[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF CALIFORNIA]

Reaction of Triphenylacetyl Chloride with Organometallic Reagents. Preparation of Alkyl Trityl Ketones

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Reaction of excess methylmagnesium iodide with triphenylacetyl chloride yields triphenylmethane, triphenylethane, and methyl trityl ketone. There could be detected no ethyl triphenylacetate, previously reported as the principal product of this reaction. It is suggested that the observed reaction products are obtained from an intermediate acylonium ion which either reacts with Grignard reagent to give ketone or decarbonylates to give the triphenylmethyl carbonium ion. Reaction of ethylmagnesium bromide with triphenylacetyl chloride yields no ketone, but a mixture of 2,2,2-triphenylethanol and ethyltritylcarbinol. The latter is believed to arise from reduction by excess Grignard reagent of initially formed ethyl trityl ketone. Methyl, ethyl, and butyl trityl ketones have been prepared in good yield by reaction of triphenylacetyl chloride with the appropriate cadmium reagents.

It has been reported[1] recently that alkyl trityl ketones have not been secured by reaction of the Grignard reagent with triphenylacetyl chloride; in fact, the only ketone of this type whose identity seems authenticated is methyl trityl ketone.[2] Reaction of ethylmagnesium iodide with triphenylacetyl chloride[1] yielded the reduction product 2,2,2-triphenylethanol rather than the previously claimed ethyl trityl ketone,[3] whereas reaction with a large excess of methylmagnesium iodide was reported[1] to result in a 67% yield of ethyl triphenylacetate. Formation of the ester in the latter case was attributed to extraction of halogen from the acid chloride by a Lewis-acid component of the Grignard reagent, and subsequent reaction of the acylonium ion, $(C_6H_5)_3\overset{+}{C}—CO$, with ether solvent. In view of the large excess of Grignard reagent that was employed, this result seems rather surprising, for the Grignard reagent would be expected to react much more rapidly with the acylonium ion than would the ether solvent. Indeed, reaction of organocadmium reagents with acid chlorides has been extensively rationalized[4] on the basis of reaction of an intermediate acylonium ion with the organocadmium reagent or a carbanion released from it.

When reaction of excess methylmagnesium iodide with triphenylacetyl chloride was re-examined during the present investigation, *no ethyl triphenylacetate could be isolated*, nor could this ester (synthesized for reference purposes) be detected in the reaction product by infrared spectroscopy, gas phase chromatography, or column chromatography on alumina. There was obtained a 17–21.5% yield of methyl trityl ketone; however, the major product of the reaction was a mixture of triphenylmethane and triphenylethane. Analysis and separation of the hydrocarbon mixture by gas chromatography indicated 17–21% yields of triphenylmethane and 31–40% yields of triphenylethane. The hydrocarbons were compared (infrared spectra and gas chromatography) with authentic samples.

The products obtained from reaction of methylmagnesium iodide with triphenylacetyl chloride do indeed indicate that the principal reaction path involves extraction of halogen to yield the acylonium ion; however, the fate of this ion does not involve reaction with the ether solvent.[5] Reaction of the acylonium ion with the Grignard reagent (or the methyl carbanion) would yield the trityl ketone, whereas the triphenylmethyl carbonium ion, formed by decarbonylation of the acylonium ion,[6] could lead to hydrocarbon formation. Reaction of the carbonium ion with the Grignard reagent would yield triphenylethane, and use of higher alkylcadmium reagents (see Table I) does lead to the corresponding higher triphenylalkanes. The ether solvent must be the source of the hydrogen required for triphenylmethane formation, possibly by an equilibrium reaction involving extraction of the *alpha* hydrogen from the ether; however, the increased formation of triphenylmethane (Table I) at higher temperature suggests a more complicated reaction path. Extraction of a hydride ion from a phenyl moiety would not be expected. The triphenylmethyl radical can hardly be the intermediate leading to hydrocarbon formation, for triphenylacetyl chloride is stable to heating under reflux in a benzene-ether mixture. Furthermore, there is apparent no reasonable mechanism leading to generation of the triphenylmethyl

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(1) J. L. Greene, D. Abraham, and H. D. Zook, *J. Org. Chem.*, **24**, 132 (1959).

(2) J. L. Greene and H. D. Zook, *J. Am. Chem. Soc.*, **80**, 3629 (1958).

(3) M. S. Kharasch and O. Reinmuth, *Grignard Reactions of Nonmetallic Substances*, Prentice Hall, Inc., Englewood Cliffs, N. J., 1954, p. 763.

(4) A recent report containing references to earlier work is: J. Cason and E. J. Reist, *J. Org. Chem.*, **23**, 1675 (1958).

(5) The origin of the ester reported by the previous investigators seems obscure; however, presence of ethanol in the ether solvent could lead to formation of magnesium ethoxide, which would react with the acylonium ion.

(6) In Friedel and Crafts reactions with trisubstituted acetyl chlorides, alkylations with the tertiary carbonium ion have been observed; for a leading reference, *cf.* E. Rothstein and R. W. Saville, *J. Chem. Soc.*, 1946 (1949).

TABLE I

REACTION OF TRIPHENYLACETYL CHLORIDE WITH ALKYLCADMIUM REAGENTS[a]

Alkyl Group	Ratio of Alkyl Halide to Acid Chloride	Yields, % $(C_6H_5)_3CH$	 $(C_6H_5)_3C-R$	 $(C_6H_5)_3C-\underset{\underset{\textstyle O}{\|}}{C}-R$
CH_3-	2:1[b]	18	33	12[c]
	2:1	0	21.5	15[c]
	5:1	0	11	73
C_2H_5-	2:1	11	13	39.5
n-C_4H_9-	2:1	11.5	17.5	46
	5:1	8.5	10.5	62.5

[a] Unless otherwise stated, after the cadmium reagent had been formed from the bromide *via* the Grignard reagent, the acid chloride was added at about 10°, then the mixture was stirred for about 1 hr. at room temperature followed by about 20 hr. at 40–43°. [b] After addition of the acid chloride in this run, the mixture was stirred for 1 hr. at about 43°, then for 1 hr. under reflux in benzene solvent. [c] The lower yields of ketone obtained with the 2:1 ratio of methyl bromide are believed due to the volatility of dimethylcadmium and its consequent loss during distillation of ether from the reaction mixture.

carbanion as an intermediate. The hydrocarbons are also formed in cadmium reactions (see Table I), and methyl trityl ketone does not suffer displacement of the triphenylmethyl carbanion on heating with dimethylcadmium under conditions used in the organocadmium reaction with an acid chloride. The ketone is recovered unchanged. Decomposition of the acylonium ion to the carbonium ion is also indicated by the fact that a higher ratio of hydrocarbon is obtained in the organocadmium reaction when it is carried out at higher temperature (Table I).

In view of the unexpected results obtained in our investigation of the reaction of triphenylacetyl chloride with methylmagnesium iodide, the reaction with the ethyl Grignard reagent was also re-examined. In agreement with the previous report,[1] 2,2,2-triphenylethanol was obtained; however, chromatography on alumina separated a second alcohol (infrared spectrum) in somewhat smaller amount than the substituted ethanol. The second alcohol, m.p. 92–93.6°, gave an analysis in agreement with that calculated for ethyltritylcarbinol. The identity of this alcohol was established by oxidation to ethyl trityl ketone and comparison of the latter with an authentic sample. Thus, ethyl trityl ketone appears to have been a primary product of the Grignard reaction, but it was reduced by excess Grignard reagent to the corresponding carbinol. Triphenylacetaldehyde is an improbable intermediate in formation of the carbinol, for the Grignard reagent would not be expected to add to such a highly hindered aldehyde.

As alkyl trityl ketones have proved difficult to synthesize and organocadmium reagents are relatively unaffected by steric hindrance,[7] the reaction of dialkylcadmium reagents with triphenylacetyl chloride was examined. If a large excess of cadmium reagent is utilized, this procedure is a simple and high-yield approach to synthesis of alkyl trityl ketones. Pertinent data are assembled in Table I. It may be noted that a hydrocarbon mixture is also obtained in these reactions, but the amount is reduced by use of excess cadmium reagent and by use of reaction temperatures below 45°. This is consistent with the view that the acylonium ion is the primary intermediate in the reaction. Decarbonylation of this ion is competitive with its reaction with the cadmium reagent or derived carbanion. As reduction products were not encountered, it would seem that the cadmium reagent is free of the reducing action which so often handicaps the Grignard reagent.

EXPERIMENTAL[8]

Triphenylacetic acid. Initial efforts to prepare this acid from commercial triphenylmethyl chloride were unsuccessful because of the presence of triphenylmethylcarbinol, which could not be removed in any convenient manner. The preparation from triphenylmethyl bromide, synthesized by the method which has been described,[9] proceeded smoothly according to a procedure somewhat different from those which have been reported.[1,10]

The Grignard reaction was initiated by addition of about 1 ml. of an ethereal solution of ethylmagnesium bromide to 2.25 g. of magnesium turnings in a stirred solution of 2 g. of triphenylmethyl bromide in a mixture of 20 ml. of ether and 40 ml. of benzene. An additional 8.2 g. of crystalline bromide was added to the stirred solution during about 2 min. After completion of the addition, which caused spontaneous warming, the mixture was heated under reflux with stirring for 1.5 hr. As stirring under reflux was continued, a stream of carbon dioxide was bubbled through the reaction mixture for a period of about 8 hr. Solvent swept out by the stream of gas was replaced periodically with benzene. At the end of the addition period, a yellow precipitate had formed in the brown solution. After addition of 60 ml. of water, followed by 40 ml. of concd. hydrochloric

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(7) J. Cason and R. D. Smith, *J. Org. Chem.*, **18**, 1201 (1953).

(8) Melting points are corrected. Infrared spectra were recorded on a Baird double beam spectrophotometer. Gas chromatography was on silicone grease partitioning agent prepared as described by J. Cason and W. T. Miller, *J. Org. Chem.*, **24**, 1814 (1959). Microanalyses were by the Microanalytical Division, Department of Chemistry, University of California.

(9) W. E. Bachmann, *Org. Syntheses*, **Coll. Vol. III**, 842 (1955).

(10) J. Schmidlin, *Ber.*, **39**, 628 (1906).

acid, the mixture was heated under reflux for 30 min. in order to decompose the complex included in the sticky yellow paste on the walls of the flask.[11] The precipitate containing the triphenylacetic acid was collected by suction filtration of the cooled mixture, washed with water, and then digested on the steam bath with a mixture of 200 ml. of 10% aqueous sodium hydroxide and 400 ml. of water. A gray precipitate was filtered from the cooled alkaline solution,[11] the clear filtrate was acidified with 100 ml. of concd. hydrochloric acid, and the mixture was heated on the steam bath for 2 hr. to coagulate the precipitated acid. The collected and dried product, which amounted to 7.62 g. (83.5%), m.p. 263–267° dec., was used for preparation of the acid chloride.

Triphenylacetyl chloride was prepared by that procedure of Zook and co-workers[1] in which thet hionyl chloride solution was poured into glacial acetic acid, except that a few drops of pyridine were added to the reaction mixture. Pyridine appeared to speed up greatly the rate of formation of acid chloride; crystallization of the product set in rapidly after addition to acetic acid, and there was an improved yield (60–64%) of product, m.p. 128–129°.

Ethyl triphenylacetate, prepared from the acid chloride as has been described,[1] was crystallized from 95% ethanol to yield material, m.p. 117–118°, with carbonyl absorption at 5.81 μ, in carbon tetrachloride solution (lit.,[1] m.p. 116–117°, 116.8–117.8°; absorption at 5.77 μ). This ester is partly separated from methyl trityl ketone by chromatography on alumina with hexane solvent. Some ester is eluted first, followed by a mixture of ester and ketone.

Methyl trityl ketone. (A) *From Grignard reagent.* A Grignard reagent was prepared in an atmosphere of nitrogen from 8.48 g. (58 mmoles) of methyl iodide and 1.22 g. (50.8 mmoles) of magnesium turnings in 40 ml. of ether. To this reagent, cooled in an ice-salt bath, there was added during 5 min. a solution of 0.9 g. (2.94 mmoles) of triphenylacetyl chloride in 15 ml. of ether. The stirred reaction mixture was allowed to warm to room temperature, then heated under reflux for 20 hr. The reaction mixture was decomposed by cautious addition of 20 ml. of a 1:1 mixture of ice and concd. hydrochloric acid. An ether extract of the product was washed with water, sodium hydroxide solution (removal of a red color), and saturated sodium chloride solution, then dried over magnesium sulfate.

The yellow oil remaining after removal of solvent from the ether extract weighed 0.636 g. and solidified on standing. Its infrared spectrum exhibited bands characteristic of methyl trityl ketone, triphenylmethane, and triphenylethane,[12] but no absorption at 5.81 μ, characteristic of ethyl triphenylacetate. Yields for the three products, based on the chromatography data in Table II, were the following: triphenylmethane, 153 mg. (21.3%); triphenylethane, 307 mg. (40.5%); methyl trityl ketone, 181 mg. (21.5%).

In a second run, carried out similarly with 1.7 g. of triphenylacetyl chloride, yields of products in the order listed above were 16.7%, 31.5%, and 17.0%.

Methyl trityl ketone. (B) *From cadmium reagent.* A Grignard reagent was prepared in 18 ml. of ether from 0.16 g. of magnesium turnings and excess methyl bromide which had been bubbled through sulfuric acid. This reagent was converted to the cadmium reagent in usual fashion[13] with 0.60 g. of anhydrous cadmium chloride. After distillation of ether and addition of 15 ml. of benzene, there was added at 10° during about 2 min. a solution of 1.0 g. of triphenylacetyl chloride in 5 ml. of benzene. After the cooling bath had been removed, there was no observable exothermic reaction as the mixture warmed to room temperature. The reaction was continued with stirring for 1 hr. at about 43°, then caked solid was scraped from the sides of the flask and the mixture was heated to reflux for 1 hr. As the temperature was raised, sudden boiling occurred and the mixture turned a bright yellow.

TABLE II

CHROMATOGRAPHY OF REACTION PRODUCT FROM METHYLMAGNESIUM IODIDE AND TRIPHENYLACETYL CHLORIDE[a]

Fraction No.	Eluting Solvent	Wt. Eluted, Mg.	Infrared Absorp. in 5–6 μ Region
1	Hexane	253[b]	none
2	Hexane	177[b]	
3	Hexane	30[b]	
4	Hexane	41[c]	
5	Hexane-benzene, 1:1	72[c]	5.88
6	Hexane-benzene, 1:3	35[c]	5.88
7	Hexane-benzene, 1:3	15	
8	Benzene	9	
9	Benzene-ether, 1:1	9	
10	Methanol	0	

[a] The crude reaction product, dissolved in 8 ml. of hexane, was applied to a column of 18 g. of alumina of activity 3, in a 20 mm. i.d. column. Except for the first fraction of 20 ml. of solvent, each fraction represents elution with 25 ml. of the indicated solvent. [b] Fractions 1–3 were taken as the yield of hydrocarbon. Analysis by gas chromatography indicated a ratio of about 2:1 for triphenylethane:triphenylmethane. Chromatography on a 3-m. column at 265°, with helium pressure of about 18 cm. of mercury, gave bands of retention times 22.2 and 27.0 min. The same retention times were observed for authentic samples of the hydrocarbons chromatographed sequentially. Samples of the hydrocarbons separated by gas chromatography gave infrared spectra identical with those of authentic samples. [c] Fractions 4–9 were taken as the yield of ketone. Recrystallization of fractions 4–6 from ethanol yielded 75 mg. of ketone, m.p. 135.5–137°, infrared absorption in carbon tetrachloride 5.88 μ (lit.,[1] m.p. 138°, infrared absorption 5.84 μ).

The reaction mixture was worked up in a usual fashion for cadmium reactions,[13] and there was obtained 0.54 g. of a yellow oil from which no significant crystallization could be obtained in ethanol. Chromatography on alumina of activity 3 gave a pattern similar to that recorded in Table III. Recrystallization of the methyl trityl ketone yielded material of m.p. 137.5–139°. Yield data are recorded in Table I.

Yield data and conditions for two additional runs are recorded in Table I.

Reaction of ethylmagnesium bromide with triphenylacetyl chloride. The Grignard reagent from 2.14 g. (19.6 mmoles) of ethyl bromide in 14 ml. of ether was added during about 10 min., at 15–20°, to a stirred suspension of 1.0 g. (3.27 mmoles) of triphenylacetyl chloride in 10 ml. of ether. A gray precipitate formed as the Grignard reagent was added. After the mixture had been stirred for 1.5 hr. at room temperature, it was decomposed with ice and acid and worked up essentially as described for the reaction with the methyl Grignard reagent.

The product of the reaction was 0.87 g. of a colorless viscous oil containing some solid. The infrared spectrum

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(11) In some instances, complex remained undecomposed after this treatment and was a part of the precipitate insoluble in sodium hydroxide. Further digestion on the steam bath of the alkali-insoluble precipitate with 100 ml. of ethanol and 40 ml. of concd. hydrochloric acid liberates the remainder of the product.

(12) The principal absorption bands (μ) for the two hydrocarbons are the following: triphenylmethane, 3.30, 3.34, 3.51, 9.27, 9.68, 13.36, 13.68, 14.33; triphenylethane, 3.30, 3.35, 3.40, 9.71, 13.14, 14.33.

(13) J. Cason and F. S. Prout, *Org. Syntheses*, **Coll. Vol. III**, 601 (1955).

showed no absorption in the carbonyl region, but a sharp band at 2.83 μ. Chromatography of this material on 25 g. of alumina of activity 3 gave rather clean-cut separation of two components present in a ratio of about 1:1.3. The first component, *ethyltritylcarbinol*, which was present in the smaller amount, was eluted with hexane. After two crystallizations from hexane, the melting point was 92–93.6°, and there was a sharp absorption band at 2.83 μ.

Anal. Calcd. for $C_{22}H_{22}O$: C, 87.4; H, 7.3. Found: C, 87.0; H, 7.3.

The second component, *2,2,2-triphenylethanol* was eluted with 1:1 hexane-benzene. After two crystallizations from hexane, the melting point was 108.8–109.9°, and there was infrared absorption at 2.82 μ, but the spectrum differed substantially in other areas from that of ethyltritylcarbinol. Melting points reported for 2,2,2-triphenylethanol are 103–105°,[1] 104–105°,[14] 107°,[15] and 110.5°.[16]

Chromic acid oxidation of ethyltritylcarbinol. A solution of 32.4 mg. of the alcohol of m.p. 92–93.6°, and of 10.7 mg. of chromic anhydride, in 1 ml. of glacial acetic acid (distilled from permanganate) was allowed to stand at room temperature for about 14 hr. At the end of this period, clear needles had crystallized from the solution. After 10 ml. of water had been added to the reaction mixture the product was collected, washed with water, and dried: wt. 25 mg. (78%), m.p. 122.8–124°. The infrared spectrum of this product was identical with that of ethyl trityl ketone, m.p. 122.5–125° (*cf.* below).

Ethyl trityl ketone was prepared from diethylcadmium and triphenylacetyl chloride according to the procedure described for preparation of methyl trityl ketone. Yield data are recorded in Table I. The ketone, separated by chromatography on alumina of activity 3, was crystallized twice from ethanol to yield material of m.p. 122.5–125°.

Anal. Calcd. for $C_{22}H_{20}O$: C, 88.0; H, 6.7. Found: C, 87.9; H, 6.8.

The hydrocarbon mixture separated by chromatography on alumina was analyzed by gas chromatography and found to exhibit only the band for triphenylmethane and that assigned to triphenylpropane. At 257°, in a 1.6-m. column, under conditions giving retention times of 5.4 and 6.5 min. for triphenylmethane and -ethane respectively, the time for the band assigned to triphenylpropane was 7.8 min.

n-Butyl trityl ketone was prepared in a cadmium reaction carried out similarly to those described for its homologs. Separation of the ketone from the hydrocarbons by chromatography on alumina of activity 3 was somewhat less clean-cut than for the lower homologs, but was satisfactory. Chromatography of a reaction product weighing 765 mg. yielded an initial fraction of 397 mg. of a mixture of ketone and hydrocarbons. Succeeding fractions of ketone contained less than 1% hydrocarbons and weighed 362 mg. The mixture in the initial fraction was analyzed by gas chromatography and found to contain 92 mg. of triphenylmethane, 171 mg. of 1,1,1-triphenylpentane, and 132 mg. of butyl trityl ketone. In a 3-m. column, at 290° and with 21 cm. of helium pressure, retention times for the three compounds, in the order mentioned above, were 15.0, 28.5, and 43 min. For analysis, the ketone was crystallized from ethanol to yield material of m.p. 82.8–83.8°.

Anal. Calcd. for $C_{24}H_{24}O$: C, 87.8; H, 7.3. Found: C, 87.5; H, 7.3.

1,1,1-Triphenylpentane was separated by gas chromatography, in a 3 m. 15 mm. o.d. column, of the first fraction of material separated by chromatography on alumina. After crystallization from ethanol, there was obtained hydrocarbon of m.p. 60–61.2°.

Anal. Calcd. for $C_{23}H_{24}$: C, 92.0; H, 8.0. Found: C, 91.8; H, 8.0.

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[14] S. Weinstein, B. K. Morse, E. Grunwald, K. C. Schrieber, and J. Corse, *J. Am. Chem. Soc.*, **74**, 1119 (1952).

[15] W. Schenk and R. Ochs, *Ber.*, **49**, 610 (1916).

[16] J. Danilow, *J. Russ. Phys. Chem. Soc.*, **51**, 122 (1920).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Factors in Aldol Condensations of Alkyl Acetates with Benzophenone and Reversals by Sodium Amide Versus Lithium Amide. Metallic Cation Effects[1]

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The condensations of ethyl, isopropyl, and *t*-butyl acetates with benzophenone to form the corresponding β-hydroxy esters were effected by sodium amide in liquid ammonia, but controlled conditions were required with the first two alkyl acetates. Certain of these conditions were the same as those previously used with lithium amide, but certain of them were different. In contrast to lithium amide, sodium amide failed to effect the condensation of ethyl acetate with acetophenone. Four β-hydroxy esters were shown to undergo cleavages with catalytic amounts, and, in certain cases, with equivalent amounts of sodium amide in liquid ammonia but not with lithium amide. Possible reasons for these cleavages are discussed. Metallic cation effects and mechanisms are considered. The condensations are suggested to require the formation of a weaker base.

In a previous investigation[3] it was shown that ethyl and isopropyl acetates can be condensed with benzophenone by means of one equivalent of lithium amide in liquid ammonia to form the corresponding β-hydroxy esters, provided the ketone is added to the reaction mixture soon after the alkyl acetate. Otherwise the alkyl acetate undergoes self-condensation. In the present investigation it was found that these condensations can be effected similarly with one equivalent or slightly more of sodium amide in liquid ammonia provided that, not only is the ketone added immediately after the ester, but also that the reaction mixture is neutralized within a few minutes. Otherwise the

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[1] Supported in part by the Office of Ordnance Research, U. S. Army.

[2] Allied Chemical and Dye Corporation Fellow, 1958–59.

[3] W. R. Dunnavant and C. R. Hauser, *J. Org. Chem.*, in press.