2. The shape of the mutarotation curve for talonic acid solutions is indicative of the formation of a dextro rotating δ-talonolactone, as well as a levo rotating γ-talonolactone.
3. γ-Talonolactone has been separated in crystalline form.

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[Contribution from the Chemical Laboratory of Harvard University]

THE REACTION BETWEEN ORGANIC MAGNESIUM HALIDES AND ALPHA-BROMO KETONES

By E. P. Kohler and M. Tishler

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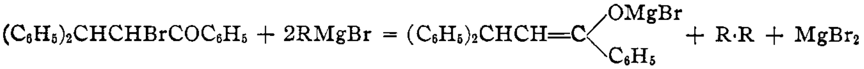
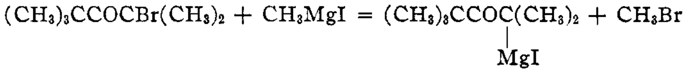
Many years ago Kohler and Johnstin[1] studied the action of organic magnesium halides on α-bromo-β,β-diphenyl propiophenone and, for reasons which seemed good at the time, represented the process with the equation



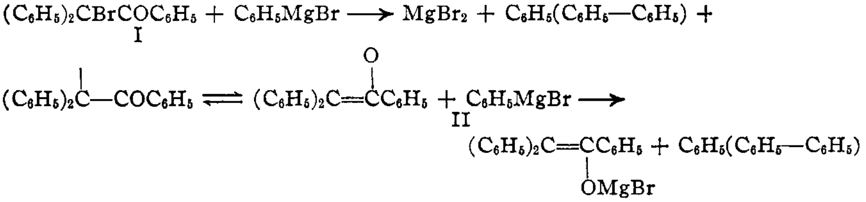
$$(C_6H_5)_2CHCHBrCOC_6H_5 + 2RMgBr = (C_6H_5)_2CHCH{=}C\begin{matrix}\diagup OMgBr\\ \diagdown C_6H_5\end{matrix} + R{\cdot}R + MgBr_2$$

A few years later Umnowa[2] treated α-bromo-pentamethyl acetone with methylmagnesium iodide and obtained a similar result, but, for reasons which likewise seemed good at the time, represented the process in a different manner



$$(CH_3)_3CCOCBr(CH_3)_2 + CH_3MgI = (CH_3)_3CCO\underset{\underset{\displaystyle MgI}{|}}{C}(CH_3)_2 + CH_3Br$$

Quite recently Löwenbein and Schuster[3] rediscovered the reaction, represented their product with a formula similar to the one adopted by Kohler and Johnstin and proposed a mechanism which, in the case studied by them, was plausible



$$\underset{\text{I}}{(C_6H_5)_2CBrCOC_6H_5} + C_6H_5MgBr \longrightarrow MgBr_2 + C_6H_5(C_6H_5{-}C_6H_5) +$$

$$(C_6H_5)_2\overset{|}{C}{-}COC_6H_5 \rightleftharpoons (C_6H_5)_2C{=}\overset{\overset{\displaystyle O}{|}}{C}C_6H_5 \underset{\text{II}}{+} C_6H_5MgBr \longrightarrow$$

$$(C_6H_5)_2C{=}\underset{\underset{\displaystyle OMgBr}{|}}{C}C_6H_5 + C_6H_5(C_6H_5{-}C_6H_5)$$

Fisher, Oakwood and Fuson,[4] who came across the same reaction when they treated tribromoacetomesitylene with alkyl magnesium halides, likewise preferred to represent their magnesium derivative as an enolate.

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[1] Kohler and Johnstin, *Am. Chem. J.*, **33,** 45 (1905).

[2] Umnowa, *Chem. Zentr.*, **84,** I, 1402 (1913); *J. Russ. Phys.-Chem. Soc.*, **45,** 881 (1913).

[3] Löwenbein and Schuster, *Ann.*, **481,** 106 (1930).

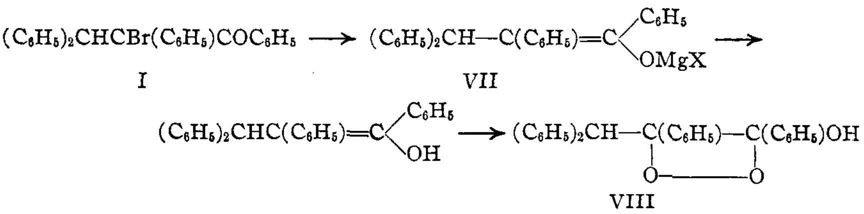
[4] Fisher, Oakwood and Fuson, This Journal, **52,** 5038 (1930).

Meanwhile, however, Kohler, Richtmyer and Hester,[5] having occasion to employ the reaction for the preparation of a sensitive bromohydrin, examined it quantitatively and found that per mole of bromo compound only one mole of the organic magnesium halide disappears. Accordingly neither Kohler and Johnstin's equation nor Löwenbein and Schuster's mechanism can be correct, even though the latter report that they isolated exactly one mole of diphenyl.

In view of these discrepancies we decided to subject the reaction to a more careful investigation in which both the structure of the resulting magnesium compound and the fate of the hydrocarbon residue in the organic magnesium halide were to be established. Quantitative determinations made with a series of α-bromo or α-iodo ketones showed that the course of the reaction is always the same, as can be seen from the results presented in the following table in which the substances listed as "products" are the compounds obtained after decomposition with water and acid. The reagent in every case was methylmagnesium iodide.

	Substances	Moles of reagent	Products
I	$(C_6H_5)_2CHC(C_6H_5)BrCOC_6H_5$	1	$(C_6H_5)_2CHCH(C_6H_5)COC_6H_5$
II	$(C_6H_5)_2CHCHBrCOC_6H_5$	1	$(C_6H_5)_2CHCH_2COC_6H_5$
III	$(C_6H_5)_2CHCHICOC_6H_5$	1	$(C_6H_5)_2CHCH_2COC_6H_5$
IV	$(C_6H_5)_2CBrCOC_6H_5$	1	$(C_6H_5)_2CHCOC_6H_5$
V	$C_6H_5COCHBrCOC_6H_5$	2	$C_6H_5COCH_2C(C_6H_5)(CH_3)OH$
VI	$C_6H_5COCBr_2COC_6H_5$	2	$C_6H_5COCHBrC(C_6H_5)(CH_3)OH$

For the purpose of establishing the structure of the resulting magnesium compound, we employed the reaction between phenylmagnesium bromide and α-bromo-triphenyl-propiophenone (I). Here the product is a colorless crystalline magnesium compound. On decomposition with iced acid in the presence of ether, this magnesium compound gave a solution which absorbed oxygen from the air, forming a peroxide of known structure.[6] The magnesium derivative is therefore an enolate.



$$\underset{\text{I}}{(C_6H_5)_2CHCBr(C_6H_5)COC_6H_5} \longrightarrow \underset{\text{VII}}{(C_6H_5)_2CH-C(C_6H_5)=C\!\begin{array}{l}\diagup C_6H_5\\ \diagdown OMgX\end{array}} \longrightarrow$$

$$(C_6H_5)_2CHC(C_6H_5)=C\!\begin{array}{l}\diagup C_6H_5\\ \diagdown OH\end{array} \longrightarrow \underset{\text{VIII}}{(C_6H_5)_2CH-\underset{\displaystyle O\text{———}}{\overset{}{C}}(C_6H_5)-\underset{\displaystyle \text{———}O}{C}(C_6H_5)OH}$$

For the purpose of establishing the fate of the hydrocarbon residue in the halide, we employed the reaction between α-iododiphenylpropiophenone and phenylmagnesium bromide. It yielded, in addition to the corresponding magnesium enolate, a liquid which was identified as iodo-

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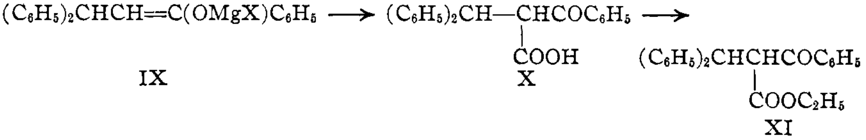
[5] Kohler, Richtmyer and Hester, THIS JOURNAL, **53**, 205 (1931).

[6] Kohler, *Am. Chem. J.*, **36**, 189 (1906).

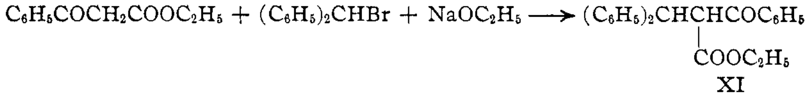
benzene by analysis and by conversion into phenyliodochloride. Diphenyl was also found, but only in the amount to be expected in the quantity of phenylmagnesium bromide used. The reaction must, therefore, be represented by the equation

$$\underset{\text{III}}{(C_6H_5)_2CHCHICOC_6H_5} + C_6H_5MgBr = \underset{\text{IX}}{(C_6H_5)_2CH{-}CH{=}C(OMgBr)C_6H_5} + C_6H_5I$$

Umnowa based her interpretation of the reaction on the fact that her magnesium derivative, corresponding to VII and IX, combined with carbon dioxide to form a salt of a carboxylic acid. Her facts are, doubtless, correct, but her conclusions are no longer valid. It is known, now, that sodium enolates readily combine with carbon dioxide, and that the products are salts of carboxylic acids.[7] Carbonation, therefore, can no longer be regarded as a reliable method for establishing the structure of metallic derivatives. Our magnesium derivatives likewise combine with carbon dioxide; in the case of the enolate represented by IX it was possible to establish the structure of the resulting acid by esterifying it and then synthesizing the same ester by a method that leaves no doubt as to its structure.



$$\underset{\text{IX}}{(C_6H_5)_2CHCH{=}C(OMgX)C_6H_5} \longrightarrow \underset{\text{X}}{(C_6H_5)_2CH{-}\underset{\displaystyle COOH}{CH}COC_6H_5} \longrightarrow \underset{\text{XI}}{(C_6H_5)_2CH\underset{\displaystyle COOC_2H_5}{CH}COC_6H_5}$$



$$C_6H_5COCH_2COOC_2H_5 + (C_6H_5)_2CHBr + NaOC_2H_5 \longrightarrow \underset{\text{XI}}{(C_6H_5)_2CH\underset{\displaystyle COOC_2H_5}{CH}COC_6H_5}$$

By benzoylating this same magnesium compound Kohler and Johnstin formed a product which had previously been obtained in a different manner and which had been formulated as a benzoate.[8]

$$C_6H_5CH{=}CHCOC_6H_5 \longrightarrow (C_6H_5)_2CHCH{=}C(OMgX)C_6H_5 \longrightarrow \underset{\text{XII}}{(C_6H_5)_2CHCH{=}C(OCOC_6H_5)C_6H_5}$$

$$\underset{\text{XIII}}{(C_6H_5)_2CH{-}CH(COC_6H_5)_2}$$

The evidence on which formula XII was preferred to formula XIII likewise is no longer valid, it being known, now, that alkylated diketones are cleaved at least as easily as esters of the type represented by XII are hydrolyzed, and also that alkylation depresses the enolization or reduces the acidity of diketones to such a degree that they no longer form copper derivatives when shaken with copper acetate. In order to decide this

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[7] Brühl, *Ber.*, **24**, 3387 (1891); Schlenk, Hillemann and Rodloff, *Ann.*, **487**, 135 (1931).

[8] Kohler, *Am. Chem. J.*, **31**, 642 (1904).

matter we synthesized the diketone XIII by a method analogous to that employed in the synthesis of the ester XI.

$$C_6H_5COCH_2COC_6H_5 + (C_6H_5)_2CHBr + NaOC_2H_5 \longrightarrow (C_6H_5)_2CHCH(COC_6H_5)_2$$

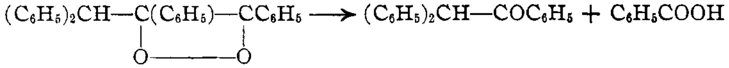
The diketone obtained in this manner and the benzoylation product proved to be the same substance; the latter is therefore not the benzoate XII but the diketone XIII.

The mechanism by which these magnesium enolates yield products which are to some extent like those obtained from Grignard reagents need not be discussed here; it is doubtless the same as that by which the corresponding sodium enolates of Schlenk form similar products. Discussion of the mechanism by which the enolates are formed can likewise be deferred until the limits of the reaction have been explored more thoroughly. It is clear, already, that the reaction is far from general and that the outcome depends not only upon the complexity of the ketone, but also, to a surprising degree, upon the chemical character of the reagent.

Experimental Part

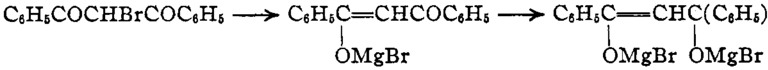
Reaction with α-Bromo-α,β,β-triphenyl-propiophenone, I.—Twenty grams of the finely powdered ketone was added, gradually, to a chilled solution of phenylmagnesium bromide which had been prepared from 1.25 g. of magnesium. The clear liquid was boiled for fifteen minutes—during which time it deposited a solid magnesium derivative—then cautiously poured into a freezing mixture of ice and hydrochloric acid. The ethereal layer was washed rapidly with water and divided into two portions of which one was exposed to a strong draft in an evaporating dish and the other evaporated in a rapid current of air while it was cooled in a freezing mixture. Both portions left an oily residue.

The oil was dissolved in a minimum quantity of acetone. The resulting solution was diluted with low boiling petroleum ether, freed from suspended water by shaking with calcium chloride and cooled. It first deposited a small quantity of triphenylpropiophenone, and then a mixture which melted at 112–114°. After repeated recrystallization from acetone and petroleum ether, this mixture yielded a pure compound which crystallized in small lustrous prisms, melted at about 126°, and had all the characteristic properties of the peroxide represented by VIII. Thus when 5 g. of the substance was heated in a large flask, it decomposed in a series of slight explosions, the products being 3.1 g. of diphenylacetophenone and 1.1 g. of benzoic acid. The same products were obtained also when the substance was digested with alcoholic potassium hydroxide



$$(C_6H_5)_2CH{-}\underset{\displaystyle |\atop O}{C}(C_6H_5){-}\underset{\displaystyle |\atop O}{C}C_6H_5 \longrightarrow (C_6H_5)_2CH{-}COC_6H_5 + C_6H_5COOH$$

Reaction with Bromodibenzoylmethane. V.—It has recently been shown that dibenzoylmethane reacts with two moles of a Grignard reagent, forming in succession a mono and a dimagnesium derivative.[9] Bromodibenzoylmethane reacts in precisely the same manner, consuming the same amount of reagent and forming the same two magnesium derivatives



$$C_6H_5COCHBrCOC_6H_5 \longrightarrow \underset{\text{A}}{C_6H_5\underset{\displaystyle |\atop OMgBr}{C}{=}CHCOC_6H_5} \longrightarrow \underset{\text{B}}{C_6H_5\underset{\displaystyle |\atop OMgBr}{C}{=}CH\underset{\displaystyle |\atop OMgBr}{C}(C_6H_5)_2}$$

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[9] Kohler and Erickson, THIS JOURNAL, 53, 2301 (1931).

Thus when a solution of phenylmagnesium bromide prepared from 1 g. of magnesium was added to an ethereal solution of 12.5 g. of the bromo ketone the result was a soluble magnesium derivative which when manipulated in the usual manner yielded 9 g. of dibenzoylmethane. And when, operating in the usual manner, the same quantity of bromo ketone was added to a solution of phenylmagnesium bromide prepared from 2.5 g. of magnesium, the result was a solid magnesium compound which yielded 10.5 g. of β-hydroxy-β,β-diphenylpropiophenone.

α-Iodo-β,β-diphenylpropiophenone. III.—The iodo ketone can be prepared by heating the corresponding bromo compound with potassium iodide in methyl alcohol, but the operation is troublesome and the yield is small. At the boiling point of methyl alcohol the reaction is too slow to be of any service. It is slow even at 100°; after the mixture had been heated at this temperature for fifty hours, the yield of impure iodo compound did not exceed 50%.

It is relatively easy, however, to transform the bromo into the iodo compound by way of the magnesium derivative. Thus 18.2 g. of the solid bromo ketone was added in the course of ten minutes to a solution of phenylmagnesium bromide which had been prepared from 1.33 g. of magnesium. The mixture was boiled for an hour, then treated while hot with 12.7 g. of iodine. The boiling was continued for another hour, during which the liquid deposited a quantity of brown solid. On decomposition with ice and dilute sulfuric acid the mixture deposited most of the iodo ketone as a finely divided crystalline solid. The solid was washed with water and thiosulfate, dried and recrystallized from benzene. The ethereal filtrate contained 1.9 g. of the same material. The yield was 19.4 g. or 94%.

Anal. Calcd. for $C_{21}H_{17}IO$: C, 61.3; H, 4.2. Found: C, 61.4; H, 4.4.

The iodo compound is very sparingly soluble in alcohol, in ether, and in cold benzene, moderately soluble in hot benzene. From its solution in boiling benzene it separates, on cooling, as a flaky white powder which melts with decomposition at 184–185°.

Reaction with Phenylmagnesium Bromide.—A solution of phenylmagnesium bromide was prepared from 39 g. of bromobenzene and, in order to remove the halide as completely as possible, a large excess of magnesium. The solution was filtered and chilled in ice water. To the cold solution 41.2 g. of the solid iodo ketone was added in small quantities with constant stirring. The mixture was stirred for an hour and a half, then boiled for half an hour and after that decomposed with iced hydrochloric acid. The washed and concentrated ethereal solution deposited 27 g. of β,β-diphenylpropiophenone, which was identified by comparison with a sample on hand. The yield was 94%.

The ethereal filtrate from the ketone, when freed from ether, left an oily residue which was distilled with steam. A small quantity of diphenyl solidified in the cold condenser, but most of the material collected as a heavy liquid in the receiver. The distillate was extracted with ether and the ethereal solution was dried and distilled. It yielded 18 g. of a colorless liquid which distilled completely between 184 and 190°. In a halogen determination 0.2200 g. of this liquid gave 0.2445 g. of a silver halide which was converted into 0.1484 g. of silver chloride. The silver halide was therefore pure silver iodide and the liquid from which it was obtained must contain at least 96.5% of iodobenzene. Assuming that diphenyl is the only impurity, the quantity contained in the liquid cannot exceed 0.7 g. and the maximum amount recovered from the reaction must be under 1 g.—approximately the quantity to be expected in the reagent.

Conversion into Phenyliodochloride.—In order to complete the identification of the iodobenzene, chlorine was passed into a solution of 5.2 g. of the liquid in 20 cc. of chloroform. A solid began to separate almost immediately and in a short time the solution deposited 6.6 g. of the characteristic yellow needles of the iodochloride—a yield of 93.6%.

Action of Carbon Dioxide on the Enolate.—Sixteen grams of solid α-bromo-β,β-diphenylpropiophenone was added in the course of ten minutes to a solution of phenylmagnesium bromide prepared from 1.2 g. of magnesium. The mixture was boiled for an hour, then chilled to 3°. Carbon dioxide was passed into the cooled liquid for five hours and then another hour at the ordinary temperature. A gummy precipitate formed at first, but the gum gradually changed to an amorphous white solid. The solid was collected on a filter in order to be able to decompose the solid and the ethereal solution separately. The ethereal filtrate, on acidification, gave 0.5 g. of unchanged bromo ketone and a small quantity of acid.

The solid was decomposed by prolonged shaking with ether and dilute sulfuric acid. The ethereal layer contained 10.6 g. of an acid—removed by extraction with sodium carbonate—and 2.5 g. of β,β-diphenylpropiophenone which may have been formed by loss of carbon dioxide from the acid. The acid was purified by recrystallization from acetone and petroleum ether.

Anal. Calcd. for $C_{22}H_{18}O_3$: C, 79.9; H, 5.5. Found: C, 79.8; H, 5.6.

Diphenylmethylbenzoylacetic Acid (X).—The acid is readily soluble in all common organic solvents except petroleum ether. It crystallizes in small colorless needles and melts with brisk evolution of carbon dioxide at 134°.

Esterification.—An attempt to esterify the ketonic acid by converting it into the sodium salt and treating a solution of the salt with diethyl sulfate was unsuccessful—the acid lost carbon dioxide and the product was the ketone. Esterification through the silver salt proved more successful.

A suspension of the salt—which had been thoroughly dried in a vacuum desiccator—in absolute ether, was boiled with excess of ethyl iodide for half an hour, during which the voluminous silver salt changed to silver iodide. After filtration, the ethereal solution was evaporated. It left an oil that solidified on cooling. The solid was purified by recrystallization from alcohol.

Anal. Calcd. for $C_{24}H_{22}O_3$: C, 80.4; H, 6.2. Found: C, 80.2; H, 6.4.

Ethyl Diphenylmethylbenzoyl Acetate. XI.—The ester is readily soluble in acetone, moderately soluble in ether and in boiling alcohol, sparingly soluble in cold alcohol. It crystallizes in very fine needles and melts at 135–136°.

Synthesis of the Ester.—To a solution of 0.6 g. of sodium in 25 cc. of absolute alcohol were added first, 5 g. of benzoyl acetic ester and then little by little, 6.5 g. of diphenylmethyl bromide. The solution gradually lost its yellow color, became cloudy, and in the course of half an hour solidified completely. The solid was collected on a filter and washed with a little alcohol, then dissolved in ether. The washed and dried ethereal solution, on concentration, deposited 5 g. of a crude product that melted at 129–133° and one gram more of the same product was obtained by suitable manipulation of the alcoholic filtrate. After recrystallization from absolute alcohol the melting point was 135–136°. The melting point of a mixture of this ester and the one obtained in the preceding experiment was 134–136°.

Synthesis of Diphenylmethyldibenzoylmethane. XIII.—To a solution of 0.5 g. of sodium in 25 cc. of absolute alcohol were added in succession 5 g. of dibenzoylmethane and 6.5 g. of diphenylmethyl bromide. Owing to the sparing solubility of the sodium derivative of the diketone, the conditions were not as favorable as in the synthesis of the ketonic ester, but the reaction yielded 1.4 g. of a product which even when crude melted at 217–220° and which was readily identified with the product obtained by treating the magnesium enolate IX with benzoyl chloride.

Summary

The reaction between an organic magnesium halide and an α-bromo ketone, in which the carbonyl group is relatively inactive, is represented by the equation

$$RCHBrCOR + R_1MgBr = RCH{=}C(OMgBr)R + R_1Br$$

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[Contribution from the Insecticide Divison, Bureau of Chemistry and Soils]

TOXICAROL. III. A RELATION BETWEEN TOXICAROL AND THE ROTENONE GROUP OF FISH POISONS

By E. P. Clark

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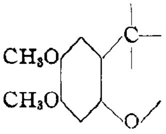
It has been shown[1] that rotenone, deguelin and tephrosin are structurally related in that, among other things, all three compounds possess the atomic grouping represented by formula A.



A

As toxicarol, the other member of this group of fish poisons, is characterized by properties so similar to those possessed by the first three, it has been assumed that, in all probability, this substance has some structure common to the others. Proof of this assumption has recently been obtained as a result of a series of experiments which are described in what follows.

Permanganate oxidation of dehydrotoxicarol in acetone has yielded risic and 2-hydroxy-4,5-dimethoxybenzoic acids. In this reaction the yield of the benzoic acid was essentially the same as that obtained from dehydrodeguelin,[1] but the risic acid, although always present, was obtained in small and variable quantities.

When dehydrotoxicarol was boiled gently with an alcoholic potassium hydroxide solution, the material formed an acid apparently analogous to deguelic[2] and derrisic[3] acids, although it was impossible to obtain it in a crystalline condition. However, when the acidic material was separated from the reaction mixture, dissolved in aqueous alkali, and oxidized with potassium permanganate, risic acid was obtained. If, instead of potassium permanganate, hydrogen peroxide was used as an oxidizing agent, a good yield of derric acid was obtained. These products are the same as those formed under identical conditions with deguelic and derrisic acids, derived, respectively, from deguelin and rotenone.

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[1] Clark, This Journal, **53**, 3431 (1931).

[2] Clark, *ibid.*, **53**, 316 (1931).

[3] Butenandt and Hildebrandt, *Ann.*, **477**, 249 (1930).