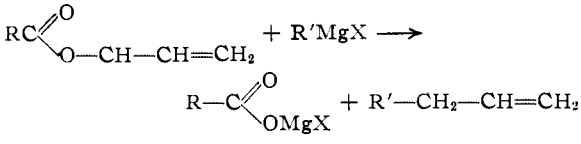
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

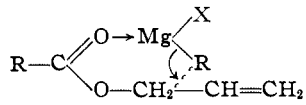
On the Mechanism of Grignard Cleavage of Allylic Esters

BY RICHARD T. ARNOLD AND SCOTT SEARLES, JR.[1]

Previous publications[2,3,4] from this Laboratory have described the reaction of allylic esters of hindered carboxylic acids to give olefinic hydrocarbons and halomagnesium salts

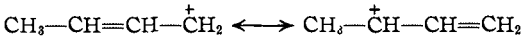


It was suggested[4] that the reaction follows a quasi six-membered ring mechanism, involving a reaction intermediate of the form



With this mechanism only one hydrocarbon product, derived from attachment of the Grignard radical to the alpha position of the allylic group, should be formed from the reaction of a Grignard reagent with an appropriate ester.

This mechanism was suggested when it was found that crotylbenzene was the only hydrocarbon product from the reaction of crotyl mesitoate and phenylmagnesium bromide. If the butenyl carbonium ion



were a reaction intermediate, a mixture of crotylbenzene and α-methylallylbenzene would be expected as the hydrocarbon product, since both crotyl and α-methylallyl halides commonly give mixtures of allylic isomers in reactions which involve the butenyl carbonium ion.

Further studies on the Grignard cleavage of esters have now been carried out. It has been found that the reaction of α-methylallyl mesitoate and phenylmagnesium bromide also produces crotylbenzene in good yield, while the isomeric α-methylallylbenzene, which would be predicted by the quasi six-membered ring mechanism to be the only product, was not detected. Identification of crotylbenzene was made by means of physical properties, isomerization to 1-butenylbenzene, and reduction to *n*-butylbenzene, from which the known diacetamido derivative was prepared. It appears, therefore, that the cyclic mechanism previously proposed for the Grignard cleavage reaction is not general. Actually inspection of models indicates α-methylallyl mesitoate is a sterically unfavorable case for quasi six-membered ring formation, as the α-carbon atom of the α-methylallyl group is well shielded by the adjacent groups.

The fact that cleavage of either the crotyl or the α-methylallyl ester gives crotylbenzene as apparently the only hydrocarbon product suggests that the same intermediate is formed in both cases. It is well known that both crotyl chloride and α-methylallyl chloride give the *n*-butenyl grouping predominately in several reactions which apparently involve the butenyl carbonium ion as a common intermediate. Pertinent examples are the reactions of these compounds with cuprous cyanide,[5] butylmagnesium bromide,[6] and allylmagnesium bromide[7]; in the first two the secondary butenyl group is found in less than 10% of the product. It is believed that the scale of our experiments was too small and our fractional distillation apparatus was inadequate to detect the small amount of α-methylallylbenzene which may have been present in the olefinic cleavage products.

In the reaction of hexen-2-yl-4 mesitoate with phenylmagnesium bromide, however, it was possible to detect the presence of the two isomeric hydrocarbons predicted by the ionic mechanism of cleavage.[2] The olefinic hydrocarbon product here was found to be a mixture of the two allylic isomers, hexen-2-yl-4-benzene and hexen-3-yl-2-benzene, identified by reduction to the corresponding alkylbenzenes and formation of solid diacetamido derivatives of the latter.

The cleavage of esters by Grignard reagents is not restricted to allylic esters, but seems to occur with any ester having the following two requirements: (1) a group attached to oxygen which is capable of forming a relatively stable carbonium ion, and (2) sufficient steric hindrance about the carbonyl group to retard the normal addition reaction. Since the *t*-butyl group is relatively stable as a carbonium ion, it should satisfy the first of these requirements. We have found that the reaction of *t*-butyl mesitoate with phenylmagnesium bromide gives *t*-butylbenzene and the bromomagnesium salt of mesitoic acid under the usual conditions employed for cleavage of allylic esters. The reaction of triphenylmethyl acetate with methylmagnesium bromide, which is reported by Fieser and Heymann[8] to give 1,1,1-triphenylethane in 61% yield, is another interesting example of the Grignard cleavage of esters. In this ester the alpha carbon atom of the O-alkyl group is shielded by three phenyl groups, so that formation of a ring-type complex would be hindered sterically, and the ease of the reaction is apparently due to the

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(2) Arnold, Bank and Liggett, THIS JOURNAL, **63**, 3444 (1941).
(3) Arnold and Liggett, *ibid.*, **64**, 2875 (1942).
(4) Arnold and Liggett, *ibid.*, **67**, 337 (1945).
(5) Lane, Fentress and Sherwood, *ibid.*, **66**, 545 (1944).
(6) Henne, Chanan and Turk, *ibid.*, **63**, 3474 (1941).
(7) Young, Roberts and Wax, *ibid.*, **67**, 841 (1945).
(8) Fieser and Heymann, *ibid.*, **64**, 376 (1942).

stability of the triphenylmethyl carbonium ion. Furthermore, it is reported that the cleavage reaction occurs with 2-methyl-10-acetoxyanthrone-9 also, but not with benzhydryl acetate or fluorenyl acetate; it thus would appear that the cleavage reaction is facilitated by structural features which stabilize the carbonium ion derived from the O-alkyl group.

Experimental[9]

α-Methylallyl Mesitoate.—A solution of 23 g. of methylvinylcarbinol, 35 g. of pyridine and 75 ml. of chloroform was added to a stirred solution of 52.5 g. of mesitoyl chloride and 65 ml. of chloroform at 5–15°. The reaction mixture was allowed to stand twelve hours at 5° and then was washed with water and 5% hydrochloric acid. After drying over calcium sulfate the solution was distilled to give 48 g. (76.5%) of the colorless product; b. p. 79–81° (10^{-3} mm.); $n^{20}D$ 1.5041.

Anal. Calcd. for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.10; H, 8.23.

Ozonization gave formaldehyde as the only volatile aldehyde, identified as its dimedon derivative; yield 74%; m. p. and mixed m. p. with authentic sample 187–188°.

Crotylbenzene.—A Grignard solution prepared from 12 g. of bromobenzene, 2.0 g. of magnesium and 25 ml. of ether was added to 13 g. of α-methylallyl mesitoate dissolved in 50 ml. of ether. After the reaction mixture was allowed to stand twenty hours at room temperature it was decomposed with slightly acidified ammonium chloride solution and the ether solution was extracted thoroughly with 5% sodium hydroxide solution. Fractional distillation of the ether layer gave 6.4 g. (81% of theory) of olefinic product; b. p. 61–62° (10 mm.); $n^{28}D$ 1.5091.

Acidification of the aqueous layer gave 8.1 g. (83%) of mesitoic acid; m. p. 151.5–152°.

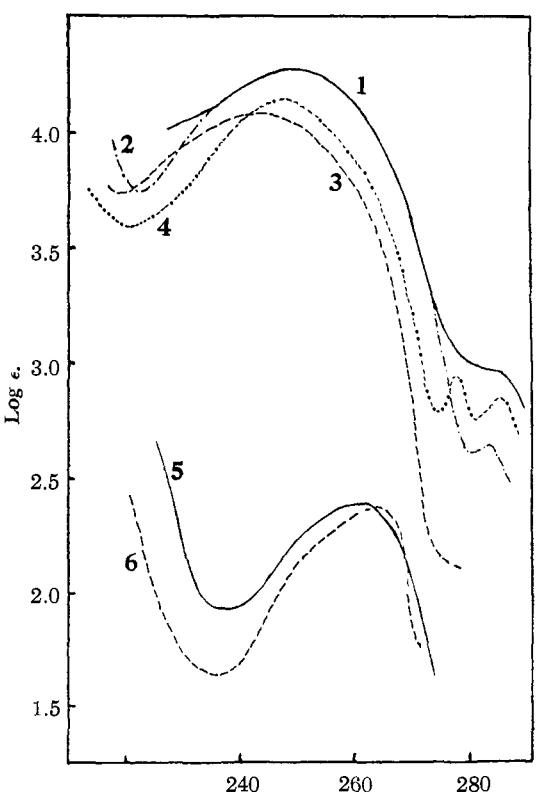


Fig. 1.—Absorption spectra: 1, 1-butenylbenzene; 2, β-methylstyrene[10]; 3, α-methylstyrene[10]; 4, styrene[11]; 5, crotylbenzene (cleavage product); 6, allylbenzene.[11]

1-Butenylbenzene.—A solution of 2 g. of crotylbenzene, 4 g. of potassium hydroxide and 18 ml. of 95% ethanol was refluxed twenty hours. After removal of the ethanol by distillation, the residue was extracted with water and ether. Distillation of the ether layer gave 1.5 g. of a colorless product; b. p. 178–180°; $n^{28}D$ 1.5160. The ultraviolet absorption spectrum (Fig. 1) shows that the side-chain double bond has been isomerized to the conjugated position.

1-Butylbenzene.—A solution of 13.4 g. of crotylbenzene (olefinic cleavage product) in 30 ml. of methanol was reduced with hydrogen over Adams platinum oxide catalyst at 25° and 2 atmospheres pressure, the theoretical up-take of hydrogen being observed. The catalyst was removed by filtration, and distillation of the solution gave 10 g. of a colorless product; b. p. 68–69° (16 mm.), 180–181° (atm. press.); $n^{20}D$ 1.4897.

The diacetamido derivative melted at 212.5–214° (lit.[12] value, 214°).

Hexen-2-yl-4 Mesitoate.—This ester was prepared from 41.5 g. of mesitoyl chloride, 26 g. of hexen-2-ol-4 and 23 g. of pyridine in chloroform as the solvent by the method described for α-methylallyl mesitoate. The ester boiled at 110–114° (10^{-3} mm.); yield 15 g. (27%).

Anal. Calcd. for $C_{15}H_{22}O_2$: C, 75.24; H, 8.68. Found: C, 75.46; H, 9.08.

Cleavage of Hexen-2-yl-4 Mesitoate.—The Grignard solution prepared from 9.5 g. of bromobenzene, 1.65 g. of magnesium and 50 ml. of ether was added to 10 g. of hexen-2-yl-4 mesitoate dissolved in 50 ml. of ether. After being warmed under reflux for an hour the reaction mixture was allowed to stand at room temperature for fifteen hours and then was processed in the manner described above for the α-methylallyl mesitoate cleavage. A 58% yield of mesitoic acid (3.9 g.) was obtained. The olefin product was hydrogenated over platinum oxide catalyst in methanol at room temperature under 2 atmospheres pressure to give 4.0 g. (61%) of a colorless hydrocarbon; b. p. 140–141° (80 mm.).

The melting point of the diacetamido derivative, prepared by the general method of Ipatieff and Schmerling[12] was 163–164° and was not changed by repeated recrystallizations. The melting points of the diacetamido derivatives of authentic samples of 2-phenylhexane and 3-phenylhexane were 178.5–179° and 201.5–202°, respectively, in close agreement with the literature values[13]; mixed m. p. of the two authentic compounds, 163–165°; mixed m. p. of either authentic compound with the derivative of the cleavage hydrocarbon, 163–165°.

***t*-Butylbenzene.**—A phenylmagnesium bromide solution prepared from 33.8 g. of bromobenzene, 5.1 g. of magnesium and 100 ml. of ether was added to 30 g. of *t*-butyl mesitoate[14] dissolved in 50 ml. of ether. The reaction mixture was allowed to stand for thirty hours and then was processed in the manner described for the cleavage of α-methylallyl mesitoate. The yield of mesitoic acid was 20 g. (50%); m. p. 152–153°. Fractional distillation of the neutral product gave 5.8 g. of *t*-butylbenzene (24%); b. p. 59–60° (14 mm.), 166–166.5° (742 mm.); $n^{18}D$ 1.4963; m. p. of diacetamido derivative, 209–210° (lit.[12] value, 210°).

Summary

The reactions of α-methylallyl mesitoate,

(9) All melting points and boiling points are reported uncorrected.

(10) Spectrograms 119 and 121, Am. Pet. Res. Proj. 44, Nat. Bur. Standards, Washington, D. C. (1945).

(11) Ramart-Lucas and Amagat, *Bull. soc. chim.*, **51**, 965 (1932).

(12) Ipatieff and Schmerling, THIS JOURNAL, **59**, 1056 (1937).

(13) Gilman and Meals, *J. Org. Chem.*, **8**, 126 (1943).

(14) Cohen and Schneider, THIS JOURNAL, **63**, 3382 (1941).

hexen-2-yl-4 mesitoate and *t*-butyl mesitoate with the phenyl Grignard reagent have been studied.

The results favor the ionic mechanism previously proposed for the cleavage reaction.

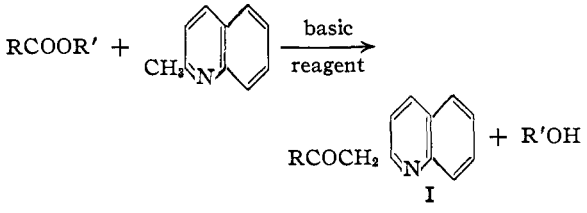
MINNEAPOLIS, MINNESOTA RECEIVED OCTOBER 18, 1948

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF DUKE UNIVERSITY]

The Acylation and Carbethoxylation of Quinaldine, Lepidine and α-Picoline Using Sodium Amide or Potassium Amide[1,2]

BY MARTIN J. WEISS[3] AND CHARLES R. HAUSER

Like methyl ketones, α- and γ-methyl pyridyl systems such as α-picoline, quinaldine and lepidine, which may be regarded as methyl ketones or their vinylogs in the ammonia system of compounds,[4] may undergo the Claisen type of acylation or carbethoxylation. For example, quinaldine may be acylated with esters in the presence of suitable basic reagents to form the corresponding acyl derivative (I).



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However, the scope of the methods for effecting such reactions has previously been somewhat limited. An alkoxide (potassium ethoxide) has been employed apparently only for the acylation of quinaldine and lepidine with ethyl oxalate,[5] which is a relatively reactive ester. Potassium amide[4] in ether has been used for the aroylation of quinaldine with ethyl benzoate and certain other aromatic esters but the method failed with α-picoline or lepidine and ethyl benzoate and also with quinaldine and ethyl acetate or ethyl oxalate. Potassium amide in liquid ammonia was later used successfully for the benzoylation of lepidine[6] but no details were given. Phenyllithium has been employed for the acylation of α-picoline with ethyl acetate,[7] acetyl chloride,[8] acetic anhydride,[7,8] benzoyl chloride,[8,9] benzoic anhydride[8] and half acid chlorides of certain dibasic acid esters,[10] but most of the yields have been low. In certain cases further condensation products have been reported.[7,8]

In the present investigation the recently developed alkali amide method[11] for the acylation and carbethoxylation of ketones has been adapted to the acylation and carbethoxylation of α-picoline, quinaldine and lepidine. The process consists in first converting the methyl pyridyl compound essentially completely to its sodium or potassium derivative by means of sodium or potassium amide and then reacting the alkali derivative with the acylating or the carbethoxylating agent. With esters and probably also with anhydrides or acid chlorides, the resulting acyl or carbethoxyl derivative is converted in the reaction mixture to its alkali derivative; this acid-base reaction may be effected either by part of the alkali derivative of the methyl pyridyl compound or by excess alkali amide. These three steps may be illustrated by the following equations in which CH_3P represents the methyl pyridyl system.

$$CH_3P + KNH_2 \longrightarrow K(CH_2P) + NH_3 \quad (1)$$

$$RCO_2R' + K(CH_2P) \longrightarrow RCOCH_2P + KOR' \quad (2)$$

$$RCOCH_2P + K(CH_2P) \longrightarrow K(RCOCHP) + CH_3P \quad (3)$$
$$\text{or } KNH_2 \qquad\qquad\qquad\qquad\qquad\qquad \text{or } NH_3$$

On the basis of this interpretation it has seemed advantageous to employ either two molecular equivalents of alkali amide to one of methyl pyridyl compound and at least one of ester (Method A)[12] or two equivalents each of alkali amide and methyl pyridyl compound to one of ester (Method B). It may be considered that, in Method A, the third step is effected by the extra equivalent of alkali amide whereas, in Method B, the third step is effected by part of the alkali derivative of the methyl pyridyl compound which is formed in the first step. Obviously half of the methyl pyridyl compound would be regenerated in the third step of Method B.

(1) Paper XLIII on Condensations; paper XLII, THIS JOURNAL, **71**, 1350 (1949).

(2) Part of this work was supported by a grant from the Duke University Research Council.

(3) Eli Lilly Fellow, 1947–1948.

(4) Bergstrom and Moffat, THIS JOURNAL, **59**, 1494 (1937).

(5) Wislicenus and Kleisinger, *Ber.*, **42**, 1140 (1909).

(6) Bergstrom, *Chem. Rev.*, **35**, 184 (1944).

(7) Beets, *Chem. Weekblad*, **39**, 187 (1942); *C. A.*, **37**, 5064 (1943).

(8) Kloppenburg and Wibaut, *Rec. trav. chim.*, **65**, 393 (1946).

(9) Bergmann and Rosenthal, *J. prakt. Chem.*, [2] **135**, 267 (1932).

(10) Graef, Fredericksen and Burger, *J. Org. Chem.*, **11**, 257 (1945).

(11) See Adams and Hauser, THIS JOURNAL, **66**, 1220 (1944); Levine and Hauser, *ibid.*, **66**, 1768 (1944).

(12) Bergstrom and Moffat[4] reported that, in the benzoylation of quinaldine with an equivalent of ethyl benzoate in ether, the use of two and one-half equivalents of potassium amide gave a 60% yield of 2-phenacylquinoline whereas the use of two equivalents gave only a 35% yield. However, we have obtained a 62% yield with two equivalents of the base. It should be mentioned also that, in the benzoylation of lepidine in liquid ammonia, the yield of 4-phenacylquinoline was actually greater (37%) with two equivalents of sodium amide than with two and one-half equivalents (28%).