85% of the theoretical. When this oil was subjected to distillation under diminished pressure, it underwent no decomposition. The main fraction distilling at 146–149° at 8-mm. pressure exhibited all the properties of a true isothiocyanate. This reacted immediately with aniline, ammonia and alcohol in accordance with the isothiocyanate structure. It would not solidify in a freezing mixture.

Anal. Calcd. for $C_9H_{11}N_3S_2$: N, 18.66. Found: N, 18.33, 18.55.

2-Ethylmercapto-5-ethyl-6-thiourea-pyrimidine.—The thiocyanate was rearranged into its isomeric form and a petroleum ether solution of the latter combined with an excess of concentrated aqueous ammonia. The corresponding thiourea was formed immediately and 2 g. of this was obtained from 3 g. of the thiocyanate. It was purified by crystallization from alcohol and melted at 143–144°.

Anal. Calcd. for $C_9H_{14}N_4S_2$: N, 23.13. Found: N, 22.94, 23.07.

2-Ethylmercapto-5-ethyl-6-phenyl-thiourea-pyrimidine.—Three grams of the rearranged thiocyanate gave 2.5 g. of this compound by treatment with aniline at ordinary temperature. This was purified by crystallization from 95% alcohol and separated in plates melting at 108–109°.

Anal. Calcd. for $C_{15}H_{18}N_4S_2$: N, 17.61. Found: N, 17.53, 17.69.

2-Ethylmercapto-5-ethyl-6-thionethylurethan-pyrimidine.—This was formed by warming the crude isothiocyanate with absolute alcohol. The alcohol was evaporated to dryness and the residue extracted with cold sodium hydroxide. On acidifying this alkaline solution with acetic acid, the urethan separated. After purification by crystallization from alcohol, it separated in the form of colorless rhombic prisms, melting at 77–78° to a clear oil.

Anal. Calcd. for $C_{11}H_{17}ON_3S_2$: N, 15.49. Found: N, 15.41, 15.48.

Experimental Conditions Influencing the Rearrangement of the Pyrimidine Thiocyanate.—A. Heating the thiocyanate (1) at 60° for twelve hours, (2) at 80° for eight hours, and (3) at 100° for three hours did not give any detectable amount of the isothiocyanate. At 140–150° rapid change takes place but the rearrangement is accompanied by secondary changes which lead to a reaction product which is very hard to purify.

B. Digestion of the pyrimidine in benzene did not produce a rearrangement until after twelve hours. Heating in toluene for six hours produces a rearrangement. At the boiling point of ethyl alcohol for two hours the pyrimidine thiocyanate undergoes a molecular rearrangement and the corresponding thiourethan was obtained.

Summary

1. A new process has been found for preparing the sodium salt of ethyl-formyl-*n*-butyrate by condensing ethyl *n*-butyrate and ethyl formate in the presence of sodium wire.

2. 2-Ethylmercapto-5-ethyl-6-chloropyrimidine has been prepared by a new procedure. Its corresponding oxypyrimidine reacts with phosphorus oxychloride in a characteristic manner.

3. 2-Ethylmercapto-5-ethyl-6-thiocyanopyrimidine is formed by the interaction of potassium thiocyanate with 2-ethylmercapto-5-ethyl-6-chloropyrimidine in boiling ethyl alcohol.

4. This thiocyanate is rearranged to its isomeric form, the isothiocyanate, (1) by heating in boiling ethyl alcohol, (2) by digestion in boiling toluene or xylene solution.

SHANGHAI, CHINA RECEIVED NOVEMBER 22, 1934

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

The Reaction between Organic Magnesium Compounds and Alpha Bromo Ketones.
II

BY E. P. KOHLER AND M. TISHLER

In our first paper[1] we showed that many α-bromo ketones react with organic magnesium compounds in accordance with the general equation

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

In view of the great activity of Grignard reagents and the fact that at the end of the reaction the magnesium halide residue is in combination with oxygen, this metathesis is not surprising; in the absence of competing reactions it would be expected to occur whenever a Grignard reagent reacts with any α-halo ketone. Three other reactions are possible, however, even with saturated ketones, namely: elimination of halogen hydride, enolization and addition to the carbonyl group. And in the case of α,β-unsaturated ketones, addition to the conjugated system may also enter the competition.

It is easy to foresee that elimination of halogen hydride will occur only in the comparatively rare cases in which there is unusually active hydrogen in the β position. It is evident also that when the halo ketone is so constituted that neither enolization nor elimination of hydrogen halide is possible, and that the hindrance to addition is prohibitive,

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[1] Kohler and Tishler, THIS JOURNAL, 54, 1594 (1932).

the result must be metathesis. In all other cases the outcome of the competition between the possible reactions cannot be foretold with certainty because it depends, in ways that at present cannot be defined accurately, upon the properties of all the substances that are involved. In these cases prediction must be based on analogies.

An examination of all the cases which have been studied shows that in some of them the result of the competition is determined largely by the character of the magnesium derivatives which enter into the reaction. Thus the products of the reaction between $(C_6H_5)_2CHCHBrCOC_6H_5$ and a series of magnesium derivatives are as follows

$CH_3MgI \quad (C_6H_5)_2CHCH{=}C(OMgI)C_6H_5 + CH_3Br$

$C_6H_5MgBr \quad (C_6H_5)CHCH{=}C(OMgBr)C_6H_5 + C_6H_5Br$

$(C_6H_5)_2C{=}C(C_6H_5)MgBr$

$(C_6H_5)CHCH{=}C(OMgBr)C_6H_5 + (C_6H_5)_2C{=}C(C_6H_5)Br$

$C_6H_5C{\equiv}CMgBr$

$(C_6H_5)_2CHCHBrC(OMgBr)(C_6H_5)C{\equiv}CC_6H_5$

$CH_2{=}C(OMgBr)C_6H_2(CH_3)_3$

$(C_6H_5)_2CHCHBrC(OMgBr)(C_6H_5)CH_2COC_6H_2(CH_3)_3$

Here the very active Grignard reagents which are obtained by the action of the metal on the halides act alike and exchange the magnesium halide residue for halogen. In contrast the less energetic reagents, which are formed indirectly by the action of feebly acidic hydrocarbons or ketones on the more active magnesium derivatives, combine with the carbonyl group and form bromohydrins. This difference in the mode of action of the two types of magnesium compounds reappears in reactions with many other halo ketones. It prevails even in the case of an unsaturated α-bromo ketone where the metathetical reaction involves the formation of an allenic compound.

$$(C_6H_5)_2C{=}CBrCOC_6H_5 + C_6H_5MgBr \longrightarrow (C_6H_5)_2C{=}C{=}C(OMgBr)C_6H_5 + C_6H_5Br$$

In other cases the result of the competition is determined largely by the ketone. With the simplest halo ketones like chloroacetone[2] and chlorocyclohexanone[3] in which the carbonyl group is unusually active or in which—from another point of view—there is little hindrance to addition, all types of magnesium compounds form only addition products. At another extreme are the halogen substitution products of ketones which are distinctly acidic, like diphenylacetophenone and dibenzoylmethane. Here also the result is determined by the character of the ketone and the process is always metathesis. In this class also belong the β-disulfones. These compounds are of special interest because although they are incapable of forming OMgX compounds without abnormally expanding the shell of valence electrons around the sulfur atom, they nevertheless form metallic derivatives. With the halogen derivatives of these β-disulfones, as with those of the β-diketones, the only reaction is metathesis.

As will be seen from the foregoing summary the facts now known provide a broad basis for prediction by analogy. Inevitably, however, there are cases in which the result cannot be foreseen. One would not have been likely to predict for example, the interchange represented by the equation

$$(C_6H_5)_2CHCH{=}C(OMgX)C_6H_5 + CH_2BrCOC_6H_2(CH_3)_3 \longrightarrow (C_6H_5)_2CHCHBrCOC_6H_5 + CH_2{=}C(OMgX)C_6H_2(CH_3)_3$$

and one would certainly not have been able to foresee that the difference between α-chloroacetomesitylene and α-bromoacetomesitylene would be sufficient to lead to enolization with the one and metathesis with the other.[4]

Concerning the mechanism of the metathetical reaction the facts here presented give but little information, but in our opinion they are completely irreconcilable with the hypothesis recently presented by Howk and McElvain.[5] According to these authors the metathetical reaction is preceded by a rearrangement of the halo ketone to the hypohalite of an enol. Even if one were disposed to believe in the possibility of such a shift of a halogen atom, it would seem incredible in compounds like α-bromo β-phenyl benzalacetophenone where it would involve a rearrangement from a conjugated to an allenic system. And it would be equally incomprehensible in the case of β-disulfones.

In some cases there is evidence for the formation of ephemeral magnesium derivatives which disappear again during the course of the reaction. It seems not improbable, therefore, that the first step in the reaction between the Grignard reagent and the halo ketone consists in the formation of a complex addition product which, depending upon space relations and the interplay of specific affinities, subsequently rearranges into a normal

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(2) Tiffeneau, *Ann. chim.*, [8] **10**, 367 (1907).

(3) Tiffeneau and Tchoubar, *Compt. rend.*, **198**, 941 (1934); Bartlett and Rosenwald, THIS JOURNAL, **56**, 1990 (1934).

(4) Fisher, Snyder and Fuson, *ibid.*, **54**, 3672 (1932).

(5) Howk and McElvain, *ibid.*, **55**, 3372 (1933).

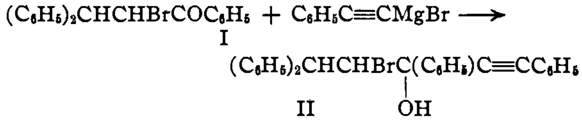
addition product or decomposes into metathetical products which are less active than those from which the complex was formed.

Experimental Part

I. Addition of Phenylethinylmagnesium Bromide

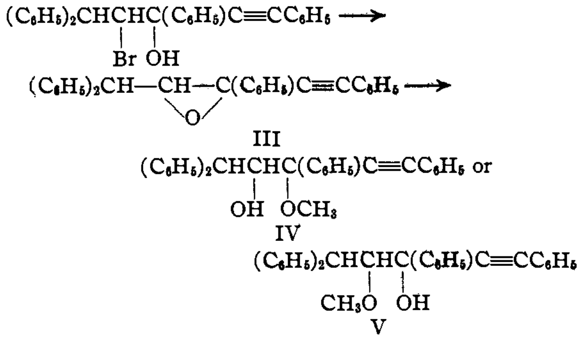
The experiments with ordinary Grignard reagents need not be described because the procedure was the same as that reported in the previous paper and all the metathetical products were identified by comparison with known substances.

The products obtained with the second type of magnesium derivatives were both more complicated and more interesting. Thus the product of the reaction between phenylethinylmagnesium bromide and α-bromo-β,β-diphenylpropiophenone was an unsaturated bromohydrin containing an acetylenic linkage.



$$\underset{\text{I}}{(C_6H_5)_2CHCHBrCOC_6H_5} + C_6H_5C\equiv CMgBr \longrightarrow \underset{\text{II}}{(C_6H_5)_2CHCHBr\underset{OH}{C}(C_6H_5)C\equiv CC_6H_5}$$

As an unsaturated compound the substance could be ozonized and thus cleaved into products which establish the chain, namely, the bromo ketone I and phenylglyoxylic acid. As a hydroxyl compound it reacted with methylmagnesium iodide, liberating one mole of gas and forming a magnesium derivative from which it was regenerated by acids. As a bromohydrin it could be converted into an ethylene oxide which combined with methyl alcohol when treated with sodium methylate.



$$(C_6H_5)_2CH\underset{Br}{C}H\underset{OH}{C}(C_6H_5)C\equiv CC_6H_5 \longrightarrow \underset{\text{III}}{(C_6H_5)_2CH{-}\overbrace{CH{-}C}^{}(C_6H_5)C\equiv CC_6H_5} \longrightarrow$$

$$\underset{\text{IV}}{(C_6H_5)_2CH\underset{OH}{C}H\underset{OCH_3}{C}(C_6H_5)C\equiv CC_6H_5} \text{ or } \underset{\text{V}}{(C_6H_5)_2CH\underset{CH_3O}{C}H\underset{OH}{C}(C_6H_5)C\equiv CC_6H_5}$$

And as an acetylenic compound it combined with iodine to form an addition product which spontaneously lost hydrogen iodide and passed into an unsaturated ketone.

$$(C_6H_5)_2CHCHBrC(OH)(C_6H_5)C\equiv CC_6H_5 + I_2 \longrightarrow \underset{\text{VI}}{(C_6H_5)_2CHCHBrC(C_6H_5){=}CICOC_6H_5} + HI$$

It is not possible at present to distinguish between the various plausible mechanisms by which the unsaturated ketone is formed. Its structure was established by the following transformations. It reacted with two moles of phenylmagnesium bromide, forming a halogen-free ketone, the bromine being replaced by phenyl and the iodine being eliminated as iodobenzene. This halogen-free ketone, on oxidation with chromic acid, yielded α,β,β-triphenyl propiophenone.

$$(C_6H_5)_2CHCHBrC(C_6H_5){=}CICOC_6H_5 \longrightarrow (C_6H_5)_2CHCH(C_6H_5)C(C_6H_5){=}CHCOC_6H_5 \longrightarrow (C_6H_5)_2CHCH(C_6H_5)COC_6H_5$$

1,3,5,5-Tetraphenyl-3-hydroxy-4-bromo-pentine-1 (II).—Preliminary experiments showed that the best yield of phenylethinylmagnesium bromide was obtained by boiling phenylacetylene with ethereal ethylmagnesium bromide for at least four hours. To a solution, prepared in this manner from 2.75 g. of magnesium, 12.5 g. of ethyl bromide and 11.5 g. of phenylacetylene, was added gradually and with constant stirring 25 g. of the bromo ketone I. The stirring was continued for two hours after all of the ketone had been added. The solid magnesium compound which separated during this time was collected on a filter, thoroughly washed with anhydrous ether, then suspended in ether and decomposed with iced sulfuric acid. The result was 19 g. of a solid which separated from ether–petroleum ether in transparent elongated prisms and which after recrystallization from the same combination of solvents melted at 135°.

Anal. Calcd. for $C_{29}H_{23}OBr$: C, 74.4; H, 4.9; Br, 17.1; mol. wt., 467. Found: C, 74.4; H, 5.0; Br, 17.5; mol. wt., 442.

Ozonolysis.—A current of ozonized oxygen containing about 6% of ozone was passed for four hours through a solution of 2 g. of the bromohydrin in carbon tetrachloride. The resulting turbid yellow solution was shaken with water and dilute sodium carbonate. From the carbon tetrachloride layer methyl alcohol precipitated 1.0 g. of the bromo ketone I and from the acidified water solutions phenylhydrazine precipitated the phenylhydrazone of phenylglyoxylic acid, melting at 161° and completely identified by comparison with an authentic sample.

1-Diphenylmethyl-2-phenyl-2-phenylethinyl-ethylene Oxide (III).—Into a solution of 1 g. of the bromohydrin in 10 cc. of chloroform was stirred drop by drop a solution of one equivalent of sodium in methyl alcohol. The chloroform solution was washed well with water, dried, concentrated, and diluted with petroleum ether. It deposited 0.75 g. of the oxide. After recrystallization from ether–petroleum ether, from which it separated in clusters of stubby needles, the oxide melted at 87.5–88.5°.

Anal. Calcd. for $C_{29}H_{22}O$: C, 90.2; H, 5.7. Found: C, 90.2; H, 5.7.

Action of Sodium Methylate on the Oxide (IV) or (V).—In order to ascertain whether the product formed by the action of one equivalent of sodium methylate on the bromohydrin was an oxide or the isomeric ketone, it was boiled for six hours with excess of 2% sodium methylate

The product, isolated in the usual manner, was a solid which crystallized from methyl alcohol in transparent prisms that contained alcohol of crystallization which was lost on exposure to the air and which melted at 119°. The composition shows that the substance is formed by the addition of methyl alcohol to an oxide. The yield was 1.05 g. from 1 g. of oxide.

Anal. Calcd. for $C_{29}H_{23}O(OCH_3)$: C, 86.2; H, 6.2; OCH_3, 7.4. Found: C, 86.2; H, 6.1; OCH_3, 7.6.

Action of Iodine on the Bromohydrin.—A solution of 1 g. of the bromohydrin and 1 g. of iodine in 15 cc. of dry ether was left to itself for twelve hours, then washed with thiosulfate, dried and allowed to evaporate. It deposited 0.7 g. of a colorless solid which, after recrystallization from ether–petroleum ether, melted at 160°.

Anal. Calcd. for $C_{29}H_{22}OBrI$: C, 58.6; H, 3.7. Found: C, 58.7; H, 3.8.

Reaction with Phenylmagnesium Bromide, $(C_6H_5)_2CHCH(C_6H_5)C(C_6H_5){=}CHCOC_6H_5$.—An ethereal solution of 2 g. of the iodo compound was added to excess of phenylmagnesium bromide and the mixture was boiled for an hour, then decomposed in the usual manner. By distillation with steam, the product was separated into phenyl iodide—identified as the iodochloride—and a yellow solid which after crystallization from methyl alcohol melted at 133°.

Anal. Calcd. for $C_{35}H_{28}O$: C, 90.5; H, 6.1. Found: C, 90.0; H, 6.3.

Oxidation.—The yellow unsaturated ketone was oxidized in the usual manner with chromic acid in glacial acetic acid. The product α,β,β-triphenylpropiophenone was identified by comparison with a sample on hand.

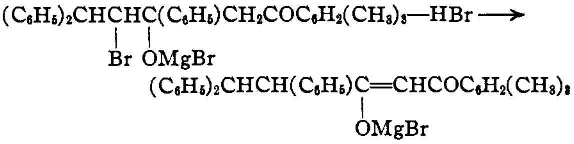
α-Bromo-β-hydroxy-β-phenyl-β-phenylethinyl Propiophenone, $C_6H_5C{\equiv}CC(C_6H_5)OHCHBrCOC_6H_5$.—A solution obtained by adding 25 g. of dibromo dibenzoyl methane gradually to 3 equivalents of phenylethinylmagnesium bromide was boiled for half an hour, then decomposed in the usual manner with iced acid. It deposited 5 g. of a solid melting at 159°. The mother liquors, on distillation with steam, left a residue from which another solid, melting at 120°, was obtained by treatment with ether and petroleum ether. The distillate contained phenylethinyl bromide which was identified by adding iodine and thus converting it into the di-iodide melting at 65°.

The two solid products proved to be two stereoisomeric carbinols, due to the two consecutive reactions which usually occur when the dibromo ketone reacts with excess of a Grignard reagent.[6]

Anal. Calcd. for $C_{28}H_{27}O_2Br$: C, 68.1; H, 4.2. Found: (159°) C, 68.1; H, 4.3; (120°) C, 68.2; H, 4.4.

II. Addition of the Magnesium Halide of Acetomesitylene

The reaction between bromo diphenyl propiophenone and the magnesium halide of acetomesitylene was not so easy to interpret because it cannot be confined to the first step. The primary product is a derivative of a bromohydrin but owing to the presence of a carbonyl group in an influential position both the magnesium compound and the bromohydrin have unusual properties. Thus in the presence of excess of reagent the magnesium compound is converted into a derivative of a β-diketone.



$$(C_6H_5)_2CH\underset{\textstyle Br}{\underset{|}{C}}H\underset{\textstyle OMgBr}{\underset{|}{C}}(C_6H_5)CH_2COC_6H_2(CH_3)_3 \text{—} HBr \longrightarrow (C_6H_5)_2CHCH(C_6H_5)\underset{\textstyle OMgBr}{\underset{|}{C}}{=}CHCOC_6H_2(CH_3)_3$$

The formation of this second magnesium compound involves a displacement of a phenyl group. The manner in which it is formed is not clear but it certainly is a secondary product which is due to the action of excess of reagent because it can be obtained equally well by heating the bromohydrin with excess of methylmagnesium iodide. It also is certainly formed directly from the magnesium derivative of the bromohydrin and not from an ethylene oxide because it cannot be obtained by heating the oxide with excess of reagent. The structure of the corresponding diketone is adequately established by the manner in which it is cleaved by bases.

$$\underset{\text{XII}}{(C_6H_5)_2CHCH(C_6H_5)COCH_2COC_6H_2(CH_3)_3} \longrightarrow (C_6H_5)_2CHCH(C_6H_5)COOH + CH_3COC_6H_2(CH_3)_3$$

The bromohydrin itself also has unusual properties. As it also is a β-hydroxy ketone it readily loses water in the presence of acids and therefore can be reduced with zinc and acetic acid to a saturated ketone which contains neither bromine nor hydroxyl.

$$\underset{\text{VII}}{(C_6H_5)_2CHCHBrC(OH)(C_6H_5)CH_2COC_6H_2(CH_3)_3} \longrightarrow \underset{\text{VIII}}{(C_6H_5)_2CHCH_2CH(C_6H_5)CH_2COC_6H_2(CH_3)_3}$$

In order to leave no doubt that all the steps leading to this reduction product are free from rearrangement, it was synthesized by two different methods. In the first method the chain was constructed by introducing the acetomesitylene residue into a ketone in which the three phenyl groups are properly disposed around the remainder of the chain. The result was a carbinol which lost water and formed an α,β-unsaturated ketone that was easily reduced. The reduction product was the saturated ketone VIII.

$$(C_6H_5)_2CHCH_2COC_6H_5 + CH_2{=}C(OMgX)C_6H_2(CH_3)_3 \longrightarrow \underset{\text{IX}}{(C_6H_5)_2CHCH_2C(OH)(C_6H_5)CH_2COC_6H_2(CH_3)_3} \longrightarrow \underset{\text{X}}{(C_6H_5)_2CHCH_2C(C_6H_5){=}CHCOC_6H_2(CH_3)_3} \longrightarrow \text{VIII}$$

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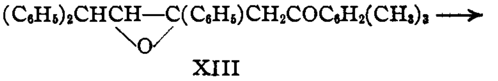
[6] Kohler, Richtmyer and Hester, THIS JOURNAL, 53, 205 (1931).

In the second method a diphenylvinyl group was introduced into benzoyl acetomesitylene which contains the rest of the chain. The resulting carbinol readily lost water, forming a butadiene derivative which on reduction likewise gave the unsaturated ketone VIII.

$$(C_6H_5)_2C{=}CHMgBr + C_6H_5COCH_2COC_6H_2(CH_3)_3$$
$$[(C_6H_5)_2C{=}CHC(OH)(C_6H_5)CH_2COC_6H_2(CH_3)_3] \longrightarrow$$
$$\underset{\text{XI}}{(C_6H_5)_2C{=}CHC(C_6H_5){=}CHCOC_6H_2(CH_3)_3} \longrightarrow \text{VIII}$$

The bromohydrin is sensitive to bases as well as acids. Weak bases convert it into the corresponding oxide, strong bases into a γ-diketone and a furan derivative. The γ-diketone is a normal rearrangement product of the ethylene oxide.



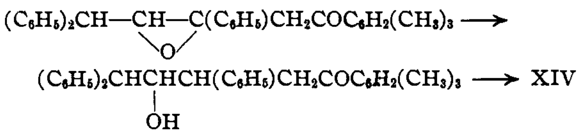
$$(C_6H_5)_2CH\underbrace{CH{-}C}_{O}(C_6H_5)CH_2COC_6H_2(CH_3)_3 \longrightarrow$$

XIII

$$(C_6H_5)_2CHCOCH(C_6H_5)CH_2COC_6H_2(CH_3)_3$$

XIV

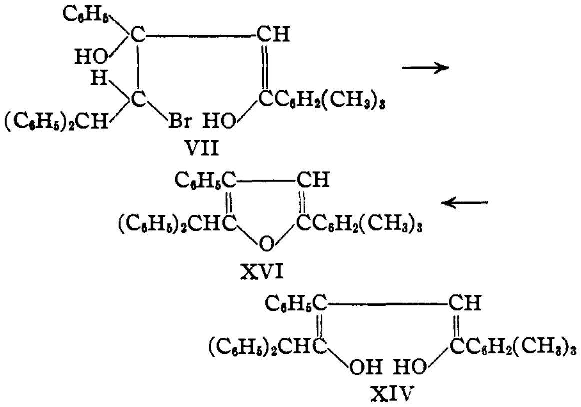
Its structure was established definitely by reducing the oxide catalytically and oxidizing the resulting hydroxy ketone—a series of reactions not subject to rearrangement.



$$(C_6H_5)_2CH{-}\underbrace{CH{-}C}_{O}(C_6H_5)CH_2COC_6H_2(CH_3)_3 \longrightarrow$$
$$(C_6H_5)_2CH\underset{\displaystyle OH}{\underset{|}{C}}HCH(C_6H_5)CH_2COC_6H_2(CH_3)_3 \longrightarrow \text{XIV}$$

XV

Acids convert the γ-diketone into the same furan derivative that is formed by the action of sodium alcoholate on the bromohydrin. As the diketone is insensitive to bases it is not an intermediate in the formation of the furan from the bromohydrin.



VII

XVI

XIV

Procedure.—In order to get satisfactory results it was necessary to prepare the magnesium halide derivative in such a manner that it remained in solution. Our procedure was as follows. A solution of ethylmagnesium bromide was prepared in the usual manner from 4.29 g. of magnesium. This solution was diluted with 500 cc. of dry benzene, then treated with a solution of 27 g. of acetomesitylene in an equal volume of benzene. The mixture was boiled for two hours, then cooled slowly (rapid cooling leads to deposition of the magnesium compound) to the ordinary temperature and used immediately.

To a solution prepared in this manner 30 g. of bromodiphenylpropiophenone was added in a single lot. The mixture was kept at 35° and stirred vigorously for about twelve minutes, then immediately poured into a saturated solution of ammonium chloride. The benzene layer and the ethereal solution which was obtained by extracting the aqueous layer were combined, dried and evaporated under diminished pressure. A solution of the residual oil in low boiling petroleum ether gradually deposited 28 g. of the bromohydrin. The mother liquor contained a mixture of bromohydrin and β-diketone that was difficult to separate.

The Bromohydrin VII.—At temperatures below 10° the bromohydrin crystallizes from ether–petroleum ether in rosettes of needles melting with decomposition at 137°, and at the ordinary temperature it crystallizes from the same solvents in cubes decomposing at 147°.

Anal. Calcd. for $C_{32}H_{31}O_2Br$: C, 72.8; H, 5.9. Found: C, 72.7; H, 6.0.

Reduction. The Bromine-Free Ketone VIII.—A solution of 1 g. of the bromohydrin in 25 cc. of glacial acetic acid was boiled with 3 g. of zinc dust for twelve hours. The ethereal solution of the reduction product which was obtained by the usual manipulations, on dilution with petroleum ether, deposited 0.6 g. of the bromine-free ketone. After recrystallization from ether–petroleum ether from which it separated in cubes, the ketone melted at 93°.

Anal. Calcd. for $C_{32}H_{32}O$: C, 88.9; H, 7.4. Found: C, 88.8; H, 7.4.

The Hydroxy Ketone IX.—As the hydroxy ketone does not crystallize readily when impure, it is best in this case to prepare and use the magnesium derivative of acetomesitylene in ether. An ethereal suspension of the magnesium derivative from 4.4 g. of acetomesitylene was boiled with 8 g. of diphenylpropiophenone for four hours, then chilled and stirred to complete the precipitation of the product. The resulting magnesium derivative was collected on a filter, thoroughly washed with ether and decomposed with ammonium chloride. It yielded 8.0 g. of the hydroxy ketone. The substance crystallizes from ether–petroleum ether in matted needles and it melts at 96°.

Anal. Calcd. for $C_{32}H_{32}O_2$: C, 85.8; H, 7.1. Found: C, 85.9; H, 7.2.

The Unsaturated Ketone X.—When a solution of the hydroxy ketone in glacial acetic acid was boiled for ten hours with excess of zinc dust, about half of it was reduced to the saturated ketone VIII while most of the remainder was left in the form of the intermediate unsaturated ketone X. The substance crystallized in yellow needles and melted at 120°.

Anal. Calcd. for $C_{32}H_{30}O$: C, 89.3; H, 7.0. Found: C, 89.0; H, 7.2.

The Butadiene Derivative XI.—The diphenylvinyl bromide needed for this experiment was made, not as heretofore from diphenylethylene, but directly from methyldiphenylcarbinol by treating it with bromine in glacial acetic acid. This method is much quicker and gives a better over-all yield as well as a purer product. The procedure was as follows. A solution of 80 g. of the carbinol and 3 g. of bromine in 400 cc. of glacial acetic acid was warmed slightly until the bromine disappeared. The remainder of the bromine—67 g.—was then added drop by drop. The resulting solution was distilled until the evolution of hydrogen bromide ceased, about 100 cc. of distillate being collected. The residue was diluted with water until further dilution no longer increased the quantity of oil. The oily layer was dissolved in ether, the ethereal solution freed from acetic acid, dried, diluted with petroleum ether and chilled. It deposited 80 g. of solid bromide which after recrystallization from ether–petroleum ether melted at 48°.

To a solution of diphenylvinylmagnesium bromide, prepared from 2.75 g. of magnesium and 39 g. of the halide, was added 10 g. of benzoylacetomesitylene. The resulting solution was boiled for five hours, then treated with iced acid in the usual manner. The result was an oil which could not be induced to crystallize. It was freed from impurities by heating it at 130° in a high vacuum, then rubbed with methyl alcohol until it solidified. The solid crystallized from methyl alcohol in bright yellow prisms melting at 102°. The yield was 14.5 g.

Anal. Calcd. for $C_{32}H_{28}O$: C, 89.7; H, 6.5. Found: C, 89.6; H, 6.7.

Reduction.—A solution of 1 g. of the buadtiene derivative in 15 cc. of glacial acetic acid was boiled with 3 g. of zinc powder until the yellow color had disappeared completely—about eight hours. The product was the saturated ketone VIII.

The β-Diketone XII.—The diketone is formed whenever the bromohydrin is heated with any Grignard reagent but it is most easily obtained by carrying out the reaction between bromodiphenylpropiophenone and the magnesium derivative of acetomesitylene at a sufficiently high temperature. Thus 10 g. of the bromo compound was added in the usual manner to a solution of excess of the magnesium compound in ether–benzene, the solution was distilled until the boiling point reached 78°, then boiled for two hours, cooled and poured into iced acid. The result was 10.6 g. of the diketone.

Anal. Calcd. for $C_{32}H_{30}O_2$: C, 86.0; H, 6.7. Found: C, 85.9; H, 6.8.

The diketone crystallizes from ethyl alcohol in prisms which melt at 180–181°. It develops a red color with ferric chloride, forms a copper derivative when shaken with aqueous copper acetate and liberates one mole of gas from methylmagnesium iodide. Like most other β-diketones it is easily brominated, forming both mono- and dibromo derivatives. The monobromo derivative—$(C_6H_5)_2CH$-$CH(C_6H_5)COCHBrCOC_6H_2(CH_3)_3$—crystallizes in prisms and melts at 171°.

Anal. Calcd. for $C_{32}H_{29}O_2Br$: C, 73.1; H, 5.5. Found: C, 73.0; H, 5.5.

The dibromo derivative—$(C_6H_5)_2CHCH(C_6H_5)COCBr_2$-$COC_6H_2(CH_3)_3$—crystallizes in cubes and melts at 121°.

Anal. Calcd. for $C_{32}H_{28}O_2Br_2$: C, 6.35; H, 4.6. Found: C, 63.5; H, 4.8.

Cleavage.—A suspension of 1 g. of the diketone in 20 cc. of 40% methyl alcoholic potassium hydroxide was heated for six hours at 150–160° in a sealed tube. The mixture was diluted with water and extracted with ether. From the aqueous layer acids precipitated an acid which melted at 219–220° and which was identified as α,β,β-triphenylpropionic acid by comparison with a sample on hand.

The Ethylene Oxide XIII.—The bromohydrin loses hydrogen bromide with the utmost ease. Thus when a solution of 1 g. of the oxide and 2 g. of potassium carbonate in 35 cc. of aqueous methyl alcohol was heated to the boiling point the bromohydrin disappeared within four minutes. The product crystallized from ether–petroleum ether in matted needles and it melted at 151°. The yield was 0.65 g.

Anal. Calcd. for $C_{32}H_{30}O_2$: C, 86.0; H, 6.7. Found: C, 85.9; H, 6.8.

Rearrangement to the γ-Diketone XIV.—The oxide is rearranged by bases and acids. Thus when a solution of 1 g. of the oxide in 25 cc. of a 2% solution of sodium methylate in methyl alcohol was boiled for six hours and then allowed to cool it deposited 0.95 g. of the diketone. And when a solution of 0.5 g. of the oxide in 25 cc. of methyl alcohol containing 1% of hydrogen chloride was boiled for one and one-half hours, it yielded 0.38 g. of the same substance. The diketone was purified by recrystallization from a mixture of acetone and methyl alcohol from which it separated in small plates melting at 125°.

Anal. Calcd. for $C_{32}H_{30}O_2$: C, 86.0; H, 6.7; mol. wt., 446. Found: C, 85.9; H, 6.8; mol. wt., 425.

Reduction of the Oxide to the Hydroxy Ketone XV.—A solution of 8 g. of the oxide in ethyl acetate was shaken with hydrogen in the presence of 0.1 g. of Adams catalyst. Reduction was slow, requiring eight hours for completion, but the alcohol was obtained in the calculated quantity. It crystallized from ethyl acetate and petroleum ether in cubes and melted at 126°.

Anal. Calcd. for $C_{32}H_{32}O_2$: C, 85.6; H, 7.1. Found: C, 85.6; H, 7.1.

Oxidation of the Hydroxy Ketone to the Diketone.—The hydroxy ketone was oxidized in acetic acid with the calculated quantity of chromic acid at the temperature of a steam-bath. The product was the γ-diketone and the yield was 0.4 g. from 0.5 g. of the hydroxy ketone.

The Furan Derivative XVI.—A suspension of 5 g. of the γ-diketone in 20 cc. of glacial acetic acid containing 3 g. of hydrogen bromide was left to itself until all of the diketone had dissolved. The deep red solution was then gradually diluted with water. It deposited a colorless solid which crystallized from acetone–methyl alcohol in transparent cubes melting at 128°. The yield was 90%. The same substance was obtained along with the diketone when the bromohydrin was treated with one equivalent of sodium methylate.

Anal. Calcd. for $C_{32}H_{28}O$: C, 89.7; H, 6.5. Found: C, 89.7; H, 6.7.

Addition to Bromoacetophenone, $CH_2BrC(OH)(C_6H_5)$ $CH_2COC_6H_2(CH_3)_3$ and $C_6H_5CH_2COCH_2COC_6H_2(CH_3)_3$.—The magnesium halide of acetomesitylene reacts with bromoacetophenone in precisely the same manner as with bromodiphenyl propiophenone. At the boiling point of ether the result is a mixture of the bromohydrin and the β-diketone and at 78° the only product is the β-diketone. The bromohydrin crystallizes from ether in leaflets melting with slight decomposition at 115°.

Anal. Calcd. for $C_{19}H_{21}O_2Br$: C, 63.2; H, 5.8. Found: C, 63.2; H, 6.0.

The diketone was purified by distillation. It was a pale yellow liquid which boiled at 161–164° under a pressure of about 10^{-4} mm. It gave a deep red color reaction with ferric chloride and formed a monoxime.

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.4; H, 7.2. Found: C, 81.0; H, 7.3.

The Monoxime $C_6H_5CH_2C({=}NOH)CH_2COC_6H_2(CH_3)_3$.—The oxime crystallized from methyl alcohol in fine matted needles melting at 140°.

Anal. Calcd. for $C_{19}H_{24}O_2N$: C, 77.2; H, 7.12. Found: C, 76.9; H, 6.8.

Addition to α-Bromo β-Phenyl Benzalacetophenone, $(C_6H_5)_2C{=}CBrC(OH)(C_6H_5)CH_2COC_6H_2(CH_3)_3$. — The bromohydrin, formed and isolated in the usual manner, crystallized from ether–petroleum ether in cubes and melted at 133°.

Anal. Calcd. for $C_{32}H_{29}O_2Br$: C, 73.1; H, 5.5. Found: C, 73.1; H, 5.8.

The Magnesium Derivative of β-Phenyl Benzalacetophenone, $(C_6H_5)_2C{=}C(COC_6H_5)_2$.—The only reaction between α-bromo-β-phenylbenzalacetophenone and methylmagnesium iodide or phenylmagnesium bromide is metathesis. The resulting yellow magnesium compound has not as yet been studied adequately; it reacts with benzoyl chloride to form unsymmetrical diphenyl dibenzoyl ethylene which crystallizes from methyl alcohol in small yellow needles and melts at 152°.

Anal. Calcd. for $C_{28}H_{20}O_2$: C, 86.5; H, 5.2. Found: C, 86.4; H, 5.3.

In proof of its structure the unsaturated diketone was reduced to the corresponding saturated diketone and the saturated compound was identified by comparison with a sample on hand.

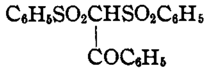
III. Experiments with Diphenylsulfonyl Methane

Diphenylsulfonyl methane can be prepared in excellent yields by the method devised by Fromm,[7] namely, by the oxidation of the corresponding disulfide. By employing as oxidizer hydrogen peroxide instead of the permanganate used by Fromm or the chromic acid used by Shriner, Struck and Jorison[8] it is easy to raise the yield from 18 to nearly 90%.

In confirmation of Fromm's conclusions we found it impossible to brominate the disulfone in pure chloroform or carbon tetrachloride. It is, however, easily brominated in polar solvents like alcohols or acetic acid, or even in water, in which it is but very sparingly soluble. When it is brominated at the ordinary temperature in these solvents or in alkaline solution the product is always the dibromo derivative, regardless of the quantity of bromine employed or the order in which the reactants are brought together. It is, nevertheless, easy to secure the monobromo derivative by boiling alcoholic solutions of equimolar quantities of the disulfone and its dibromo derivative.

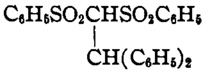
$$\underset{\text{XVII}}{C_6H_5SO_2CH_2SO_2C_6H_5} + \underset{\text{XVIII}}{C_6H_5SO_2CBr_2SO_2C_6H_5} \longrightarrow \underset{\text{XIX}}{2C_6H_5SO_2CHBrSO_2C_6H_5}$$

These bromo disulfones give metathetical products with all organic magnesium derivatives. With one equivalent of reagent the dibromo sulfone forms a magnesium derivative of the monobromo compound and with two equivalents the product is a crystalline di-magnesium of the sulfone. Attempts to replace the two magnesium halide groups with two benzoyl groups were not successful, only one of them being replaceable. And only one also could be replaced with a diphenylmethyl group.



$$C_6H_5SO_2\underset{\displaystyle COC_6H_5}{\underset{|}{C}}HSO_2C_6H_5$$

XX



$$C_6H_5SO_2\underset{\displaystyle CH(C_6H_5)_2}{\underset{|}{C}}HSO_2C_6H_5$$

XXI

Preparation.—To a cold solution of 5 g. of methylene phenyl sulfide in 75 cc. of acetic acid and 20 cc. of acetic anhydride was added 12.3 g. of 30% hydrogen peroxide. The solution was kept at 10° for two hours and then at the ordinary temperature for twenty-four. On dilution with water it deposited a crystalline precipitate of the disulfone which after recrystallization melted at 119–120°. The yield was 5.6 g. or 88%.

The Dibromo Derivative XVIII.—A solution of 16 g. of the disulfone in 200 cc. of 5% sodium hydroxide was added slowly to a solution of 20 g. of bromine in 250 cc. of an 8% solution of sodium hydroxide. The mixture deposited 22.2 g. of the dibromo derivative. The compound crystallized from alcohol in large needles melting at 158°.

Anal. Calcd. for $C_{13}H_{10}S_2O_4Br_2$: C, 34.4; H, 2.2. Found: C, 34.5; H, 2.3.

The Monobromo Derivative XIX.—A solution of 0.65 g. of the disulfone and 1 g. of its dibromo derivative in 50 cc. of methyl alcohol was boiled for two hours, then diluted with water and extracted with ether. The monobromo derivative was extracted from the ethereal solution with 2% potassium hydroxide and precipitated by acidifying the alkaline solution. It crystallized from ether–benzene in leaflets melting at 120°—yield 1.4 g.

Anal. Calcd. for $C_{13}H_{11}S_2O_4Br$: C, 41.6; H, 2.9. Found: C, 41.6; H, 3.2.

The Dimagnesium Bromide Derivative of the Disulfone. In order to establish the character of the crystalline mag-

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(7) Fromm, *Ann.*, **253**, 161 (1889).

(8) Shriner, Struck and Jorison, THIS JOURNAL, **52**, 2060 (1930).

nesium derivative which is formed whenever the dibromo derivative reacts with organic magnesium compounds, several samples obtained with ethylmagnesium bromide were analyzed. As the substance could not be recrystallized its composition was found to be somewhat variable but the results show that it is a dimagnesium bromide derivative.

Anal. Calcd. for $C_{13}H_{10}S_2O_4Br_2Mg_2$: C, 31.0; H, 2.0; S, 12.7; Br, 31.8; Mg, 9.7. Found: C, 31.1; H, 2.3; S, 12.7; Br, 29.0; Mg, 9.5.

The Mono Benzoyl Derivative XX.—A suspension of the dimagnesium derivative which had been obtained in the usual manner in ether–benzene was treated with benzoyl chloride; the mixture was boiled for four hours, during which time it had turned into an orange-brown powder. The usual manipulations resulted in the isolation of a compound which crystallized from acetone–alcohol in colorless cubes melting at 180°.

Anal. Calcd. for $C_{20}H_{16}S_2O_5$: C, 60.0; H, 4.0. Found: C, 59.9; H, 4.2.

The benzoyl derivative does not give a ferric chloride reaction but is soluble in dilute aqueous alkalies and can be recovered from the alkaline solution by acidification.

The Diphenylmethyl Derivative XXI.—When diphenylmethyl bromide was substituted for benzoyl chloride in the preceding experiment the product was a compound which crystallized from acetone–alcohol in small needles melting at 193°.

Anal. Calcd. for $C_{28}H_{22}S_2O_4$: C, 67.5; H, 4.8. Found: C, 67.3; H, 5.0.

Summary

Reactions between organic magnesium compounds and α-halo ketones may result in enolization, metathesis, addition, or elimination of halogen hydride. This communication contains a number of examples which supply a basis for predicting which of these possible reactions is most likely to occur in a given case.

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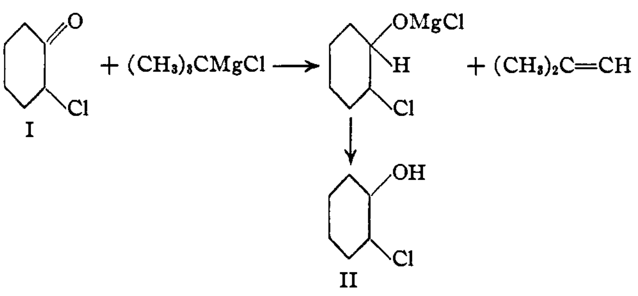
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA AND FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

Cis- and *Trans-*Chlorohydrins of Cyclohexene[1]

BY PAUL D. BARTLETT

It has been observed in two cases[2] that cyclic α-chloro ketones react with the Grignard reagent to give chlorohydrins (designated as "B-isomers") which do not form epoxy compounds, and which on strong alkaline treatment give instead ketones. It is well known that the reaction of secondary and tertiary Grignard reagents upon highly branched ketones[3] and even upon cyclohexanone[4] is primarily one of reduction rather than of addition. If this reduction, applied to 2-chlorocyclohexanone (I), occurs in the same stereochemical sense as the addition of methylmagnesium bromide, then it should yield the hitherto unknown "B"-isomer of 2-chlorocyclohexanol (II). The "A"-isomer of this compound is well known.[5]

Reductions of 2-chlorocyclohexanone were carried out with the cyclohexyl, isopropyl, and tertiary butyl Grignard reagents, with yields of 27, 64 and 72%, respectively, of crude reduction product. Fractionation of this product yielded an oil of b. p. (26 mm.) 93–94°, closely resembling the A isomer.



Refluxed with aqueous sodium hydroxide it gave cyclohexanone, together with a smaller amount of cyclohexene oxide. Since neither the A-isomer, nor cyclohexene oxide itself, is capable of giving cyclohexanone under these conditions, there was evidently a new chlorohydrin present.

The rate of reaction of this product with sodium hydroxide in 50% alcohol was measured at 25° by acid titration. The results, plotted in Fig. 1, show that 27% of the chlorohydrin reacts rapidly, the remainder slowly, with alkali. The fast-reacting fraction has the same rate of reaction with alkali as was determined separately for

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[1] Presented in part before the Organic Division at the Cleveland meeting of the American Chemical Society, September 12, 1934.

[2] Bartlett and Rosenwald, THIS JOURNAL, **56**, 1990 (1934); Bartlett and White, *ibid.*, **56**, 2785 (1934).

[3] Conant and Blatt, *ibid.*, **51**, 1229 (1929).

[4] Kohler and Thompson, *ibid.*, **55**, 3822 (1933).

[5] "Organic Syntheses," Coll. Vol. 1, John Wiley and Sons, 1932, p. 151.