(m.p. 94–105°) obtained in the demethylation of XI melted at 103–108°.

Anal. Calcd. for $C_9H_7ClO_2$: C, 59.19; H, 3.86; Cl, 19.42. Found: C, 59.34; H, 3.92; Cl, 19.27.

Acknowledgment.—The authors are indebted to J. R. Kubic and A. K. Kuder for the analyses.

BRECKSVILLE, OHIO

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STATE UNIVERSITY OF IOWA]

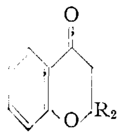
The Reaction of Grignard Reagents with 4-Hydroxy- and 4-Ethoxycoumarin

BY S. WAWZONEK, R. C. NAGLER[1,2] AND L. J. CARLSON[1]

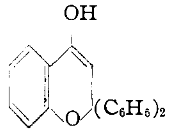
RECEIVED OCTOBER 5, 1953

4-Ethoxycoumarin was found to react with phenylmagnesium bromide and methylmagnesium iodide and to give 2,2-diphenyl-4-chromanone and 2,2-dimethyl-4-chromanone, respectively, if the intermediate carbinol was decomposed with acid. The intermediate when decomposed with ammonium chloride gave a mixture of the corresponding chromanone and products formed by a reverse aldol reaction. 4-Hydroxycoumarin was found to be resistant to the addition reaction of Grignard reagents. The results obtained differ from those reported previously by Heilbron and Hill.

A further study of the action of Grignard reagents with 4-hydroxycoumarin and its derivatives was suggested by the conflicting reports of previous investigators on the properties of 2,2-dimethyl-4-chromanone (I, R = CH_3) and 2,2-diphenyl-4-chromanone (I, R = C_6H_5).



I



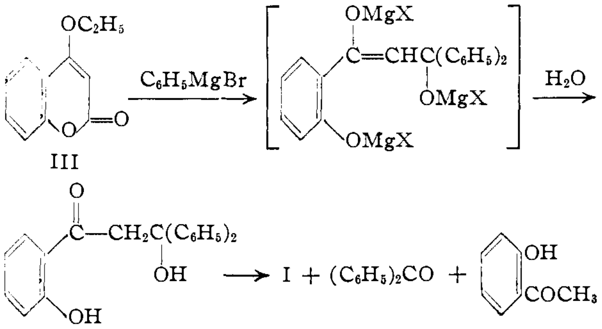
II

The former (I, R = CH_3) was found to be a neutral compound[3] while the diphenyl compound (I, R = C_6H_5), made by the addition of phenylmagnesium bromide to 4-hydroxycoumarin, was reported to be acidic[4] and to exist as the enol, 4-hydroxy-2,2-diphenyl-Δ^3-chromene (II).

Repetition of the reaction of excess phenylmagnesium bromide with 4-hydroxycoumarin gave upon decomposition of the Grignard product mainly 4-hydroxycoumarin and a small amount of tar. Similar results were obtained using methylmagnesium iodide under normal and forcing conditions.

This discrepancy in results from those reported previously[4] was partially resolved when the preparation of the chromene II from its ether was undertaken. The latter was reported to be formed by the addition of phenylmagnesium bromide to 4-methoxycoumarin.[4] The use of identical conditions to those of Heilbron and Hill's[4] with 4-ethoxycoumarin instead of 4-methoxycoumarin, gave a product with the same melting point as that reported for 4-methoxy-2,2-diphenyl-Δ^3-chromene. That this product was 2,2-diphenyl-4-chromanone (I, R = C_6H_5) and not the chromene was indicated by its insolubility in alkali, by the formation of a 2,4-dinitrophenylhydrazone, by the products isolated from the ammonium chloride hydrolysis of the Grignard addition product and by an independent synthesis.

When an ammonium chloride solution was substituted for the hydrochloric acid in the decomposition of the Grignard addition product, a mixture of 2,2-diphenyl-4-chromanone (I, R = C_6H_5), benzophenone and *o*-hydroxyacetophenone was formed. This behavior points to the formation of *o*-hydroxy-(β-hydroxy-β,β-diphenyl)-propiophenone (IV) as an intermediate, even though it was not isolated. This carbinol (IV) in weakly acid medium apparently is only slowly cyclized to 2,2-diphenyl-4-chromanone (I, R = C_6H_5) and therefore can undergo a reverse aldol to benzophenone and *o*-hydroxyacetophenone.



III

IV

The cleavage of the ether by the Grignard reagent must occur after the opening of the ring, since if a limited amount of the reagent is used, a mixture of 4-ethoxycoumarin (III) and 2,2-diphenyl-4-chromanone (I, R = C_6H_5) is obtained. The ethylbenzene formed in this cleavage was isolated in a very small amount and its structure demonstrated by oxidation to benzoic acid.

The synthesis of 2,2-diphenyl-4-chromanone (I) was accomplished by condensing benzophenone with *o*-hydroxyacetophenone in the presence of sodium *t*-butoxide. The crude product obtained was converted to a mixture of 2,4-dinitrophenylhydrazones from which the golden 2,2-diphenyl-4-chromanone derivative was separated mechanically. The remaining dark red crystalline product had an elementary analysis which corresponded to the 2,4-dinitrophenylhydrazone of *o*-hydroxy-(β-hydroxy-β,β-diphenyl)-propiophenone and gave upon cyclization only trace amounts of the corresponding derivative of 2,2-diphenyl-4-chromanone (II, R = C_6H_5). The amount of red product obtained, however, was too small to be characterized further.

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(1) Abstracted in part from the Ph.D. thesis, August, 1953, of R. C. Nagler and the M.S. thesis, February, 1950, of L. J. Carlson.

(2) du Pont Fellow, 1951–1952.

(3) K. V. Auwers and W. Mauss, *Ber.*, **61**, 2545 (1928).

(4) I. Heilbron and D. J. Hill, *J. Chem. Soc.*, 2005 (1927).

The reaction of excess methylmagnesium iodide with 4-ethoxycoumarin gave similar results to those obtained with phenylmagnesium bromide. Acid decomposition of the Grignard mixture gave 2,2-dimethyl-4-chromanone which was identical with an authentic sample.[3] The intermediate carbinol was not isolated when ammonium chloride was used, but the presence of *o*-hydroxyacetophenone, which would result from a reverse aldol, was demonstrated by the formation of its 2,4-dinitrophenylhydrazone.

The results obtained in this work indicate that the 4-methoxy-2,2-diaryl-Δ^3-chromenes obtained by Heilbron and Hill are actually the 2,2-diaryl-4-chromanones. The analyses offered by these investigators as proof of structure would likewise fit for the chromanones.

Since 2,2-diphenyl-4-chromanone (I, R = C_6H_5) shows the properties of a normal ketone and is neutral, the 4-hydroxy-2,2-diphenyl-Δ^3-chromene (II) reported[4] was probably impure 4-hydroxycoumarin. The acidic properties reported fit this possibility, but the high melting point and elementary analysis do not support this structure.

Experimental[5]

Reaction of 4-Hydroxycoumarin with Excess Grignard Reagent.—The directions of Heilbron and Hill[4] were followed for this reaction. Hydroxycoumarin[6] (5 g.) in benzene (300 ml.) was refluxed with phenylmagnesium bromide (0.1 mole) in ether (100 ml.) for 5 hours. Hydrolysis with dilute hydrochloric acid followed by steam distillation of the biphenyl gave a solution from which a small amount (0.1 g.) of a black tar was filtered off. Upon cooling the filtrate to 0°, 4-hydroxycoumarin (4.5 g.) (90%) was recovered.

The substitution of methylmagnesium iodide for the phenylmagnesium bromide with either benzene, di-*n*-butyl ether or xylene as solvents for the 4-hydroxycoumarin gave similar results.

Reaction of 4-Ethoxycoumarin with Excess Phenylmagnesium Bromide.—4-Ethoxycoumarin (4.8 g., 0.025 mole)[7] in ether (300 ml.) was refluxed with phenylmagnesium bromide (0.15 mole) in ether (200 ml.) for 20 hours. The initial precipitate which formed disappeared during this period. The product obtained depended upon the method used for hydrolyzing the Grignard intermediate.

a. Acid Hydrolysis.—Addition of the Grignard mixture to 1 *N* hydrochloric acid (600 ml.) was followed by stirring for one-half hour. The ether solution was separated and the aqueous layer extracted twice with 200-ml. portions of ether and the ether solutions combined. Removal of the solvent followed by steam distillation gave less than 0.3 g. of volatile solids. The oily crude residue (5.9 g.) contained only a trace of alkali-soluble material and melted below 100°. Recrystallization four times from dilute acetic acid and twice from ethanol–water gave 2,2-diphenyl-4-chromanone melting at 134–135°.

Anal. Calcd. for $C_{21}H_{16}O_2$: C, 83.97; H, 5.37. Found: C, 83.73; H, 5.54.

The 2,4-dinitrophenylhydrazone formed golden crystals from ethanol–ethyl acetate and melted at 289–291°.

Anal. Calcd. for $C_{27}H_{20}N_4O_5$: C, 67.45; H, 4.18; N, 11.64. Found: C, 67.05; H, 4.27; N, 11.39.

b. Ammonium Chloride Hydrolysis.—Treatment of the Grignard product with ammonium chloride was followed by extraction of the aqueous layer with three 100-ml. portions of ether. The combined ether solutions were concentrated to 250 ml. and extracted with 5% sodium hydroxide. The ether solution upon removal of the solvent gave an oil which on steam distillation gave benzophenone (3.7 g.). Purification by sublimation gave a sample melting at 47–48° which did not lower the melting point of an authentic sample. The oil (0.7 g.) remaining after steam distillation crystallized from ethanol–water after six weeks and melted at 110–122°. A second recrystallization gave a product melting at 128–131° which did not depress the melting point of the 2,2-diphenyl-4-chromanone obtained from the acid hydrolysis. The dinitrophenylhydrazone after four crystallizations from ethanol–ethyl acetate melted at 289–291°.

The sodium hydroxide extract was acidified with hydrochloric acid and steam distilled. Extraction of the distillate with ether gave an oil (1.2 g.) which gave a dark brown-violet ferric chloride test comparable to that of *o*-hydroxyacetophenone. The 2,4-dinitrophenylhydrazone from this oil after one crystallization from ethanol melted at 210–212° and did not lower the melting point of the 2,4-dinitrophenylhydrazone of *o*-hydroxyacetophenone.

The material (0.8 g.) which was not volatile with steam crystallized very slowly and melted at 95–115°. The 2,4-dinitrophenylhydrazone (m.p. 285–287°) was identical with that of 2,2-diphenyl-4-chromanone.

Refluxing a limited amount of phenylmagnesium bromide (0.04 mole) with 4-ethoxycoumarin (3.8 g.) in ether for 18 hours gave a solution which was decomposed with 1 *N* hydrochloric acid. Separation of the ether layer was followed by extraction of the aqueous layer with three 100-ml. portions of ether. Steam distillation after removal of the solvent gave a liquid (0.7 ml.) boiling at 118–132°. Oxidation of this product with alkaline potassium permanganate gave benzoic acid and pointed to the presence of ethylbenzene.

From the steam non-volatile portion was recovered 4-ethoxycoumarin (1.3 g.) and 2,2-diphenylchromanone (2.3 g.).

Synthesis of 2,2-Diphenylchromanone.—To a well-stirred refluxing mixture of benzophenone (54.6 g.), anhydrous benzene (250 ml.), sodium *t*-butoxide (from 5 g. of sodium), and *t*-butyl alcohol (25 ml.), was added *o*-hydroxyacetophenone (4 g.) in benzene (150 ml.) at the rate of one drop per second. The resulting mixture was refluxed for 20 hours and poured into a cold mixture of concentrated hydrobromic acid (100 ml.) and glacial acetic acid (150 ml.). Removal of the benzene layer was followed by steam distillation and gave 6.7 g. of a non-volatile brown glass. A portion of this material when recrystallized five times from ethanol and water gave 2,2-diphenylchromanone melting at 132–135°.

The remainder of the crude product was converted to a mixture of 2,4-dinitrophenylhydrazones. Recrystallization from ethanol–ethyl acetate gave a mixture of dark red and golden crystals. The golden plates melted at 290–291° and were identical with the 2,4-dinitrophenylhydrazone of 2,2-diphenylchromanone.

The dark red crystalline compound separated mechanically melted at 238–240° and from its analysis was probably the 2,4-dinitrophenylhydrazone of *o*-hydroxy-β-hydroxy-β,β-diphenylpropiophenone.

Anal. Calcd. for $C_{27}H_{22}N_4O_6$: C, 65.40; H, 4.48. Found: C, 65.60; H, 4.81.

This hydrazone when refluxed with acetic anhydride for an hour was converted into the dinitrophenylhydrazone of 2,2-diphenylchromanone in only trace amounts. The possibility that this compound may have been present as an impurity was not eliminated completely.

Reaction of 4-Ethoxycoumarin with Excess Methylmagnesium Iodide.—To 4-ethoxycoumarin (9.5 g.) in ether (500 ml.) was added methylmagnesium iodide (0.3 mole) in ether (350 ml.) and the resulting white solid formed refluxed for 20 hours. During this time the solid dissolved. Hydrolysis with ammonium chloride and ice was followed by extraction of the water layer three times with 100-ml. portions of ether. The combined ether solution was extracted with 5% sodium hydroxide. Acidification of the alkaline solution gave an oil (3.7 g.) which gave a strong ferric chloride test. The 2,4-dinitrophenylhydrazone formed gave, after two recrystallizations from ethanol–ethyl acetate, orange-red needles melting at 212–213°. A mixture with the 2,4-dinitrophenylhydrazone made from *o*-hydroxyacetophenone gave no depression.

Anal. Calcd. for $C_{14}H_{12}N_4O_5$: C, 53.16; H, 3.82; N, 17.72. Found: C, 53.17; H, 3.88; N, 17.45.

The oil (2 ml.) when allowed to stand in the presence of a saturated ammonium chloride solution at room temperature for 15 hours and then taken up in ether was found to contain the alkali-insoluble 2,2-dimethylchromanone (0.99), m.p.

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[5] Melting points are not corrected.

[6] M. A. Stahmann, I. Wolff and K. P. Link, THIS JOURNAL, **65**, 2285 (1943).

[7] R. Anschütz, *Ann.*, **367**, 189 (1909).

67–75°. Purification by sublimation gave a sample melting at 87–88° which did not depress the melting point of an authentic sample.[3]

The ether solution containing the alkali-insoluble portion from the Grignard gave an oily solid (5.3 g.) melting at 57–69°. Sublimation under reduced pressure gave the white 2,2-dimethylchromanone melting at 87–88° and gave no depression with an authentic sample.

The 2,4-dinitrophenylhydrazone crystallized from ethanol–ethyl acetate melted at 225–226°.

Anal. Calcd. for $C_{17}H_{16}N_4O_5$: C, 57.32; H, 4.53; N, 15.72. Found: C, 57.31; H, 4.65; N, 15.37.

A mixture with the 2,4-dinitrophenylhydrazone of authentic 2,2-dimethylchromanone showed no depression.

IOWA CITY, IOWA

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Reaction of Thiacyclopropanes (Olefin Sulfides) and Thiacyclobutanes with Organolithium Compounds[1]

BY F. G. BORDWELL, HARRY M. ANDERSEN AND BURNETT M. PITT

RECEIVED SEPTEMBER 29, 1953

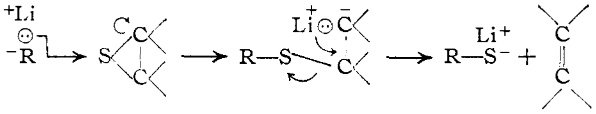
Alkyl- and aryllithium reagents were found to effect a 1,2-elimination reaction with thiacyclopropanes giving rise to olefins and lithium mercaptides. This reaction constitutes a new method for preparing thiols; it is chiefly useful for preparing thiophenols. With thiacyclobutane ring opening occurred, but attack of R^- (or Ar^-) was again on sulfur rather than on carbon (thiacyclopentane gave no reaction). The reaction gave a mixture of products, which can be formulated as coming from the initial substance, $RSCH_2CH_2CH_2Li$. Lithium aluminum hydride reacted with thiacyclopropanes to give secondary lithium mercaptides.

Thiacyclopropanes (olefin sulfides) react with some nucleophilic reagents including lithium diethylamide,[2a] primary and secondary amines,[2b] and mercaptide ions[2b,c] to give products of ring opening which are comparable to those formed from epoxides. In the course of a program of study of the methods of synthesis and reactions of divalent sulfur compounds, an attempt was made to prepare mercaptans by the reaction of thiacyclopropanes with organometallic compounds in a manner analogous to the formation of alcohols by the coupling of epoxides with Grignard reagents or organolithium compounds. However, the reactions did not proceed as anticipated. Alkyl- or aryllithium reagents appropriated the sulfur from the thiacyclopropane molecule to form alkyl or aryl mercaptides and olefins.

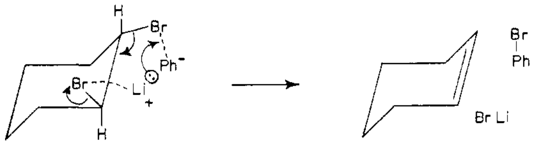
The reaction of phenyllithium with 2-thiabicyclo-[4,1,0]heptane (cyclohexene sulfide) gave 60% of thiophenol (as the lithium salt) and 52% of cyclohexene. Butyllithium gave 63% of 1-butanethiol and 67% of cyclohexene. Similarly, 81% of thiophenol was obtained from phenyllithium and methylthiacyclopropane (propylene sulfide). From comparable experiments using thiacyclopropane (ethylene sulfide) 51% of thiophenol and 27% of 1-butanethiol were obtained.

The reaction of aryllithium reagents and the readily available propylene sulfide[3] constitutes a new method for preparing thiophenols. It serves as an alternative to the reaction of aryl Grignard reagents and sulfur (S_8), which is awkward due to the insolubility of sulfur in ether, and usually gives very poor yields. The method has also been applied in our laboratory to the preparation of *m*- and *p*-dimethylaminothiophenols in yields of 70–80%.[4]

These reactions probably can best be formulated as an attack by the alkyl- or arylcarbanion on sulfur, facilitated by coördination of sulfur with the lithium cation. Breaking of the carbon–sulfur



bond gives rise to an electron pair which can simultaneously or subsequently initiate a 1,2-elimination reaction to form the olefin and liberate the sulfur in the form of lithium mercaptide. The attack of the incipient carbanion on sulfur in olefin sulfides and on carbon in olefin oxides may be rationalized by pointing to the fact that (1) sulfur is more electropositive and polarizable than oxygen, (2) the carbon–sulfur dipole is small, and (3) divalent sulfur in disulfides, sulfenyl halides, etc., is known to be susceptible to attack by nucleophilic agents in displacement type reactions. A similar difference in susceptibility to attack was observed between chlorine and bromine in reactions with phenyllithium.[5] Whereas 1,2-dichlorides react with the elimination of hydrogen chloride (nucleophilic attack on hydrogen), 1,2-dibromides, such as cyclohexene dibromide, react with the elimination of bromine (nucleophilic attack on bromine).



Reactions of thiacyclopropanes with Grignard reagents were less clear-cut. Although an 87% yield of cyclohexene was obtained by the reaction of phenylmagnesium bromide and cyclohexene

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[1] This investigation was supported by the American Petroleum Institute as part of Research Project 48B. An account of this work was presented at the Milwaukee Meeting of the American Chemical Society, March, 1952.

[2] (a) H. Gilman and L. A. Woods, THIS JOURNAL, **67**, 1843 (1945); (b) H. R. Snyder, J. M. Stewart and J. B. Ziegler, *ibid.*, **69**, 2672, 2675 (1947); (c) C. C. J. Culvenor, W. Davies and N. S. Heath, *J. Chem. Soc.*, 282 (1949).

[3] French Patent 797,621; *C. A.*, **30**, 7122 (1936); C. C. J. Culvenor, W. Davies and K. H. Pausacker, *J. Chem. Soc.*, 1050 (1946); F. G. Bordwell and H. M. Andersen, THIS JOURNAL, **75**, 4959 (1953).

[4] Pierre J. Boutan, unpublished results.

[5] G. Wittig and G. Harborth, *Ber.*, **77B**, 306 (1944).