The Reaction between Lactones and Grignard Reagents. I. Diphenyl-1,8-naphthalide

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A possible structure for a compound obtained in the course of another investigation was that of 1-isobutyryl-8-(α-hydroxybenzhydryl)-naphthalene or its ring tautomer, the hemiketal II. The synthesis of this compound by the reaction between isopropylmagnesium bromide and diphenyl-1,8-naphthalide (I) was carried out and certain of its properties, as well as some aspects of the reaction of the lactone (I) with Grignard reagents, have proved interesting enough to cause us to extend the study.

It has already been shown by Wittig, Leo and Wiemer[1] that diphenyl-1,8-naphthalide (I) reacts with phenylmagnesium bromide to yield only the monoaddition product VI, none of the expected 1,8-bis-(α-hydroxy-benzhydryl)-naphthalene being formed. Alkylmagnesium halides have now been found to react in an analogous manner, the Grignard reagents from isopropyl, ethyl, n-butyl and s-butyl bromides yielding compounds which, on the basis of their composition and properties, have been formulated as the hemiketals II, III, IV and V. No other compounds were isolated from the reactions in which these hemiketals were formed; indeed, unchanged diphenylnaphthalide was recovered in every case even though the Grignard reagent was used in excess.
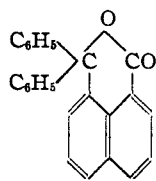
I
III, R = C₂H₅
IV, R = n-C₄H₉
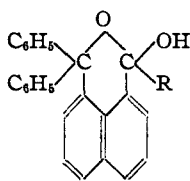
II, R = i-C₃H₇
V, R = s-C₄H₉
VI, R = C₆H₅

Since the reaction of a lactone with a Grignard reagent to yield a glycol necessarily involves a ring opening at some stage in the process, the failure of the lactone I to react further than the monoaddition stage undoubtedly depends upon the great stability of the *peri*-ring. The favorable spatial relationships existing in the case of the *peri*-ring of I, coupled with the influence of the

disubstituted carbon atom[2] combine to produce this stability, further evidence of which is found in the lack of ketonic character of the compounds II–VI toward ketone reagents and in the extreme stability of the lactone I toward alkali, treatment with boiling 20% alcoholic potassium hydroxide being insufficient to open the ring. In view of these facts it also follows that the reaction of one mole of a Grignard reagent with the lactone involves addition to the carbonyl group and not a cleavage of the bond between the carbonyl carbon atom and the ring oxygen atom.
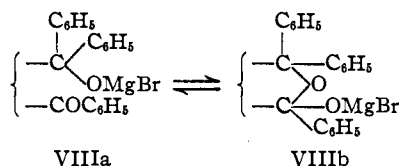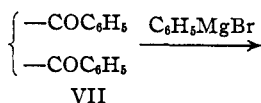
An alternative explanation for the non-reactivity of the compounds II–VI toward the further addition of Grignard reagents if it be considered that they may actually possess the structures of the 1-acyl-8-(α-hydroxybenzhydryl)-naphthalenes might be that the α-hydroxybenzhydryl group *peri* to the carbonyl group in these structures offers hindrance to the addition of the reagent. In this connection another reaction described by Wittig[1] and one described by Tschitschibabin[3] are of interest. Wittig found that 1,8-dibenzoyl-naphthalene reacts with phenyllithium to yield the hemiketal VI and not the glycol which might be expected. Tschitschibabin showed that the reaction between 2,2'-dibenzoylbiphenyl and phenylmagnesium bromide also stops after one mole of reagent has added, the product being a similarly constituted hemiketal. While the possibility of steric hindrance might be adequate to explain the first of these two observations, it cannot be applied to the latter case since in this case it would be possible for the groups to rotate sufficiently to remove the possibility of such hindrance. The reason for the reaction of 1,8-dibenzoylnaphthalene and of 2,2'-dibenzoylbiphenyl with no more than one mole of phenyllithium or Grignard reagent, respectively, is probably due to the formation, in the course of the reaction, of an intermediate whose stability in a

(1) Wittig, Leo and Wiemer, *Ber.*, **64**, 2405 (1931).

(2) (a) Fuson in Gilman's "Organic Chemistry," John Wiley, New York, N. Y., 1938, p. 16; (b) Hjelt, *Ber.*, **24**, 1237 (1891); (c) Tasman, *Rec. trav. chim.*, **46**, 653 (1927); numerous papers by Ingold, Thorpe, *et al.*, for example, *J. Chem. Soc.*, **119**, 305 (1921); **121**, 1430, 1765 (1922); **123**, 113, 327, 1683 (1923).

(3) Tschitschibabin and Ssergejeff, *Ber.*, **59**, 654 (1926).

cyclic form is such as to cause the reaction to stop at that point:

$$\begin{cases} -COC_6H_5 \\ -COC_6H_5 \end{cases} \xrightarrow{C_6H_5MgBr}$$

VII

$$\begin{cases} -C\overset{C_6H_5}{\underset{OMgBr}{\diagdown}}C_6H_5 \\ -COC_6H_5 \end{cases} \rightleftharpoons \begin{cases} -C\overset{C_6H_5}{\underset{O}{\diagup}}C_6H_5 \\ -C\overset{OMgBr}{\underset{C_6H_5}{\diagdown}} \end{cases}$$

VIIIa   VIIIb

In the more general case of a lactone which reacts with a Grignard reagent to yield a glycol it must be assumed that the product of the first step of the reaction, the lactol derivative corresponding to VIIIb, must, in view of the evidence adduced above, react in the form VIIIa: that is, except when considerations of ring stability enter in, the forms VIIIa and VIIIb must be freely interconvertible.[4]

The hemiketals II, III, IV, and V undergo an unusual decomposition when heated, regenerating diphenylnaphthalide (I) and liberating what has been proved in one case to be the saturated hydrocarbon corresponding to the alkyl group and in another case what appears to be the corresponding olefin and hydrogen. The hemiketals II and V, containing *secondary* alkyl groups, decompose in this manner at their melting points, while III and IV, the *primary* alkyl derivatives, melt without decomposition but decompose at slightly higher temperatures or at comparable temperatures but lower pressures. Attempts were made to prepare the benzyl and 3-pentyl derivatives corresponding to II–V but the products could not be crystallized. The oils obtained, however, decomposed when heated to temperatures in the range of the melting points of II–V with the evolution of gas and the formation of diphenylnaphthalide. In contrast to the relatively smooth decomposition of the alkyl derivatives, the phenyl derivative (VI) decomposed only on heating to relatively high temperatures to yield indefinite tarry products.
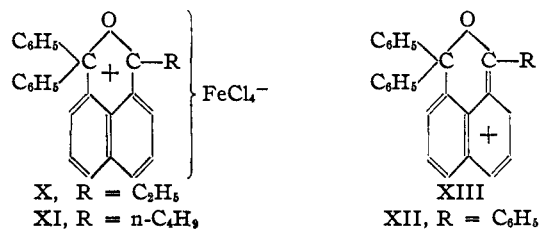
These observations suggest that the decomposition of hemiketals of the type IX is rather general according to the equation

(4) Evidence that this is so has been obtained in other studies now in progress in this Laboratory and will be presented in a future communication.

IX
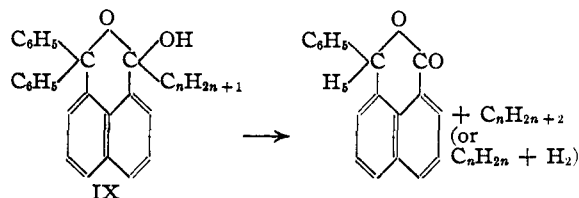
where R = alkyl, the ease of the decomposition increasing in the order R = primary < R = secondary. No closely analogous reaction has been described and it is felt that the present evidence is not sufficient to form a foundation for a general mechanism for the reaction. A pyrolytic disproportionation of certain tertiary alcohols studied by Ramart–Lucas[5] and by Grignard[6] bears a certain resemblance to this decomposition. These workers found that many tertiary alcohols decompose at elevated temperatures to form ketones and hydrocarbons by simple disproportionation; for example, Ramart–Lucas found

$$(C_2H_5)_3C-C\overset{C_6H_5}{\underset{C_6H_5}{\diagdown}}OH \xrightarrow{\Delta} (C_2H_5)_3CH + (C_6H_5)_2CO$$
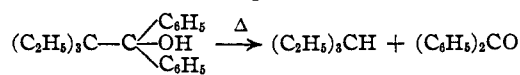
Certain other properties and reactions of the compounds II–V are of interest since they serve to indicate that the structures assigned to these substances are correct. They all give yellow colors in concentrated sulfuric acid, an indication that they do not possess the alternative hydroxyketone structures since the colors produced in sulfuric acid by triaryl carbinols are deeper (red to blue) than the yellows given by these compounds. They show no ketone reactions. The ethyl (III) and *n*-butyl (IV) derivatives yield deeply colored solutions when they are treated with hydrogen chloride in acetic acid solution. The addition of ferric chloride to the resulting solutions causes the formation of crystalline ferrichlorides (X and XI). The phenyl derivative also forms a ferrichloride (XII). The salts X and XI are deeply colored compounds, an indication that they possess structures in which resonance forms, probably such as XIII, are involved.


X, R = C₂H₅
XI, R = n-C₄H₉

XII, R = C₆H₅
XIII

(5) Ramart–Lucas, Ann. chim., [8], 30, 349 (1913).

(6) Grignard, et al., Compt. rend., 176, 1860 (1923); 182, 299 (1926); Ann. chim., [10], 2, 298 (1924).

The isopropyl (II) and s-butyl (V) derivatives, on the other hand, show very little color change (at most to yellow) when their solutions in acetic acid are treated with hydrogen chloride, and no ferrichlorides are formed. It is possible that dehydration to the alkylidene-peri-naphthopyrans occurs, but these compounds could not be isolated from these reactions.

Treatment of the ethyl derivative (III) with boiling acetic anhydride (containing a little sodium acetate) led to the formation of the dehydration product XIV. Similar treatment of the isopropyl derivative (II) led in one case to the corresponding derivative (XV) but this result was difficult to reproduce since decomposition into diphenylnaphthalide (I) also tended to occur at the boiling point of acetic anhydride and under milder conditions the reaction either did not proceed to completion or took both possible courses with the result that difficultly resolvable mixtures were usually obtained.
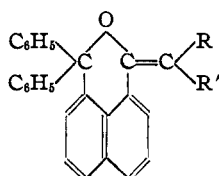
XIV, R = CH₃, R' = H
XV, R = R' = CH₃

Experimental

Diphenyl-1,8-naphthalide (I).—Treatment of 1,8-naphthalic anhydride with phenyllithium as described by Wittig yielded diphenyl-1,8-naphthalide, m. p. 202°. The compound gives a crimson color in concentrated sulfuric acid. A sample refluxed overnight in 20% alcoholic potassium hydroxide solution was precipitated unchanged upon dilution with water.

Hemiketals of 1-Acyl-(8-α-hydroxybenzhydryl)-naphthalenes (II-VI) (II); R = i-C₃H₇.—To a solution of 10.0 g. of diphenylnaphthalide (I) in 100 ml. of dry benzene was added a solution of twice the calculated amount of isopropylmagnesium bromide in ether. After six hours the light orange solution was decomposed with ice and ammonium chloride solution and the solvents removed with steam. The residue was taken up in isopropyl ether and the (insoluble) unreacted diphenylnaphthalide removed by filtration. The filtrate was evaporated and the residue recrystallized from alcohol. It formed short, colorless needles, m. p. 176° (dec.).

Anal. Calcd. for C₂₇H₂₄O₂: C, 85.23; H, 6.36. Found: C, 85.07; H, 6.54.

The compound gives a yellow color in concentrated sulfuric acid. When dry hydrogen chloride was passed into a solution of the compound in glacial acetic acid plus a little acetyl chloride some yellow color was produced and the addition of ferric chloride yielded no precipitate.

The compound decomposed upon melting leaving a residue which was found to be diphenylnaphthalide (m. p., mixed m. p.).

(III), R = C₂H₅.—The reaction between diphenylnaphthalide and ethylmagnesium bromide was carried out as in the preparation of compound II. The hemiketal (III) formed colorless prisms from alcohol, m. p. 142–143°.

Anal. Calcd. for C₂₆H₂₂O₂: C, 85.25; H, 6.01. Found: C, 85.28; H, 6.09.

The compound gave a yellow color with concentrated sulfuric acid. When a sample of the compound was heated at 100° under reduced pressure (25 mm.) the colorless crystals changed to a tan resin which upon treatment with warm isopropyl ether left undissolved diphenylnaphthalide; from the ether solution was recovered unchanged III. Heating of III at 200° at atmospheric pressure also caused the decomposition into diphenylnaphthalide but with the formation of tarry by-products.

(IV), R = n-C₄H₉.—The preparation of IV from diphenylnaphthalide and n-butylmagnesium bromide was carried out as described for II and III. Recrystallized from acetic acid the compound formed large, granular crystals, m. p. 114–115°.

Anal. Calcd. for C₂₈H₂₆O₂: C, 85.25; H, 6.64. Found: C, 85.35; H, 6.61.

The color in concentrated sulfuric acid was yellow. The behavior of the compound on heating was essentially like that described for the ethyl derivative (III), diphenylnaphthalide being formed.

(V), R = s-C₄H₉.—Diphenylnaphthalide was treated with excess s-butylmagnesium bromide as described for the other compounds of the series. The product was separated from unreacted diphenylnaphthalide by treating the crude mixture with isopropyl ether and the compound (V) isolated from the ether solution. Recrystallized from ethanol it formed small white crystals, m. p. 135–136° (dec.).

Anal. Calcd. for C₂₈H₂₆O₂: C, 85.25; H, 6.64. Found: C, 85.19; H, 6.75.

The color in concentrated sulfuric acid was yellow. The residue left after a sample of the compound was melted proved to be diphenylnaphthalide. A quantitative decomposition gave an 83% yield of diphenylnaphthalide. The s-butyl derivative, like the isopropyl and unlike the ethyl and n-butyl derivatives (see below) gave no appreciable color when treated with hydrogen chloride in acetic acid solution and yielded no iron salt when ferric chloride was added to this reaction mixture.

(VI), R = C₆H₅.—The phenyl derivative (VI) was prepared by the method of Wittig[1] for comparison with the alkyl derivatives. It crystallized from benzene with one molecule of solvent, m. p. ca. 115° (dec.). A sample was heated to constant weight.

Anal. Calcd. for C₃₀H₂₂O₂·C₆H₆: C₆H₆, 15.85. Found: C₆H₆, 15.35.

Recrystallized from ligroin (b. p. 90–110°) it melted at 200–201° (Wittig gives 202°).

After heating VI at a variety of temperatures, only intractable tars were formed or unchanged material was recovered.

Ferrichlorides (X, XI, XII) (X), R = C₂H₅.—Dry hydrogen chloride was passed into a solution of 0.5 g. of the

hemiketal III in a mixture of 10 ml. of glacial acetic acid and 1.5 ml. of acetyl chloride. The solution became dark red in color. Seven-tenths of a gram of ferric chloride was added. On cooling olive-green crystals separated. After washing with acetic acid and drying in air the ferrichloride melted at 150–153° (dec.).

Anal. Calcd. for $C_{28}H_{21}OFeCl_4$: C, 57.04; H, 3.84; Fe, 10.24. Found: C, 57.15; H, 2.86; Fe, 10.46.

(**XI**), R = $n\text{-}C_4H_9$.—Prepared as described above for the ethyl derivative, this compound formed red-orange crystals, m. p. 134–135° (dec.).

Anal. Calcd. for $C_{28}H_{25}OFeCl_4$: Fe, 9.70. Found: Fe, 9.73.

(**XII**), R = C_6H_5.—Wittig prepared the chloride of the hemiketal VI, but it was found that the ferrichloride was more stable and more easily prepared. It was formed when ferric chloride was added to a solution of the phenyl derivative VI in acetic acid saturated with hydrogen chloride. It formed bright carmine crystals, m. p. 148–150°.

Anal. Calcd. for $C_{30}H_{21}OFeCl_4$: Fe, 9.37. Found: Fe, 9.72.

1,1 - Diphenyl - 3 - ethylidene - *peri* - naphthopyran (XIV).—A solution of 50 mg. of the hemiketal III and a few mg. of anhydrous sodium acetate in 1 ml. of acetic anhydride was refluxed for five minutes. On cooling the product separated as iridescent needles, m. p. 134°.

Anal. Calcd. for $C_{26}H_{20}O$: C, 89.60; H, 5.74. Found: C, 88.97; H, 5.67.

1,1 - Diphenyl - 3 - isopropylidene - *peri* - naphthopyran (XV).—Treatment of the hemiketal II as described for the preparation of compound XIV yielded the dehydration product, m. p. 190–194°.

Anal. Calcd. for $C_{27}H_{22}O$: C, 89.45; H, 6.13. Found: C, 89.15; H, 5.96.

The compound gave a yellow color in concentrated sulfuric acid.

Decomposition of the Hemiketal (II, R = $i\text{-}C_3H_7$).—A sample of the hemiketal II weighing 52.7 mg. was heated to its melting point and reheated repeatedly, until constant weight was reached. The loss in weight amounted to 5.1 mg. From these data the fragment lost has a molecular weight of 36; propane requires 44.

The evolved gas showed no unsaturation toward bromine in chloroform. When the tube in which a sample of the hemiketal had been decomposed was shaken with a little dry benzene, no cloudiness was observed showing that no water had been formed in the decomposition.

A sample of the evolved gas was collected by sweeping it into a Dumas azotometer in a stream of carbon dioxide and then transferring it to a sample tube over mercury. The gas was analyzed by microcombustion methods.[7] Two analyses gave ratios of water–carbon dioxide of 1.358 and 1.351. Propane requires 1.333.

Decomposition of the Hemiketal (III, R = C_2H_5).—A sample of the gas produced from the decomposition of the hemiketal III was collected as described above. The results of microanalyses showed 21% unsaturation, 27% hydrogen and, within experimental error, no saturated hydrocarbons. The remainder was air. Two microcombustions gave ratios of water–carbon dioxide of 1.42 and 1.60. An equimolar mixture of ethylene and hydrogen requires 1.50.[7]

Summary

1. Diphenyl-1,8-naphthalide reacts with Grignard reagents to yield compounds which are the result of the addition of only one mole of the reagent.

2. The significance of this type of reaction is discussed in relation to the question of the mode of reaction of lactones and Grignard reagents.

3. It has been shown that certain of the *peri*-naphthopyranols derived from the reaction of diphenyl-1,8-naphthalide with Grignard reagents decompose on heating at moderate temperatures to regenerate the lactone and to yield a hydrocarbon fragment corresponding to the Grignard reagent used.