(1.89 g.) were obtained. These were recrystallized from an equal mixture of benzene and alcohol, m. p. 155.0–155.5°. *Anal.* Calcd. for $C_{30}H_{22}$: C, 94.20; H, 5.80. Found: C, 94.57; H, 5.67.

(B) 3-(3-Xenyl)-Δ^2-cyclohexenone (III) was prepared as described above.

A 40-ml. dry ether solution of the substance (17.6 g.) was added to a 40-ml. dry ether solution of 4-xenyllithium, prepared from 4-xenyl bromide (35.0 g.) and lithium (0.76 g.). Hydrolysis of the complex formed was effected as before with 10% sulfuric acid (50 ml.) and the resulting mixture was steam-distilled until there was no further appearance of organic material in the distillate. The residue was extracted with benzene, the extract being then washed successively with sodium bicarbonate solution and with water and finally dried over magnesium sulfate. This was filtered and the solvent allowed to evaporate. The resulting residue of 1-(3-xenyl)-3-(4-xenyl)-cyclohexediene-1,3 was not purified further.

This crude product (3.60 g.) was aromatized as described in procedure A, and the residue taken up in benzene. After filtration and addition of about four times the volume of ethyl alcohol, crystals of 1-(4-xenyl)-3-(3-xenyl)-benzene (IX) were obtained which upon recrystallization from an equal mixture of benzene and ethyl alcohol melted at 153–154°. Mixed melting point with the product obtained by procedure A showed no depression.

Preparation of 1,3-Di-(3-xenyl)-benzene (X).—A Grignard solution prepared in dry ether (40 ml.) from 3-xenyl bromide (30.3 g.) and magnesium (3.2 g.) was treated with a dry ether solution (20 ml.) of 3-(3-xenyl)-Δ^2-cyclohexenone (III). The Grignard complex was isolated as before by rapid filtration of the chilled ether reaction mixture. The precipitate obtained was hydrolyzed with cold 10% sulfuric acid and then extracted with ether. The extract was washed with water and sodium bicarbonate solution and dried over magnesium sulfate. After removal of the solvent, distillation of the residue in the Hickmann apparatus yielded a very viscous yellow liquid (11.36 g.). Attempts to crystallize this material were unsuccessful.

Dehydrogenation of this substance was accomplished as before, by adding dropwise the 1,3-di-(3-xenyl)-cyclohexediene-1,3 (7.55 g.) to a refluxing mixture of 5% palladinized charcoal (4 g.) in *p*-cymene (25 ml.). The reaction mixture was worked up as before using ethyl alcohol, but crystallization from this solution yielded an oil. A portion of this oil was dissolved in benzene–petroleum ether (30–60°) and, upon cooling, crystalline material precipitated, which upon recrystallization from benzene and petroleum ether, yielded 1,3-di-(3-xenyl)-benzene, melting at 97–98°. *Anal.* Calcd. for $C_{30}H_{22}$: C, 94.20; H, 5.80. Found: C, 94.60; H, 5.89.

Summary

The reaction of the monoethyl ether of dihydroresorcinol with organo-metallic reagents has been extended to include the preparation of 1-phenyl-3-(3-xenyl)-benzene, 1-(4-xenyl)-3-(3-xenyl)-benzene and 1,3-di-(3-xenyl)-benzene.

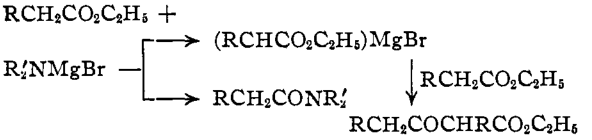
COLLEGE PARK, MD. RECEIVED SEPTEMBER 23, 1948

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF DUKE UNIVERSITY]

Condensations of Esters by Diisopropylaminomagnesium Bromide and Certain Related Reagents[1]

BY FREDERICK C. FROSTICK, JR., AND CHARLES R. HAUSER

Dialkylaminomagnesium bromides may react with esters either at the α-hydrogen, effecting their condensations, or at the carbonyl carbon to form the corresponding N,N-dialkylamide, thus



$$\mathrm{RCH_2CO_2C_2H_5} + \mathrm{R'_2NMgBr} \begin{cases} \longrightarrow (\mathrm{RCHCO_2C_2H_5})\mathrm{MgBr} \xrightarrow{\mathrm{RCH_2CO_2C_2H_5}} \mathrm{RCH_2COCHRCO_2C_2H_5} \\ \longrightarrow \mathrm{RCH_2CONR'_2} \end{cases}$$

Diethylaminomagnesium bromide has recently been shown[2] to effect the self-condensation of ethyl phenylacetate, *t*-butyl acetate and certain other esters but not ethyl *i*-valerate and ethyl *i*-butyrate with which the amide is presumably formed. This reagent self-condensed ethyl *n*-butyrate, but the condensation product was contaminated with the amide. The condensation product from ethyl propionate was reported free of the amide, but later work has shown that this condensation product also is generally contaminated with the amide.[3]

In the present investigation, diisopropylaminomagnesium bromide has been found to be a more suitable condensing agent than diethylaminomagnesium bromide. The diisopropyl reagent effects in good yield the self-condensation not only of the straight chain esters, ethyl propionate, ethyl *n*-butyrate and methyl laurate, but also that of the branched chain esters, ethyl *i*-valerate and ethyl *i*-butyrate, which are known to be more difficult to condense. The results are summarized in Table I. The yields have been based on the diisopropylaminomagnesium bromide since a 10% excess of the ester was employed; however, the yields would be approximately the same if they were based on the ester used minus that recovered. The condensation products were shown by the sodium fusion test for nitrogen to be free from the amide with the exception of that from ethyl *i*-valerate when the reaction time was twenty hours; in this case, secondary reactions appeared to have occurred. The products obtained when the reac-

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[1] Paper XLII on "Condensations"; paper XLIII, THIS JOURNAL, 71, 770 (1949).

[2] Hauser and Walker, *ibid.*, 69, 295 (1947).

[3] In a private communication, Dr. Robert W. Holley of the State College of Washington, Pullman, Washington, has stated that the condensation product he obtained from ethyl propionate using diethylaminomagnesium bromide was contaminated with the amide. We have similarly found that this condensation product is contaminated with the amide (as detected by the sodium fusion test) when the reaction is carried out for either one-half hour or for four hours.

tion time was four hours were converted by ketonic cleavage to the corresponding ketones which were obtained in good yields. With ethyl diethylacetate, diisopropylaminomagnesium bromide gave, after a reaction time of two and one-half hours, a mixture containing nitrogen. An attempt to self-condense ethyl diphenylacetate with this reagent failed even after twenty hours, 55% of the original ester being recovered. However, the magnesium enolate of ethyl diphenylacetate was evidently formed since, on treatment of the reaction mixture with benzoyl chloride after one-half hour, ethyl benzoylidiphenylacetate was obtained in 38% yield.

$$(C_6H_5)_2CHCO_2C_2H_5 \xrightarrow{[(CH_3)_2CH]_2NMgBr} [(C_6H_5)_2CCO_2C_2H_5]MgBr \xrightarrow{C_6H_5COCl} C_6H_5COC(C_6H_5)_2CO_2C_2H_5$$

The present method for self-condensing esters is conveniently carried out and the condensing agent, diisopropylaminomagnesium bromide, is readily prepared from standardized ethylmagnesium bromide and diisopropylamine which is available commercially. Diisopropylaminomagnesium bromide is particularly suitable for the self-condensations of ethyl *i*-valerate and ethyl *i*-butyrate which are not condensed by sodium alkoxides. Although sodium hydride[4] self-condenses ethyl *i*-valerate, and sodium[5] and potassium triphenylmethide[6] and mesitylmagnesium bromide[7] self-condense both ethyl *i*-valerate and ethyl *i*-butyrate, diisopropylaminomagnesium bromide is probably more convenient to use.

Certain esters have also been condensed by means of dicyclohexylaminomagnesium bromide and di-*n*-butylaminomagnesium bromide. With the dicyclohexyl reagent, both ethyl *n*-butyrate and ethyl *i*-valerate were self-condensed to form β-keto esters which were free from the amide. However, the yields were somewhat lower than those obtained with the diisopropyl reagent. Moreover, working up the reaction mixture is more convenient with the diisopropyl reagent than with the dicyclohexyl reagent. With the di-*n*-butyl reagent, some amide formation appeared to occur along with the self-condensation of ethyl *i*-valerate since the condensation product gave a positive test for nitrogen.

These results indicate that, as the complexity of the basic reagent is increased, the α-hydrogen reaction of an ester is favored over the reaction at the carbonyl carbon. Similarly, the relatively complex mesitylmagnesium bromide[7] and sodium[5] and potassium triphenylmethides[6] react with the α-hydrogen of ethyl *i*-valerate or ethyl *i*-butyrate effecting self-condensation whereas simpler basic reagents such as methyl or ethyl magnesium bromide[8] and sodium amide[9] appear to react mainly at the carbonyl carbon of the ester.

In these Claisen condensations by dialkylaminomagnesium bromides, the magnesium cation as well as the dialkylamino anion (both of which are present at least potentially) appears to be involved in the mechanism.[2] However, the magnesium appears to influence mainly the rate of the reaction[2] whereas the basic anion may influence both the rate and the equilibrium. Actually, the condensation has been possible only when a sufficiently weaker base is formed.[10] A study of these factors is in progress.

Experimental

Self-condensations of Esters by Diisopropylaminomagnesium Bromide.—In a 500-ml., three-necked flask equipped with a mercury-sealed stirrer, dropping funnel and reflux condenser (having a drying tube), was placed the appropriate quantity (0.2–0.4 mole) of standardized[11] ethylmagnesium bromide in ether solution. To the stirred mixture was added an equivalent number of moles of dry diisopropylamine in 50 ml. of dry ether at such a rate that the ether refluxed and stirring was continued for fifteen to thirty minutes to complete the formation of the diisopropylaminomagnesium bromide.[12] The ester (molar equivalent plus 10% excess) in 100 ml. of dry ether was added at such a rate that the ether refluxed gently. This addition required about one-half hour. In most cases, stirring was continued at room temperature (25–30°) for a longer period.

The reaction mixture was poured with stirring onto 300 g. of crushed ice mixed with 40–70 ml. of concentrated hydrochloric acid and the flask rinsed with some of the solution. After acidification, the ether phase was separated and the aqueous layer extracted twice with ether. The combined ether solution was washed with water, 10% sodium bicarbonate solution, and again with water, dried over Drierite, and the solvent distilled from a steam-bath. The residue was distilled *in vacuo* or recrystallized. Approximately 10–15% of the original ester was recovered in a low-boiling fraction obtained before the product distilled. The products were tested qualitatively for nitrogen by the sodium fusion method,[13] and certain of them were subjected to ketonic cleavage in the presence of acid.[14] The results are summarized in Table I.

With ethyl diethylacetate (b. p. 148.7–150°, 26.9 g., 0.187 mole), there was obtained, after a total reaction time of two and one-half hours, 9.5 g. (35% recovery) of the ester, b. p. 147–151°, and 13.8 g. of material boiling at 110–132° at 11 mm. which gave a positive test for nitrogen.

With ethyl diphenylacetate (m. p. 59.0–59.5°),[15] after refluxing on a steam cone for five hours and standing at room temperature for fifteen hours, 55% of the ester (m. p. 57–58°, mixed m. p. 57–59°) was recovered.

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(4) Swamer and Hauser, THIS JOURNAL, **68**, 2647 (1946).

(5) (a) Hauser and Renfrow, *ibid.*, **59**, 1823 (1937); (b) Hudson and Hauser, *ibid.*, **63**, 3156 (1941).

(6) Levine, Baumgarten and Hauser, *ibid.*, **66**, 1230 (1944).

(7) Spielman and Schmidt, *ibid.*, **59**, 2009 (1937).

(8) Runge, "Organometallverbindungen," Wissenschaftliche Verlagsgesellschaft m. b. H., Stuttgart, 1944, p. 377.

(9) Hauser, Levine and Kibler, THIS JOURNAL, **68**, 26 (1946).

(10) Renfrow and Hauser, *ibid.*, **60**, 463 (1938).

(11) One liter of two to four moles of ethylmagnesium bromide was prepared in the usual manner. The solution was standardized as described by Gilman, Wilkinson and Meyers, *ibid.*, **45**, 150 (1923).

(12) The complete formation of this reagent is indicated when ethane ceases to be evolved or when a test for the Grignard reagent with Michler's ketone is negative (see ref. 2).

(13) (a) McElvain, "The Characterization of Organic Compounds," The Macmillan Company, New York, N. Y., 1946, p. 40. (b) Shriner and fuson, "Identification of Organic Compounds," 3rd ed., John Wiley and Sons, Inc., New York, N. Y., 1948.

(14) Hudson and Hauser, THIS JOURNAL, **63**, 3163 (1941).

(15) The ester was prepared by the carbonation of diphenylmethane using potassium amide and esterifying the resulting acid; Yost and Hauser, *ibid.*, **69**, 2325 (1947).

TABLE I

SELF-CONDENSATIONS OF ESTERS BY DIISOPROPYLAMINOMAGNESIUM BROMIDE

Ester, ethyl	Reaction time, hr.[a]	β-Keto ester	B. p., °C., uncor.	Mm.	Yield, %
Propionate	4	Ethyl α-*n*-propionylpropionate[b]	92.5–94	19[j]	73[c]
n-Butyrate	1	Ethyl α-*n*-butyryl-*n*-butyrate[b]	101.5–104.5	11.5	65
n-Butyrate	4	Ethyl α-*n*-butyryl-*n*-butyrate[b]	102–104.5	12[k]	66[d]
i-Butyrate	1.3	Ethyl α-*i*-butyryl-*i*-butyrate[b]	88–92.5	15	48
i-Butyrate	2	Ethyl α-*i*-butyryl-*i*-butyrate[b]	90.5–93.5	15	55
i-Butyrate	4	Ethyl α-*i*-butyryl-*i*-butyrate[b]	91.5–94.5	15[l]	55[e]
i-Valerate	1	Ethyl α-*i*-valeryl-*i*-valerate[b]	117–118.5	15	61
i-Valerate	4	Ethyl α-*i*-valeryl-*i*-valerate[b]	116–118	14[m]	71[f]
i-Valerate	20	Ethyl α-*i*-valeryl-*i*-valerate	110–118	15	(55)[h]
Laurate (methyl)	4	Methyl α-lauryl-laurate[b,i]	37–39[n]	M. p.	92[g]

[a] Reaction time includes one-half hour for adding the ester and one-half hour on a steam-bath; additional time was at room temperature (25–30°). [b] Product gave a negative test for nitrogen. [c] Ketonic cleavage gave a 41% yield of diethyl ketone, b. p. 98–102°; m. p. of semicarbazone, 138–139° (ref. 13a, p. 240). [d] Ketonic cleavage gave an 84% yield of di-*n*-propyl ketone, b. p. 135–143°; m. p. of semicarbazone, 131–132° (ref. 13a, p. 240). [e] Ketonic cleavage gave a 68% yield of diisopropyl ketone, b. p. 120–125°; m. p. of 2,4-dinitrophenylhydrazone, 94–95° (ref. 13b, p. 262). [f] Ketonic cleavage gave a 69% yield of diisobutyl ketone, b. p. 163–166; m. p. of 2,4-dinitrophenylhydrazone, 91–92° (ref. 13a, p. 240). [g] Ketonic cleavage gave an 88% yield of laurone, m. p. 68–69° (ref. 13b, p. 264). [h] Product gave a positive test for nitrogen. [i] Product recrystallized from methanol at −5° after all traces of ether had been removed under vacuum. [j] Reported b. p. 92–93° at 20 mm. [Dieckmann and Kron, *Ber.*, **41**, 1269 (1908)]. [k] See ref. 17. [l] Hudson and Hauser, THIS JOURNAL, **63**, 3159 (1941). [m] Reported b. p. 118–119° at 15 mm. (see ref. 6). [n] Reported m. p. 38–40° [Hansley, U. S. Patent 2,158,071 (1939)].

Benzoylation of Ethyl Diphenylacetate.—To a solution of 0.227 mole of diisopropylaminomagnesium bromide in ether was added slowly 43.0 g. (0.179 mole) of ethyl diphenylacetate (m. p. 57–59°)[15] dissolved in 150 ml. of dry ether. The reaction mixture was refluxed on a steam cone for ten minutes during which time a thick cream-colored precipitate was formed. After stirring an additional thirty minutes, 35.0 g. (0.250 mole) of benzoyl chloride was added and the resulting mixture stirred for thirty minutes. The reaction mixture was poured with stirring onto 50 ml. of concentrated hydrochloric acid and 500 ml. crushed ice. The ether phase was separated and the white solid left with the aqueous phase was dissolved in ether after several extractions with this solvent. The combined ether solution was washed with water, dried with Drierite and the solvent distilled. The residue was treated with hydriodic acid and glacial acetic acid according to the procedure described previously.[16] There was obtained 23.1 g. (38% yield) of ethyl benzoyldiphenylacetate, m. p. 146–147.5°; a mixed melting point with a known sample, m. p. 147–148°,[16] was 146–148°.

Self-condensations of Esters by Other Dialkylaminomagnesium Bromides.—Dicyclohexylaminomagnesium bromide and di-*n*-butylaminomagnesium bromide were prepared by the action of ethylmagnesium bromide on equivalent amounts of dicyclohexylamine and di-*n*-butylamine, respectively. With the latter amine, the reaction mixture was refluxed for about one hour.

In the usual manner, ethyl *n*-butyrate was self-condensed by the dicyclohexyl reagent for one hour (total time) to form ethyl α-*n*-butyryl-*n*-butyrate, b. p. 103–106° at 12 mm. (reported b. p. 102–103° at 12 mm.)[17] in 46% yield. Ethyl *i*-valerate was self-condensed by this reagent for four hours to form ethyl α-*i*-valeryl-*i*-valerate, b. p. 116–118° at 14 mm. (reported b. p. 118–119° at 15 mm.)[6] in 55% yield. In these cases, approximately six liters of water was required to dissolve the aminomagnesium halide complex formed on pouring the reaction mixture onto the acid. Tests for nitrogen on these condensation products were negative.

Ethyl *i*-valerate was treated with di-*n*-butylaminomagnesium bromide for three hours to form a product boiling at 126–144° at 14 mm. which gave a positive test for nitrogen.

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Summary

1. Diisopropylaminomagnesium bromide effects satisfactorily the self-condensation of various esters including ethyl *i*-butyrate and ethyl *i*-valerate.

2. This reagent converts ethyl diphenylacetate to its magnesium enolate which has been benzoylated.

3. Certain esters have been condensed by dicyclohexylaminomagnesium bromide and by di-*n*-butylaminomagnesium bromide.

4. Comparisons have been made between various basic reagents in their reactions with esters where attack may occur at the α-hydrogen or at the carbonyl carbon atom.

DURHAM, N. C. RECEIVED SEPTEMBER 27, 1948

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(16) Hauser, Saperstein and Shivers, THIS JOURNAL, **70**, 608 (1948).

(17) Roberts and McElvain, *ibid.*, **59**, 2007 (1931).