[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

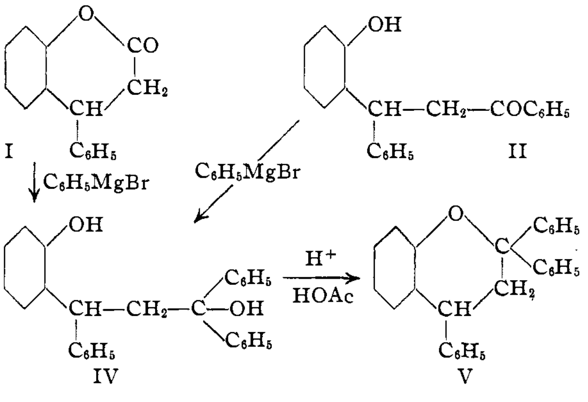
The Reaction of *o*-Hydroxybenzhydrylacetophenone and *o*-Hydroxybenzaldiacetophenone with Phenylmagnesium Bromide

BY T. A. GEISSMAN

The reactions of 4-phenyldihydrocoumarin (I) and ω-(*o*-hydroxybenzhydryl)-acetophenone (II) with phenylmagnesium bromide have been studied, originally in an attempt to correlate the results with the question of the mode of reaction of Grignard reagents with lactones of the dihydrocoumarin type.[1] The reaction between alkylmagnesium halides and a substance which may be either a chromanol or the corresponding hydroxyketone was first carried out by John and Schmeil.[1a] The choice of the hydroxyketone (II) used in the present study was based upon Löwenbein's[2] statement that the compound possesses neither phenolic nor ketonic properties and thus has the structure of the chromanol (III).

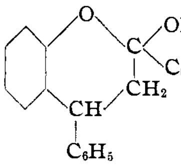
The present work has shown, however, that the properties of the compound are in agreement with its formulation as the hydroxyketone (II), a result which invalidated the original purpose of the study. The so-called chromanol is readily soluble in methanolic potassium hydroxide and forms a semicarbazone, thus showing both phenolic and ketonic characteristics.

The product of the reaction of both the dihydrocoumarin (I) and the hydroxyketone (II) was 1,1,3-triphenyl-3-(*o*-hydroxyphenyl)-propanol-1 (IV). The latter compound was readily dehydrated to 2,2,4-triphenylchromane (V).



The preparation in this way of the carbinol IV and chromane V constitutes, in the light of previous work[1] on the reaction between dihydrocoumarins and Grignard reagents, a proof of their structures. Consequently it became of interest to examine a report by Gomm and Hill[3] who claimed to have prepared these compounds by the reaction of phenylmagnesium bromide with *o*-hydroxybenzaldiacetophenone (VI). The products of this reaction have properties different from those of IV and V prepared as described above, and so the reaction of *o*-hydroxybenzaldiacetophenone with phenylmagnesium bromide has been reinvestigated in an attempt to elucidate the structures of the products obtained

When *o*-hydroxybenzaldiacetophenone is treated with phenylmagnesium bromide in boiling benzene and the reaction mixture decomposed with iced ammonium chloride, the product is an uncrystallizable oil, probably the glycol VII. This oil on treatment with a trace of sulfuric acid in acetic acid solution yields 2,2-diphenyl-4-benzhydrylidenemethylchromane (VIII). The structure of VIII was proved by its synthesis from methyl dihydrocoumarin-4-acetate (IX), the first product of the reaction between this ester and phenylmagnesium bromide being again an uncrystallizable oil, probably VII, which was converted smoothly to VIII by dehydration. Gomm and Hill obtained VIII (to which they assigned the structure of V) as the direct product of the reaction between VI and the Grignard reagent, a result which was undoubtedly due to the fact that they decomposed the reaction mixture with, and steam-distilled from, dilute acid dehydration of the glycol (VII) occurring during these operations.



III

When the reaction between *o*-hydroxybenzaldiacetophenone and phenylmagnesium bromide was carried out in cold ether solution the product was a crystalline compound to which has been assigned the structure (X) (it is this compound to which

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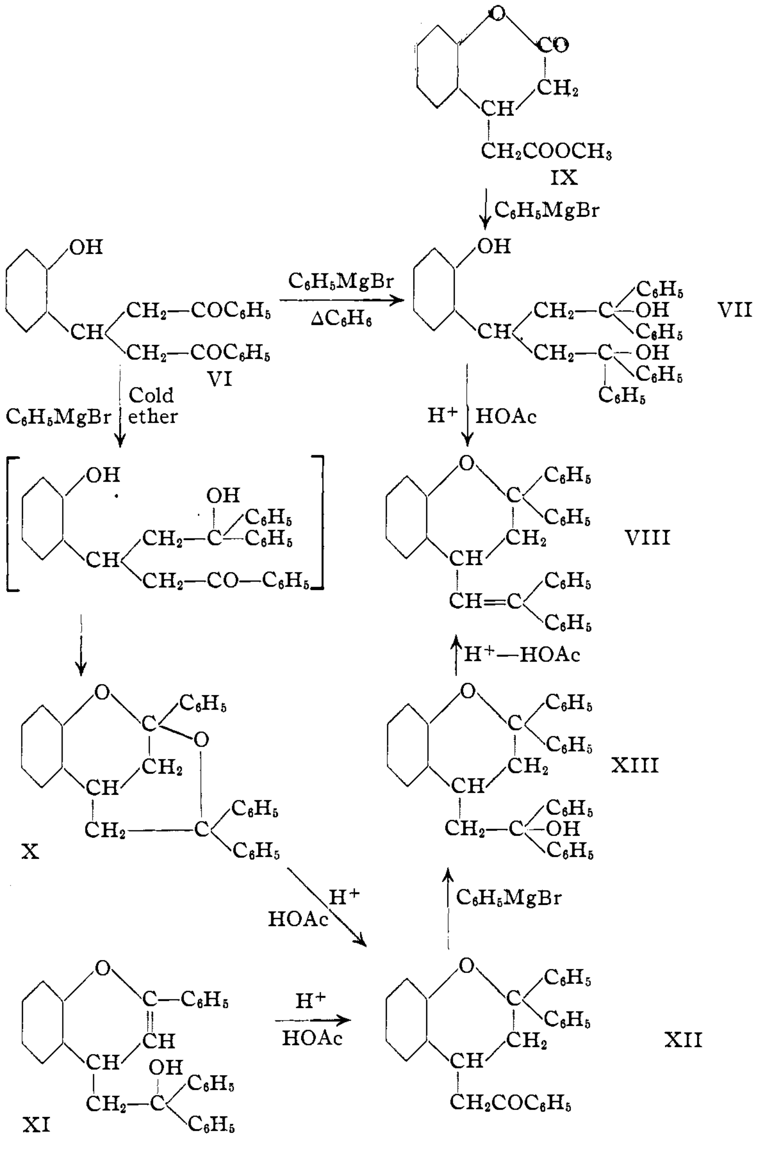
[1] (a) John and Schmeil, *Ber.*, **72**, 1653 (1939); (b) Smith, Ungnade and Prichard, *J. Org. Chem.*, **4**, 358 (1939); (c) Smith and Ruoff, THIS JOURNAL, **62**, 145 (1940).

[2] Löwenbein, *Ber.*, **57**, 1517 (1924).

[3] Gomm and Hill, *J. Chem. Soc.*, 1118 (1935).

Gomm and Hill assigned the structure of IV), on the basis of the following evidence. The compound does not react with carbonyl reagents in neutral or basic solution and is recovered unchanged after treatment with phenylmagnesium bromide in ether. It is isomeric with 1,1-diphenyl-2-(4-flavenyl)-ethanol-1 (XI), prepared by the addition of phenylmagnesium bromide to 4-phenacylflavene, and upon treatment with a trace of acid in acetic acid solution both X and XI are converted to the same (isomeric) compound (XII). Structures X and XI contain groupings which are known to be unstable in acid media, and it is probable that the course of the isomerization involves attack upon these centers leading by ring-opening and subsequent closure to XII, which contains a chromane ring system and would be stable under the conditions of the reaction. The structure of XII was established by the facts that it formed a 2,4-dinitrophenylhydrazone and upon treatment with phenylmagnesium bromide was converted into a crystalline carbinol (XIII). The carbinol XIII readily underwent dehydration to yield the chromane VIII, the structure of which has been proved by its preparation as described above. The dinitrophenylhydrazone of XII can be formed directly from X or XI by treatment of these compounds with 2,4-dinitrophenylhydrazine in boiling glacial acetic acid solution.



Tricyclic structures analogous to that proposed for X have been suggested for certain chromane derivatives by Boehme and Themlitz.[4] The reactions discussed above are shown on the accompanying chart. It is probable that compound X (as the tricyclic acetal) is not produced directly, since the product obtained after careful decomposition of the reaction mixture with iced ammonium chloride is an oil which crystallizes only slowly from such solvents as ligroin or alcohol, even when seeded with crystalline material, but which rapidly deposits the compound X from glacial acetic acid solution. The direct product of the reaction is thus probably a carbinol (shown in brackets) which under the mild dehydrating action of the acetic acid is cyclized to X.

The reaction of phenylmagnesium bromide with *o*-hydroxybenzaldiacetophenone is thus seen to involve the addition of either one or two moles of the reagent to the diketone, depending upon experimental conditions, and is not a cleavage reaction as reported by Gomm and Hill.

Experimental

ω-(*o*-Hydroxybenzhydryl)-acetophenone (II).—This was prepared from *o*-hydroxybenzalacetophenone and phenyl-

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[4] Boehme and Themlitz, *Arch. Pharm.*, **272**, 406 (1934).

magnesium bromide according to the directions of Löwenbein.[2] The material melted at 167–167.5° (reported, 166°). The pyrilium ferrichloride derived from it[2] melted at 167° (reported, 168°).

Semicarbazone of II.—A solution of 0.5 g. of semicarbazide hydrochloride and 1.5 g. of sodium acetate in a little water was added to a solution of 0.5 g. of the hydroxyketone (II) in 10 cc. of alcohol. The solution was heated to boiling and allowed to stand overnight. The following day water was added to cloudiness at the boiling point and the solution digested at this temperature for fifteen minutes. On cooling white prisms separated. Recrystallized from dilute alcohol the product melted at 177–178°.

Anal. Calcd. for $C_{22}H_{21}O_2N_3$: N, 11.70. Found: N, 11.57.

4-Phenyldihydrocoumarin (I).—The procedure of Liebermann and Hartmann[5] was followed. The compound was recrystallized from dilute alcohol, stout needles, m. p. 82–84° (reported, 82°).

1,1,3-Triphenyl-3-(*o*-hydroxyphenyl)-propanol-1 (IV).—(a) **From** (II).—To the Grignard reagent prepared from 6.3 g. of bromobenzene and 0.97 g. of magnesium in 40 cc. of dry ether was added 3.0 g. of the (solid) hydroxy ketone (II). The resulting solution was refluxed for thirty minutes, decomposed with iced ammonium chloride solution and the solvents removed by steam-distillation. The oily residue was extracted with ether and upon removal of the ether was obtained as a viscous oil which could not be induced to crystallize.

In a second experiment using 5.0 g. of the chromanol and equivalent amounts of the other reagents, the oil crystallized on seeding with some of the material obtained as described in (b) and yielded 4.3 g. of crystalline product after recrystallization from ligroin (b. p. 75–135°); m. p. 109–110°. Recrystallized from benzene–petroleum ether the material appeared as transparent colorless prisms containing solvent and melting indefinitely at around 85° with loss of solvent. Dried at 80° (20 mm.) or recrystallized from ligroin the compound melted at 112–113°.

(b) **From** (I).—A solution of 2.25 g. of 4-phenyldihydrocoumarin in 10 cc. of dry benzene was added to a solution of phenylmagnesium bromide prepared from 6.50 g. of bromobenzene and 1.00 g. of magnesium in 50 cc. of dry ether. The solution was refluxed for thirty minutes, decomposed with iced ammonium chloride solution and steam-distilled. The oily residue was removed with ether and after removal of the solvent was obtained as a pale yellow oil. This material could not be induced to crystallize when first obtained and 1.0 g. of it was removed for dehydration to the chromane. The remainder crystallized upon standing in ether–petroleum ether and yielded 1.5 g. of white prisms, m. p. 106–108°. Recrystallized from ligroin (b. p. 75–135°), it melted at 111–112°, showed no depression when mixed with a sample of the material obtained in (a), and caused rapid crystallization of the oil obtained in (a) when used as seed.

The compound is difficultly soluble in dilute aqueous alkali, readily soluble in methanolic potassium hydroxide, gives no color with ferric chloride and a red-orange color with concentrated sulfuric acid.

Anal. Calcd. for $C_{27}H_{24}O_2$: C, 85.22; H, 6.37. Found: C, 85.20, 85.40; H, 6.54, 6.53.

2,2,4-Triphenylchromane (V).—To a hot solution of 0.50 g. of the crystalline carbinol (IV) in 5 cc. of glacial acetic acid was added two drops of concentrated sulfuric acid. Upon cooling and scratching the walls of the flask the product crystallized. There was obtained 0.47 g. of white prisms, m. p. 162–163°.

The chromane was also obtained by a similar treatment of the oily product first obtained (above, part a) as the product of the reaction between the hydroxyketone (II) and phenylmagnesium bromide. From 1.0 g. of the oily carbinol was obtained 0.9 g. of V, m. p. 161–162°, a result which indicates that the reluctance of the oil to crystallize cannot be laid to the presence of significant amounts of impurities.

The chromane gives no immediate color with concentrated sulfuric acid, but on standing a yellow color develops which gradually turns reddish. It is insoluble in methanolic potassium hydroxide and does not absorb bromine in carbon tetrachloride solution.

Anal. Calcd. for $C_{27}H_{22}O$: C, 89.45; H, 6.13. Found: C, 89.27; H, 6.16.

The Reaction between *o*-Hydroxybenzaldiacetophenone and Phenylmagnesium Bromide.—(a) In Ether: Compound (X).—A solution of phenylmagnesium bromide prepared from 57.1 g. of bromobenzene and 7.2 g. of magnesium in 150 cc. of ether was added to a well-cooled (5–10°) suspension of 35.4 g. of *o*-hydroxybenzaldiacetophenone in 150 cc. of dry ether. The initial reaction resulted in the formation of a heavy white precipitate which upon the addition of more of the reagent became semi-solid and finally formed a viscous liquid phase insoluble in the ether solution. The mixture was stirred for six hours at 5°, allowed to stand overnight and decomposed with iced ammonium chloride. After the solvents and diphenyl were removed by steam distillation, the product was isolated by taking up the residue from the steam-distillation in ether, drying the solution and evaporating the solvent. The product, a viscous oil, was dissolved in an equal volume of alcohol and allowed to stand overnight. The 3.5 g. of material which crystallized was unchanged starting material. The alcohol was removed in a stream of dry air and a further amount (3.0 g.) of starting material separated. This was removed, after dilution of the residual oil with ligroin, by filtration. The ligroin solution deposited no crystalline material, even on seeding with a sample of the expected product (obtained in a previous run). The ligroin was removed and the oil dissolved in glacial acetic acid. Crystallization began immediately and on standing a total of 10.9 g. of crystalline material separated.

Recrystallized from *n*-butanol, the product formed hard, colorless prisms, m. p. 185–186°.

Anal. Calcd. for $C_{29}H_{24}O_2$: C, 86.10; H, 6.00. Found: C, 86.39; H, 6.22.

The compound is insoluble in 10% methanolic potassium hydroxide; it instantly decolorizes bromine in chloroform solution with hydrobromic acid evolution, and reacts with bromine in acetic acid in the cold. It did not react with semicarbazide in dilute propanol solution, nor with phenylmagnesium bromide in ether solution.

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(5) Liebermann and Hartmann, *Ber.*, **24**, 2586 (1891).

The acetic acid mother liquor from the crystallization of the 185° compound was heated to boiling and several drops of sulfuric acid added. Formation of a crystalline precipitate quickly began and on cooling there was obtained 12.0 g. of compound VIII, described below (part b).

(b) In **Ether–Benzene: Compound** (VIII).—To a solution of phenylmagnesium bromide prepared from 27.5 g. of bromobenzene and 4.1 g. of magnesium in 150 cc. of ether was added a solution of 10.0 g. of *o*-hydroxybenzaldiacetophenone in 100 cc. of dry benzene. The solution was refluxed for two and one-half hours, decomposed with iced ammonium chloride solution and, after steam distillation, the product was removed with ether. Removal of the ether left 15.5 g. of a sirupy oil which could not be crystallized.

The oily material was soluble in alcoholic alkali (its solution in alcohol remained clear upon the addition of dilute alkali, but became cloudy when water was added), absorbed bromine in carbon tetrachloride solution and gave a deep red color with sulfuric acid.

When to a solution of the oily product in hot glacial acetic acid was added a trace of concentrated sulfuric acid, a crystalline precipitate formed rapidly. The material so obtained (VIII) formed soft, white needles from acetic acid, m. p. 219–220°.[6]

Anal. Calcd. for $C_{35}H_{28}O$: C, 90.48; H, 6.09. Found: C, 90.43; H, 6.24.

The compound is insoluble in 10% methanolic potassium hydroxide and is unattacked by bromine in chloroform or acetic acid solution. In contrast to its extremely difficult solubility in acetic acid, ether, alcohols and even acetic anhydride, it is readily soluble in warm benzene.

4-Phenacylflavene.—This was prepared from *o*-hydroxybenzaldiacetophenone according to the directions of Hill.[7] It was found necessary to buffer the ordinary glacial acetic acid by the addition of a small amount of sodium acetate in order to prevent the formation of large amounts of 4-phenacylideneflavene,[8] a colored impurity difficult to remove. The product formed soft, white needles, m. p. 95–96° (reported,[7] 96°).

1,1-Diphenyl-2-(4-flavenyl)-ethanol-1 (XI).—This was prepared in good yield according to the directions of Gomm and Hill.[3] The compound forms soft, white needles from *n*-butanol, m. p. 193–193.5° (reported[3] 194°).

Anal. Calcd. for $C_{29}H_{24}O_2$: C, 86.10; H, 6.00. Found: C, 86.09; H, 6.20.

The compound is insoluble in 10% methanolic potassium hydroxide and was recovered unchanged when treated with 2,4-dinitrophenylhydrazine in propyl alcohol. It decolorizes bromine in chloroform or acetic acid solution with the evolution of hydrobromic acid. A mixture of the m. p. 193° compound and compound X, m. p. 185–186°, melted at 165–170°.

4-Phenacyl-2,2-diphenylchromane (XII).—(a) From Compound (X).—To a solution of 1.0 g. of X, m. p. 185–186°, in 15 cc. of glacial acetic acid was added two drops of concentrated sulfuric acid. The solution was boiled for a minute, diluted slightly and cooled. The product crystallized as colorless needles weighing 0.82 g., m. p. 115–116°. Crystallized from ligroin (b. p. 75–135°) it separated as crisp white needles, m. p. 115–116°.

Anal. Calcd. for $C_{29}H_{24}O_2$: C, 86.10; H, 6.00. Found: C, 85.73; H, 6.02.

(b) **From Compound XI.**—Treatment of compound XI in the manner described in (a) resulted in the formation of the same substance, m. p. 115–116° (mixed m. p. 115–116°), as that obtained from X.

Anal. Calcd. for $C_{29}H_{24}O_2$: C, 86.10; H, 6.00. Found: C, 85.90; H, 6.04.

The compound (XII, m. p. 115–116°) is insoluble in 10% methanolic potassium hydroxide and does not react in the cold with bromine in chloroform or acetic acid; on warming with bromine in either solvent reaction occurs with evolution of hydrobromic acid.

2,4-Dinitrophenylhydrazone from X, XI, and XII.—To a solution of 0.5 g. of 2,4-dinitrophenylhydrazine in 10 cc. of glacial acetic acid was added 0.5 g. of (XII). The deep red solution was refluxed gently for five minutes; crystallization began while the solution was still boiling. On cooling there was obtained 0.66 g. of orange-red crystals which on recrystallization from chloroform–petroleum ether formed bright red-orange leaflets, m. p. 243–244° dec.

The same compound was formed when X (m. p. 185–186°) or XI (m. p. 193°) was treated with 2,4-dinitrophenylhydrazine in boiling glacial acetic acid.

Anal. Calcd. for $C_{35}H_{28}O_5N_4$: C, 71.90; H, 4.83; N, 9.50. Found: C, 71.46; H, 4.73; N, 9.51.

1,1 - Diphenyl - 2 - (2,2 - diphenyl - 4 - chromanyl)-ethanol-1 (XIII).—A solution of 2.0 g. of XII in a mixture of ether and benzene was added to an excess of phenylmagnesium bromide in ether. After one hour of refluxing the solution was decomposed with iced ammonium chloride solution and steam-distilled. The product was a viscous oil which crystallized slowly from ether–petroleum ether to form colorless prisms, m. p. 148–149°. Recrystallized from benzene–petroleum ether the compound formed colorless prisms, m. p. 149–149.5°.

Anal. Calcd. for $C_{35}H_{30}O_2$: C, 87.07; H, 6.29. Found: C, 87.06; H, 6.35.

The substance is insoluble in 10% methanolic potassium hydroxide and does not decolorize bromine in acetic acid solution.

Dehydration of XIII.—To a solution of 0.20 g. of the carbinol (XIII) in 5 cc. of warm glacial acetic acid was added a trace of concentrated sulfuric acid. Crystallization began immediately. On cooling there was obtained 0.18 g. of soft white needles of compound VIII, m. p. 219–220°.

Methyl Dihydrocoumarin-4-acetate (XII).—Dihydrocoumarin-4-acetic acid was prepared by hydrolysis of the addition product of coumarin and cyanoacetamide, according to the directions of Seshadri.[9] The acid was esterified with methanol and sulfuric acid in the usual way. The ester is a colorless, viscous oil, b. p. 208–210° (20 mm.); n^{22}_{D} 1.5369.

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[6] In their experiment in which the Grignard reaction was run as just described, Gomm and Hill[3] decomposed the reaction mixture with dilute acid and obtained as the direct product a crystalline compound, m. p. 216–217°.

[7] Hill, *J. Chem. Soc.*, 1255 (1934).

[8] Feuerstein and Kostanecki, *Ber.*, **31**, 710 (1898).

[9] Seshadri, *J. Chem. Soc.*, 166 (1928).

Anal.[10] Calcd. for $C_{12}H_{12}O_4$: C, 65.42; H, 5.50. Found: C, 64.87, 65.10; H, 5.82, 5.91.

Reaction of Phenylmagnesium Bromide with Methyl Dihydrocoumarin-4-acetate.—A solution of 2.1 g. of the redistilled ester in 20 cc. of dry ether was added to an excess of phenylmagnesium bromide in ether. A vigorous reaction occurred with the formation of a white precipitate which quickly dissolved. The solution was refluxed for thirty minutes and decomposed with ice–ammonium chloride solution. The product, after steam distillation and recovery with ether, was a viscous oil which could not be induced to crystallize.

The addition of a trace of sulfuric acid to a solution of the oil in acetic acid transformed it quickly into a white crystalline material. Recrystallized from acetic anhydride this product formed soft white needles, m. p. 216–218°. Mixed with a sample of VIII, m. p. 218–219°, the melting point was 216–218°.

Summary

1. It has been shown that the compounds produced by the reaction of phenylmagnesium bromide with *o*-hydroxybenzaldiacetophenone do not have the structures proposed for them by Gomm and Hill.[3]

2. The structure of one of these compounds has been established by a different method of synthesis, and a structure for the other proposed on the basis of its properties and its relationship to compounds of known structure.

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[10] Analysis by Dr. J. Haagen-Smit, California Institute of Technology, Pasadena, Calif.

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF NOTRE DAME]

Chlorides and Hydrochlorides from 1-Hexyne[1]

BY G. F. HENNION AND CHARLES E. WELSH

Introduction

When 1-hexyne is chlorinated in various oxygen-containing media a complex mixture of products results, some of which contain oxygen as well as chlorine.[2] Various chlorine derivatives of 1-hexyne are thus obtained together and may be separated by fractional distillation. It was thought advisable to prepare these separately, by chlorination in inert solvents, in order to obtain pure substances for the determination of reliable physical data. It was desired also to prepare the mono and dihydrochlorides of 1-hexyne for comparison with the chlorides. During this investigation certain observations were made which may be of interest, and hence are recorded here.

Chlorination of 1-hexyne in either carbon tetrachloride or *n*-heptane containing a small amount of antimony pentachloride gave a mixture of *trans*-1,2-dichloro-1-hexene and 1,1,2,2-tetrachlorohexane only. When the antimony pentachloride was omitted the product was much less tractable and boiled over a wide range.

Direct addition of hydrogen chloride to 1-hexyne, with or without a solvent, was unsuccessful in the absence of a catalyst. Numerous metal chlorides were studied for catalytic activity. Of these bismuth chloride appeared to be best and with its use hydrogen chloride added readily to 1-hexyne to yield both 2-chloro-1-hexene and 2,2-dichlorohexane. By heating with potassium hydroxide in propyl alcohol the latter product could be reverted to the former.

Chlorination of 2-chloro-1-hexene in carbon tetrachloride containing antimony pentachloride was of particular interest because the reaction did not lead to 1,2,2-trichlorohexane, as anticipated. Instead a mixture of *cis*-1,2-dichloro-1-hexene and 1,1,2,2-tetrachlorohexane was obtained. Attempts to prepare 1,2,2-trichlorohexane by the addition of hydrogen chloride to both *cis*- and *trans*-1,2-dichloro-1-hexene likewise were unsuccessful. No reaction was observed in either case, even when bismuth chloride was present.

Physical data for the compounds prepared are given in Table I.

Experimental

Chlorination of 1-Hexyne.—A solution of 41 g. (0.5 mole) of 1-hexyne in 200 ml. of carbon tetrachloride was placed in a one liter, three-necked flask equipped with an efficient stirrer, a reflux condenser, and a chlorine inlet tube. To the solution was added slowly, with stirring, 50 ml. of carbon tetrachloride containing 1.5 ml. of antimony pentachloride. Chlorine was then passed over the solution in a fairly rapid stream, at a temperature of 45 ± 5°, until 35.5 g. (0.5 mole) was absorbed. The solution was washed with water, dilute sodium carbonate solution, again with water, dried over calcium chloride, and fractionally distilled: yield, 15 g. (19.6%) of *trans*-1,2-dichloro-1-hexene and 39.3 g. (30.6%) of 1,1,2,2-tetrachlorohexane.

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[1] Paper XXXVIII on the chemistry of substituted acetylenes and their derivatives; previous paper, THIS JOURNAL, **62**, 653 (1940).

[2] Norris, Vogt and Hennion, *ibid.*, **61**, 1460 (1939); **62**, 449 (1940).