excellent purity.

PHILADELPHIA, PA. RECEIVED JULY 14, 1942

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF PENNSYLVANIA]

The Reactions of Retenequinonimine and Phenanthraquinonimine with Schiff Bases. A New Example of an Aldol-Type of Condensation[1]

BY CHARLES W. C. STEIN[2] AND ALLAN R. DAY

It was noted in the previous paper in this series[3] that the interaction of retenequinonimine or phenanthraquinonimine with aldehydes, in the presence of amines, gave excellent yields of 2-substituted retenoxazoles or phenanthroxazoles. It was shown that where secondary or tertiary amines were used, the first step in the reaction consisted of a basically catalyzed aldol-type of condensation between the aldehyde and the quinonimine. However, where a primary amine such as *n*-butylamine was employed, it was realized that another possible course of reaction existed. The amine and aldehyde may react to form a Schiff base and the latter then might undergo an aldol-type of condensation with the quinonimine. Schiff bases are known to behave like aldehydes in many respects (the =NR acting as the carbonyl oxygen) and so it appeared to be quite reasonable to expect them to undergo a similar condensation with the quinonimine.

To test this possibility, benzal-*n*-butylamine was prepared and treated with retenequinonimine. A rapid reaction took place, with the formation of good yields of 2-phenylretenoxazole. Since these reactions were carried out under anhydrous conditions, the possibility that the benzal-*n*-butylamine underwent hydrolysis before reaction was practically excluded. Definite proof was obtained, however, by testing the benzal-*n*-butylamine for free aldehyde in dry toluene solution. Addition of phenylhydrazine to the solution of the Schiff base produced no precipitate of benzaldehyde phenylhydrazone, even when heated on the water-bath for thirty minutes, the approximate time of many of the reactions. A similar test carried out with a sample of freshly distilled benzaldehyde gave an immediate precipitate of phenylhydrazone. It was further noted that *n*-butylamine was evolved in nearly quantitative amounts when retenequinonimine and benzal-*n*-butylamine in equivalent quantities were heated at 100° in dry solvents.

A consideration of all the evidence available at

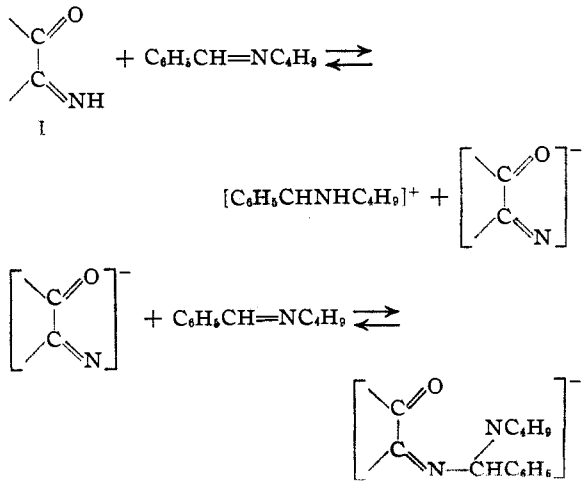
(1) Presented at the Memphis Meeting of the American Chemical Society in April, 1942.

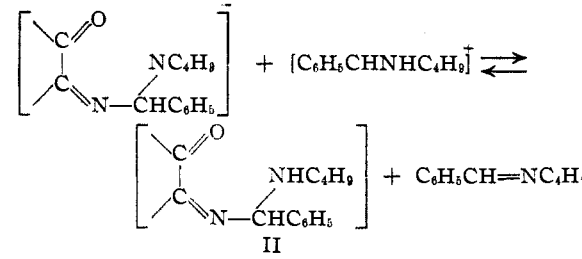
(2) Present address, General Aniline Works, Grasselli, N. J.

(3) Stein and Day, THIS JOURNAL, **64**, 2567 (1942).

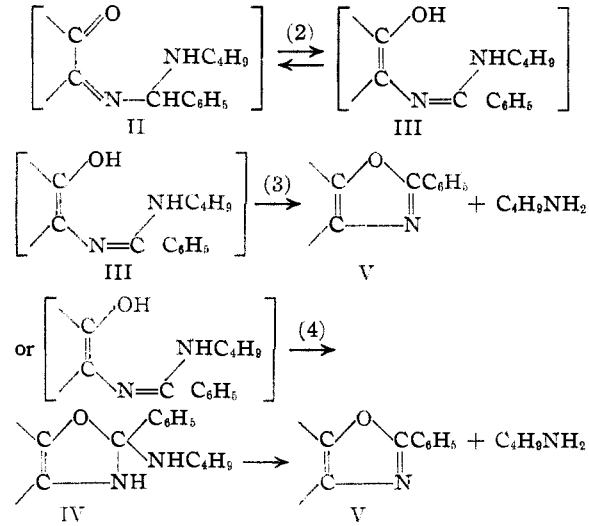
this point showed that any suggested mechanism for this reaction must meet the following requirements. (1) The reaction between the quinonimine and benzal-*n*-butylamine must evolve *n*-butylamine, equivalent in quantity to the amine (present in combined form) in the Schiff base at the start of the reaction; and (2) the substituent in position two of the oxazole ring is derived from the aldehyde portion of the Schiff base.

In accord with these requirements, a mechanism is suggested which involves an aldol-type of condensation between the aldehyde and the quinonimine (step 1). Since the hydrogen of the imino group may be said to be an active hydrogen, it appears reasonable to believe that addition to the Schiff base occurs as the initial step. Indirect evidence for this may be deduced from the fact that when retenequinone is used in place of the quinonimine, no oxazole is formed. Hence the presence of the imino group is essential for the reaction. The addition of the quinonimine to the Schiff base involves an aldol-type condensation where the base acts as an aldehyde and the quinonimine supplies the active hydrogen. The Schiff base also acts as the basic catalyst for the reaction, at least in the case where benzal-*n*-butylamine was used. Such condensations are conditioned by the basic strength of the catalyst and it is interesting to note that when benzalaniline is substituted for the benzal-*n*-butylamine, the reaction is very slow and low yields of oxazole result, unless a more basic catalyst such as piperidine is added. The initial reaction between the quinonimine and benzal-*n*-butylamine, step (1), may be written as





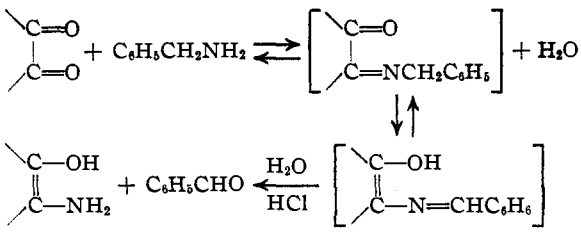
This is followed by two allylic-type shifts of hydrogen, step (2), and subsequently by the splitting out of *n*-butylamine to form the oxazole, step (3) or (4).



There is a considerable amount of information in the literature which may be offered in support of the above mechanism. The addition of various types of active hydrogen compounds to the double bond in Schiff bases has been reported by Mayer.[4] In all of the reactions reported by Mayer, the course of reaction involved addition of the active hydrogen to the nitrogen atom and addition of the other group to the unsaturated carbon atom of the Schiff base. These additions are undoubtedly basic catalyzed reactions for they occur under the influence of basic reagents.

Step (2) in the postulated mechanism also is quite reasonable, for allylic-type shifts of hydrogen would be expected in the type of structure shown. Direct evidence for this shift is difficult to obtain, but in closely related work McCoy[5] has been able to establish such a shift. The hydrolysis of the interaction products of retenequinone and benzylamine yields benzaldehyde. This can be explained only on the basis of a hydrogen shift.

(4) Mayer, *Bull. soc. chim.*, [3] **33**, 157, 395, 498 (1905).
(5) McCoy and Day, unpublished work.



In the final reaction (ring closure to form the oxazole), step (3) appears to be more reasonable in view of the close similarity between Schiff bases and aldehydes in addition reactions. Furthermore, the postulated intermediate III, being a substituted amidine, would be expected to undergo such a condensation.[6] However, step (4) cannot be ruled out. The addition of a hydroxyl group across a double bond with the formation of a heterocyclic ring has been reported in the synthesis of the tocopherols and related compounds.[7] The postulated intermediate (IV) resulting from such an addition would be a dihydroretenoxazole. Such a derivative would be expected to pass readily into the oxazole. A search of the literature disclosed the fact that in cases where 2,3-dihydro-oxazoles or 2,3-dihydroimidazoles might be expected to be the end-products, only the corresponding oxazoles or imidazoles were isolated. The last step, then, may represent spontaneous conversion (oxidation) of a dihydro-oxazole to the oxazole (with the elimination of an amine rather than hydrogen). This assumption is in agreement with the absence of 2,3-dihydro-oxazoles in the literature. Either course suggested for the last step in the reaction, (3) or (4), would explain the liberation of *n*-butylamine.

The use of different types of Schiff bases has yielded some interesting results: benzal-*n*-butylamine yielded up to 93% of 2-phenylretenoxazole; benzalaniline gave a 21% yield of 2-phenylretenoxazole; *n*-butylidene-*n*-butylamine gave only a 7% yield of 2-propylretenoxazole; and *n*-butylideneaniline gave no oxazole. In considering the variation in yields produced by the different types of Schiff bases, it was thought that a relationship might be shown between the yields of oxazole and the basic strength and (or) molecular aggregation of the Schiff bases. Since the initial reaction is a basically catalyzed condensation, the basic strength of the Schiff base should be an important factor. When retenequinonimine and benzalaniline were heated in dry alcohol solution in the presence of one equivalent of piperidine, a 90% yield of 2-phenylretenoxazole was obtained, as compared with a 21% yield in the absence of piperidine. This result agrees with the fact that benzalaniline is a weaker base than benzal-*n*-butylamine. When retenequinonimine and *n*-butylidene-*n*-butylamine were heated in dry alcohol with one equivalent of piperidine, the yield of 2-propylretenoxazole was raised from 7% to 23%. Under similar conditions *n*-butylideneaniline yielded no oxazole. In the last two cases, it is apparent that some other factor is important.

In the dimerization of certain Schiff bases[8] a hydrogen atom on the alpha carbon of the aldehyde part of the base adds to the nitrogen atom of another molecule of the Schiff base. Hence it may be assumed that alpha hydrogen is necessary for dimerization to occur. Since oxazole formation probably depends on the existence of the Schiff base monomer in the reaction mixture, lower yields or no yield of oxazole might be expected when alpha hydrogen is present in the Schiff base. As a check on this hypothesis, a qualitative study of the molecular weights of *n*-butylidene-*n*-butylamine, benzal-*n*-butylamine, and benzalaniline was made by the Rast method. *n*-Butylideneaniline has been shown previously to be a dimer.[8] Values were obtained which were sufficiently reproducible to indicate the probable state of molecular aggregation. With benzalaniline a value was obtained which indicated that the base was essentially monomeric. Benzal-*n*-butylamine gave a somewhat similar result. *n*-Butylidene-*n*-butylamine, however, proved to be trimeric. Since at temperatures of 80–100° the associations (monomer–polymer relationships) are probably reversible, the values cannot be used for a quantitative interpretation but may be used as suggestive evidence for the presence or absence of the monomeric forms at these temperatures.

These results confirm the supposition that the Schiff bases which yield appreciable quantities of oxazole exist preponderantly as the monomers, whereas those which yield little or no oxazole are mostly dimeric or more highly associated. The types $ArCH{=}NCH_2R$ and $ArCH{=}NAr$ are among the former, while the types $(RCH{=}NCH_2R)_n$ and $(RCH{=}NAr)_n$ are among the latter.

The use of phenanthraquinonimine in place of retenequinonimine gave similar results.

(6) Dains, *Ber.*, **35**, 2496 (1902).

(7) Smith, *Chem. Revs.*, **27**, 287 (1940).

(8) Kharasch, Richlin and Mayo, THIS JOURNAL, **62**, 494 (1940); Emerson, Hess and Uhle, *ibid.*, **63**, 872 (1941).

Since the completion of the above work, a general study of basically catalyzed additions to Schiff bases has been started. It is believed that such an investigation will lead to a better understanding of the factors involved and in some cases lead to improved synthetic methods.

Experimental

Analyses and Melting Points.—See previous paper.[3]

Retenequinone, Retenequinonimine, Phenanthraquinone and Phenanthraquinonimine.—These compounds were prepared by the methods noted in the previous paper.

Benzal-*n*-butylamine.—This derivative apparently has not been reported previously. Twenty-five grams (0.236 mole) of freshly distilled benzaldehyde was dissolved in 25 cc. of absolute alcohol and 19 g. (0.26 mole) of *n*-butylamine added gradually with cooling. The solution was allowed to stand over anhydrous potassium carbonate for two days. The alcohol was removed by distillation and the crude benzal-*n*-butylamine was distilled under reduced pressure, b. p. 112–113° at 14 mm., yield 34%, d^{24}_4 0.906, $n^{24}D$ 1.5229. The addition of phenylhydrazine to a solution of the benzal-*n*-butylamine in dry toluene gave no precipitate of benzaldehyde phenylhydrazone, even when heated on the water-bath for thirty minutes. A similar test carried out with freshly distilled benzaldehyde gave an immediate precipitate of the phenylhydrazone. *Anal.* Calcd. for $C_{11}H_{15}N$: N, 8.70; mol. wt. calcd. for monomer, 161, dimer 322. Found: N, 8.64; mol. wt., 220 (in naphthalene), 227 (in triphenylmethane).

Preparation of Benzalaniline.—This was prepared by the procedure described by Bigelow and Eatough.[9] It was recrystallized from 85% alcohol; yield, 84%; m. p. 51°. *Mol. wt.* Calcd.: monomer 181, dimer 362. Found: mol. wt., 216 (in naphthalene).

Preparation of *n*-Butylidene-*n*-butylamine.—At the time this work was undertaken, this compound had not been reported, but it was reported about one month later by Emerson, Hess and Uhle.[8] The method used here is a modification of the method of Chancel.[10] *n*-Butyraldehyde (21.6 g., 0.30 mole) was slowly added to 21.9 g. (0.30 mole) of cooled *n*-butylamine. After standing for one hour, the layers were separated and the upper layer dried over potassium hydroxide. The dried product was distilled at atmospheric pressure, b. p. 141–145°. *Mol. wt.* Calcd. for trimer: 383. Found: 383 and 414 (13% solution in naphthalene).

Preparation of *n*-Butylideneaniline.—This was prepared by the method of Kharasch, Richlin and Mayo;[8] yield 32%. It was reported to be a dimer.

Reactions of Retenequinonimine with Schiff Bases.—In general 2 g. (0.0076 mole) of the quinonimine and one equivalent of the Schiff base were added to 50–100 cc. of dry alcohol and refluxed for a suitable length of time on the water-bath. In most cases the solution was then cooled and the product removed by filtration.

Reaction of Retenequinonimine with Benzal-*n*-butylamine.—The solution was refluxed for nineteen minutes. The crude 2-phenylretenoxazole was recrystallized from absolute alcohol; yield 78%; m. p. 174–175°. *Anal.* Calcd. for $C_{25}H_{21}NO$: N, 3.99. Found: N, 3.96.

Reaction of Retenequinonimine with Two Equivalents of Benzal-*n*-butylamine.—The solution was refluxed for ninety minutes. The product was purified as described above; yield 93.5%; m. p. 175–177°.

Reaction of Retenequinonimine with Benzal-*n*-butylamine in Dry Toluene. (a) Test for *n*-Butylamine as a Reaction Product.—The solution was heated on the water-bath for three hours. After cooling the mixture, the 2-phenylretenoxazole was removed by filtration. The filtrate was distilled and the distillate collected in hydrochloric acid. The acid solution was evaporated to about 20 cc., made alkaline with sodium hydroxide and treated with *m*-nitrobenzenesulfonyl chloride. The filtrate on acidification yielded N-butyl-*m*-nitrobenzenesulfonamide which was recrystallized from alcohol and water; m. p. 67°. A mixed m. p. with an authentic sample showed no depression. **(b) Determination of the Amount of *n*-Butylamine Liberated.**—A run similar to the one described above was carried out in dry alcohol. At the end of the heating period the mixture was steam distilled and the distillate collected in 4% boric acid solution containing methyl red. The boric acid solution was then titrated with standard hydrochloric acid. The volume of the acid used corresponded to 96.58% of the *n*-butylamine originally held in the benzal-*n*-butylamine. In this particular experiment an 82% yield of 2-phenylretenoxazole was obtained.

Reaction of Retenequinone with Benzal-*n*-butylamine.—The solution was refluxed for one hour. No oxazole formation was observed.

Reaction of Retenequinonimine with Benzalaniline.—After refluxing for four hours, the mixture was cooled and the orange-yellow solid removed by filtration. The crude product was recrystallized from 80% dioxane–water to separate the 2-phenylretenoxazole from retenequinone. Final purification was effected from dry alcohol with the use of decolorizing carbon; yield 21.6%; m. p. 177–178.5°. *Anal.* Calcd. for $C_{25}H_{21}NO$: N, 3.99. Found: N, 3.95.

Reaction of Retenequinonimine with *n*-Butylidene-*n*-butylamine.—After refluxing for two hours, the solution was evaporated to a small volume and cooled. The crude 2-propylretenoxazole, so obtained, was recrystallized from 80% dioxane–water, with the aid of decolorizing carbon, until colorless; yield 7%; m. p. 98.5–100.5°. *Anal.* Calcd. for $C_{23}H_{23}NO$: N, 4.42. Found: N, 4.43.

Reaction of Retenequinonimine with *n*-Butylidene-aniline.—No oxazole could be isolated from the reaction mixture after refluxing for four hours.

Reaction of Retenequinonimine with Benzalaniline in the Presence of One Equivalent of Piperidine.—The solution was refluxed for four hours and the crude 2-phenylretenoxazole was recrystallized from dioxane and water; yield 90.5%; m. p. 178–180°.

Reaction of Retenequinonimine with *n*-Butylidene-*n*-butylamine in the Presence of One Equivalent of Piperidine.—After refluxing for four hours, the solution was evaporated to dryness and the gummy residue extracted with a small amount of methyl alcohol, leaving 0.65 g. of a yellow solid. Recrystallization from 80% alcohol, with

(9) Bigelow and Eatough, "Organic Syntheses," John Wiley and Sons, New York, N. Y., 1941, Coll. Vol. I, p. 80.

(10) Chancel, *Bull. soc. chim.*, [3] **11**, 933 (1894).

the use of decolorizing carbon, gave white, fluffy needles of 2-propylretenoxazole; yield 23%; m. p. 100–100.5°.

Reaction of Retenequinonimine with *n*-Butylideneaniline in the Presence of One Equivalent of Piperidine.—No oxazole could be isolated from this reaction mixture after refluxing for fourteen hours.

Reaction of Phenanthraquinonimine with Benzal-*n*-butylamine.—The solution was refluxed for forty-five minutes and the crude 2-phenylphenanthroxazole recrystallized from 80% dioxane–water using decolorizing carbon and finally alcohol; yield 79%; m. p. 205–205.8°. *Anal.* Calcd. for $C_{21}H_{13}NO$: N, 4.74. Found: N, 4.57.

Reaction of Phenanthraquinonimine with Benzalaniline.—The 2-phenylphenanthroxazole obtained after refluxing the solution for four hours was recrystallized from 80% dioxane–water with the use of decolorizing carbon; yield 21.7%; m. p. 206–207°. *Anal.* Calcd. for $C_{21}H_{13}NO$: N, 4.74. Found: N, 4.72.

Reaction of Phenanthraquinonimine with Benzalaniline in the Presence of One Equivalent of Piperidine.—In the presence of piperidine, the yield of 2-phenylphenanthroxazole increased from the 21.7% noted above to 85%, after only two hours of refluxing.

Reaction of Phenanthraquinonimine with *n*-Butylidene-*n*-butylamine.—The solution was refluxed for four hours. After three weeks of standing in the cold, a small amount of yellowish-brown solid separated and was removed. Evaporation of the filtrate yielded only an intractable gum. The crude 2-propylphenanthroxazole was recrystallized from 80% alcohol and finally from 50% alcohol and obtained as colorless needles; yield 0.8%; m. p. 84.3–86.2°. Several runs were necessary to obtain sufficient material for the analyses. *Anal.* Calcd. for $C_{16}H_{15}NO$: C, 82.73; H 5.79; N, 5.36. Found: C, 82.56; H, 5.71; N, 5.30.

Reaction of Phenanthraquinonimine with *n*-Butylidene-*n*-butylamine in the Presence of One Equivalent of Piperidine.—After refluxing for four hours, the solution was evaporated and the viscous residue stirred with 50% methyl alcohol and a few pellets of sodium hydroxide until it had solidified. The 2-propylphenanthroxazole was then recrystallized from 80% alcohol, with the aid of decolorizing carbon; yield 30%; m. p. 85–86°. *Anal.* Calcd. for $C_{18}H_{15}NO$: N, 5.36. Found: N, 5.27.

Reaction of Phenanthraquinonimine with *n*-Butylideneaniline.—No 2-propylphenanthroxazole could be isolated in the absence or the presence of piperidine, after four hours of refluxing.

Summary

1. Retenequinonimine and phenanthraquinonimine have been shown to react with most types of Schiff bases to form 2-substituted retenoxazoles or phenanthroxazoles.

2. The first step in the reaction has been shown to consist of an aldol-type of condensation, with the quinonimine supplying the labile hydrogen. Some Schiff bases are sufficiently basic to catalyze the condensation.

3. This base-catalyzed reaction is a new and useful method for the synthesis of 2-substituted retenoxazoles and phenanthroxazoles.

PHILADELPHIA, PENNA. RECEIVED JULY 14, 1942

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Para Acylation of Polyalkylbenzophenones by Aryl 2,4,6-Trialkylbenzoates

BY REYNOLD C. FUSON, E. M. BOTTORFF, R. E. FOSTER AND S. B. SPECK

Alkylmagnesium halides and arylmagnesium halides that carry a substituent in the para position have been shown to condense with aryl mesitoates to produce ketones.[1] A much more remarkable result was obtained with arylmagnesium halides that had no substituent in the para position. *p*-Tolyl mesitoate and phenylmagnesium bromide, for example, yielded *p*-cresol and a substance that proved to be *p*-dimesitoylbenzene (III). The structure of this compound was proved by synthesizing it from terephthalyl chloride and mesitylene by the Friedel–Crafts method.

The first step in this transformation appeared to be the formation of benzoylmesitylene, which then condensed with unchanged mesitoic ester to produce the diketone (III). In confirmation of this hypothesis, it was discovered that the diketone could be made also by condensing benzoylmesitylene with *p*-tolyl mesitoate.

$$MesCO_2C_6H_4CH_3 \xrightarrow{C_6H_5MgBr} MesCOC_6H_5 \text{ and } CH_3C_6H_4OH$$

$$MesCO_2C_6H_4CH_3 + MesCOC_6H_5 \longrightarrow MesCO\text{—}C_6H_4\text{—}COMes + CH_3C_6H_4OH$$

III

This condensation is without parallel. The net result is the acylation, under the influence of the Grignard reagent, of a benzene ring in the position *which is para to the meta-directing carbonyl group*. The condensation can be formulated as a Claisen reaction in which a nuclear hydrogen atom is replaced by an acyl group. This point of view is supported by the fact that the condensation between the ketone and the ester can be effected with the aid of a number of alkaline cata-

(1) Fuson, Bottorff and Speck, THIS JOURNAL, **64**, 1450 (1942).