EXPERIMENTAL

The volume of the solution contained in the sealed Carius tube (50 ml.) and the total volume of the tube (140 ml.) were determined by measuring an equivalent volume of water in a tube of comparable size. The volume of the diethyl ether solution of methylmagnesium iodide had not decreased appreciably during the twenty years of storage as the level of the top of the solution prior to opening the tube was even with the top of a blank label which had been placed on the tube to mark the initial volume. The tube had been wrapped in a towel and kept in a shatter-proof container throughout the twenty years it had remained sealed. There was no detectable rush of gas when the tube was opened after having been cooled for 4 hr. in an ice bath. By working promptly in an inert atmosphere according to the usual techniques employed when handling reactive organometallic compounds, all quantitative determinations were completed within 8 hr. after opening the tube. The samples used were removed by a pipette of previously determined volume which had been drawn out long enough to easily reach the solution in the tube and small enough to readily pass through the constricted neck of the tube.

The analytical procedures were essentially those reported earlier from this laboratory,[2] the chief difference being in the size of the sample used. The sulfuric acid in the gas wash bottle used in the gas analysis was replaced with fresh acid between the analyses of samples 6 and 7.

Acet-α-naphthalide (m.p. 159.5–160°) was prepared by the procedure previously reported from this laboratory,[8] and methylmercuric iodide (m.p. 146–147°) was prepared by the procedure of Marvel, Gauerke, and Hill.[9] A mixed melting point of a sample of each derivative with its respective authentic specimen was not depressed.

AMES, IOWA

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY, UNIVERSITY OF WISCONSIN]

Addition of Organometallic Reagents to α,β-Unsaturated Amides

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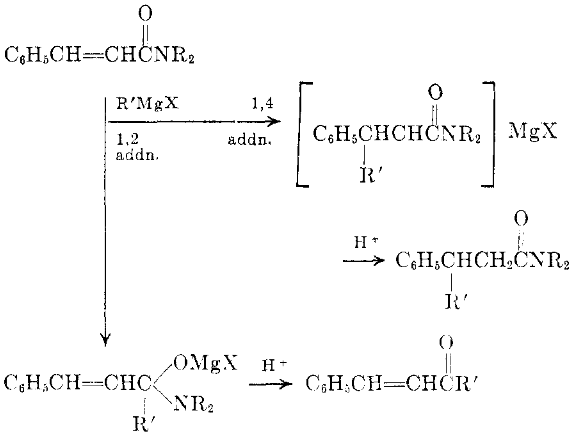
Phenyllithium adds *via* conjugate addition to *N,N*-dicyclohexylcinnamamide with no evidence of 1,2 addition, but adds 1,2 to *N,N*-dimethylcinnamamide.

N,N-Disubstituted α,β-unsaturated amides add phenyl and ethyl Grignard reagents by conjugate addition despite wide variations in the substituents. In contrast, methylmagnesium iodide yields some 1,2 addition and some unchanged starting material. The latter appears to involve a complex which regenerates the amide on hydrolysis. Enolization does not occur to an important extent in the formation of this intermediate.

An organometallic reagent may add to an unsaturated amide by normal addition to form an unsaturated ketone or by conjugate addition to form a saturated amide.



The reaction of phenylmagnesium bromide with *N*-ethylcinnamanilide was reported by Kohler and Heritage[3] to yield conjugate addition products. The investigation was extended by Maxim and Ioanid[4] to the condensation of several cinnamanilides with ethyl- and phenylmagnesium bromides and with methylmagnesium iodide.

In the present work, it was desired to determine the effect of wider variations in the structure of the amide on the course of the condensation. As the study progressed and the conjugate nature of the addition of the Grignard reagents was confirmed, the addition of phenyllithium to α,β-unsaturated amides became a further object of investigation.

The extent of 1,2 addition was found by comparison of the ultraviolet absorption spectrum of the products with a standard curve of the ketone produced. The extent of conjugate addition was determined by isolation of the saturated amide. The results of these and previously reported experiments are summarized in Table I. They illustrate a marked tendency of the unsaturated amides to undergo conjugate addition somewhat like that shown by the unsaturated ketones. For example, the reaction of phenylmagnesium bromide with *N,N*-dimethylcinnamamide yields 93% 1,4 addition[5] while isopropyl styryl ketone, which is almost identical sterically, yields 88% of the conjugate addition product.[6] However, the analogy is not

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[2] Rohm & Haas Co., Bridesburg, Philadelphia, Pa.

[3] E. P. Kohler and G. Heritage, *Am. Chem. J.*, **33**, 21 (1905).

[4] N. Maxim and N. Ioanid, *Bul. Soc. Chim. România*, 10, 29 (1928).

[5] G. Gilbert, *J. Am. Chem. Soc.*, **77**, 4413 (1955).

[6] E. P. Kohler, *Am. Chem. J.*, **38**, 511 (1907).

complete since phenylmagnesium bromide will produce 1,2-addition products with some unsaturated ketones, although none were obtained from the unsaturated amides. Even the relatively unhindered crotonylpiperidine showed no evidence of 1,2-addition with phenylmagnesium bromide. The method thus appears useful for the synthesis of β-substituted propionamides and their derivatives when the unsaturated amide and Grignard reagent are available.

TABLE I

SUMMARY OF ADDITION REACTIONS

Amide	Organometallic Reagent	Products % 1,2	Products % 1,4
N,*N*-Diphenylcinnamamide	C_6H_5MgBr[a]	0	100
	C_2H_5MgI	0	65
	C_2H_5MgBr[a]	0	100
	CH_3MgI[b]	45	0
Cinnamoyl piperidine	CH_3MgI[c]	10	0
N,*N*-Dicyclohexylcinnamamide	C_6H_5MgBr	0	97
	CH_3MgI[d]	10	0
	C_6H_5Li	0	68
N,*N*-Dimethylcinnamamide	C_6H_5MgBr[e]	0	93
	C_6H_5Li	72	0
Crotonylpiperidine	C_6H_5MgBr	0	51

[a] See ref. 4. [b] 42% recovered starting material. [c] 76% recovered starting material. [d] 87% recovered starting material. [e] See ref. 5.

In view of its well-known tendency to add *via* the normal route, phenyllithium was condensed with *N*,*N*-dimethyl- and *N*,*N*-dicyclohexylcinnamamide to determine whether it, too, would undergo conjugate addition. The cyclohexyl substituted amide did, indeed, yield 68% of *N*,*N*-dicyclohexyl-β,β-diphenylpropionamide, the conjugate addition product. There was no indication of benzalacetophenone, the 1,2 addition product, in the ultraviolet absorption spectrum of the crude product, a significant departure from the usual reactions of organolithium compounds. *N*,*N*-Dimethylcinnamamide yielded 72% benzalacetophenone on condensation with phenyllithium. It seems likely, therefore, that steric hindrance of the amide carbonyl by the bulky cyclohexyl substituents is at least partly responsible for the conjugate addition of phenyllithium.

The behavior of methylmagnesium iodide contrasts significantly with the other organometallic reagents studied. In reactions involving this reagent no 1,4 products, but some normal addition products and some starting material, were recovered. This anomalous behavior is particularly illustrated by comparison with the other alkylmagnesium halides. With *N*,*N*-diphenylcinnamamide, ethylmagnesium bromide and ethylmagnesium iodide both yielded only 1,4 addition products, while methylmagnesium iodide yielded 42% unchanged starting material and 45% benzalacetone, the product of 1,2 addition. Other investigators have also noted anomalies in the reactions of methylmagnesium iodide as evidenced by an unusual tendency to undergo 1,2 addition with unsaturated ketones. Smith and Hanson[7] added methylmagnesium iodide to benzalpropiophenone in the hope of obtaining 1,4 addition. However, all of the products isolated were those of 1,2 addition. When ethyl- or phenylmagnesium bromide were added to this ketone, only conjugate addition was observed.[6] Similarly, methyl propenyl ketone yields 75% 1,4 addition with methylmagnesium bromide[6] and 80% 1,2 addition with methylmagnesium iodide.[8]

In the reaction of methylmagnesium iodide with *N*,*N*-dicyclohexylcinnamamide, precipitation occurred on addition of the amide solution, indicating the formation of a stable intermediate. Essentially no gaseous products were evolved during the reaction, eliminating the possibility that an enol salt is the precursor of the recovered starting material. It seems likely, therefore, that methylmagnesium iodide forms a complex with the unsaturated amides which may be hydrolyzed to obtain the starting amide, but which does not undergo addition under the conditions of the reaction.

The coincidence of high yields of 1,2 addition products and the recovery of starting material as exclusive properties of methylmagnesium iodide seems to indicate that these two properties stem from the same difference in behavior with the other Grignard reagents studied here. Relation of this difference to the structure of the Grignard reagents probably must await a detailed explanation of the nature of Grignard reagents in solution and especially of the mechanism of addition of organometallic reagents to conjugated systems. Although considerable effort has been devoted to these ends, no generally accepted theory has as yet been evolved.[9]

EXPERIMENTAL

The organometallic reagents were prepared by the usual procedures in dry ether and brought to room temperature. In order to avoid the formation of complex products[3] the addition of the ethereal amide solution was carried out slowly and only to the point of persistence of the precipitate.

Condensation of ethylmagnesium iodide and N,N-diphenylcinnamamide. To the ethylmagnesium iodide prepared from 4.67 g. (0.03 mole) of ethyl iodide was added 2.9 g. (0.0097 mole) of *N*,*N*-diphenylcinnamamide, prepared by the method of Bernthsen,[10] in 200 ml. of ether and stirring was continued for 3 hr. After hydrolysis with dilute HCl, the ether solution was dried and the solvent evaporated, yielding 3.8

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[7] L. I. Smith and L. I. Hanson, *J. Am. Chem. Soc.*, **57**, 1326 (1935).

[8] L. P. Kyriakides, *J. Am. Chem. Soc.*, **36**, 661 (1914).

[9] See, for example, E. R. Alexander and G. R. Coraor, *J. Am. Chem. Soc.*, **73**, 2721 (1951); R. E. Lutz and W. G. Reveley, *J. Am. Chem. Soc.*, **63**, 3184 (1941); H. Gilman and R. G. Jones, *J. Am. Chem. Soc.*, **62**, 1243 (1940); C. G. Swain and L. Kent, *J. Am. Chem. Soc.*, **72**, 518 (1950); E. R. Alexander, *Principles of Ionic Organic Reactions*, John Wiley and Sons, New York, 1950, p. 190.

[10] A. Bernthsen, *Ber.*, **20**, 1554 (1887).

g. of a viscous yellow oil. Distillation of 3.5 g. yielded 1.9 g. boiling at 195–210° (0.2 mm.), a clear, viscous oil, *N*,*N*,β-triphenylvaleramide, which could not be crystallized. Refluxing with concentrated HCl for 6 hr. yielded 0.63 g. of β-phenylvaleric acid, m.p. 62–64° from 40–60° petroleum ether. The basic fraction of the hydrolyzate gave a positive nitric acid test for diphenylamine.[11] The ultraviolet absorption spectrum of the crude product showed no maximum in the region in which ethyl styryl ketone would be expected to absorb.

Condensation of methylmagnesium iodide with N,N-diphenylcinnamamide. To a solution of methylmagnesium iodide prepared from 3.55 g. (0.025 mole) of methyl iodide was added 2.48 g. (0.0083 mole) of *N*,*N*-diphenylcinnamamide in ether and stirring continued for 4 hr. The mixture was hydrolyzed with dilute acid, and the crude product (2.43 g.) isolated as usual. Recovered starting material (1.04 g., 42%) was identified by a mixture melting point with an authentic sample.

The ultraviolet absorption spectrum indicated a yield of 45% of benzalacetone.

Condensation of methylmagnesium iodide with cinnamoylpiperidine. To a solution of methylmagnesium iodide prepared from 1.70 g. (0.012 mole) of methyl iodide was added 1.15 g. (0.0053 mole) of cinnamoylpiperidine in 200 ml. of ether and the mixture was stirred at room temperature for 3.5 hr. After hydrolysis, 1.07 g. of brownish crystalline solid was obtained which yielded 0.18 g. of 94% (by ultraviolet analysis) benzalacetone on steam distillation. The yield of benzalacetone was 23%.

The residue from the steam distillation yielded 0.81 g. (76%) of starting material, identified by a mixture melting point with an authentic sample and hydrolysis with concentrated HCl to cinnamic acid.

N,N-Dicyclohexylcinnamamide. To 19.6 ml. (18.1 g., 0.1 mole) of dicyclohexylamine in 50 ml. of benzene was added 8.4 g. (0.05 mole) of cinnamoyl chloride in 50 ml. of benzene. The mixture was refluxed 2 hr., the precipitated hydrochloride filtered, and the benzene solution extracted with 10% aqueous HCl, 10% aqueous NaOH, and water.

The product obtained on removal of the solvent was recrystallized from 90–100° petroleum ether, m.p. 115–115.5°.

Anal. Calcd. for $C_{21}H_{29}NO$: C, 80.96; H, 9.39. Found: C, 81.20; H, 9.45.

Evolution of gaseous products in the condensation of methylmagnesium iodide with N,N-dicyclohexylcinnamamide. A 100-ml. Erlenmeyer flask with ground-glass joint and side arm was connected by a rubber tube to a 30-ml. bottle. The mouth of the flask was stoppered with a soda lime drying tube. Magnesium (0.06 g., 0.00247 mole) was placed in the flask and converted to methylmagnesium iodide with a slight excess of methyl iodide.

After cooling to room temperature, the flask was attached to a gas measuring apparatus and the bottle was filled with an ethereal solution of the substance to be added. This solution was added to the methylmagnesium iodide through the side arm of the flask while maintaining a closed system and the changes in volume were measured. After stirring for 3 hr., a solution of 1 ml. of ethanol in 18 ml. of ether was added slowly through the side arm and the resulting volume increment was again noted.

Three runs were carried out in this manner. In a blank run, 14% of the total gas was collected before hydrolysis. In the second run, 0.3 g. of *N*,*N*-dicyclohexylcinnamamide and in the third 0.6 g. of *N*,*N*-dicyclohexylcinnamamide were added. These yielded 24 and 18% of the evolved gas before hydrolysis. The theoretical amounts expected if methane were a product in the reaction were 0, 39, and 78%, respectively.

Condensation of methylmagnesium iodide with N,N-dicyclohexylcinnamamide. The Grignard reagent was prepared from 3.55 g. (0.025 mole) of methyl iodide. On addition of 3.11 g. (0.01 mole) of *N*,*N*-dicyclohexylcinnamamide a white precipitate formed. The mixture was stirred for 3 hr. and hydrolyzed with dilute HCl. On removal of the solvent, 2.95 g. of product containing 2.74 g. (87%) of starting material, m.p. 114–115°, was obtained. A mixture melting point with an authentic sample showed no depression. Ultraviolet analysis of the steam distillate indicated a yield of 10% of benzalacetone.

Condensation of phenylmagnesium bromide with N,N-dicyclohexylcinnamamide. To phenylmagnesium bromide, prepared from 2.26 g. (0.0145 mole) of bromobenzene, was added a dilute ethereal solution of 1.5 g. (0.0048 mole) of *N*,*N*-dicyclohexylcinnamamide and stirring was continued for several hours. On hydrolysis there was obtained 3.22 g. of crude product which yielded 97% of the theoretical quantity of *N*,*N*-dicyclohexyl-β,β-diphenylpropionamide, m.p. 125.6–127.0°. A mixture melting point with an authentic sample prepared from β,β-diphenylpropionyl chloride and dicyclohexylamine showed no depression.

Anal. Calcd. for $C_{27}H_{35}ON$: C, 83.24; H, 9.06. Found: C, 82.99; H, 9.01.

Condensation of phenyllithium with N,N-dicyclohexylcinnamamide. An ethereal solution of 1.59 g. (0.0051 mole) of *N*,*N*-dicyclohexylcinnamamide was added slowly to phenyllithium, prepared from 0.14 g. (0.02 mole) of lithium and 1.57 g. (0.01 mole) of bromobenzene, and the mixture was stirred for 3 hr. The intermediate was hydrolyzed with 15 ml. of water.

The product solidified on standing and was recrystallized from alcohol-water, m.p. 124–125.4°. A mixture melting point with an authentic sample of N,N-dicyclohexyl-β,β-diphenylpropionamide showed no depression; yield 1.32 g. (68%).

The ultraviolet absorption spectrum of the crude product showed no peak in the region of 310 mμ.

Condensation of phenyllithium with N,N-dimethylcinnamamide. Phenyllithium was prepared from 0.18 g. (0.026 mole) of lithium and 2.04 g. (0.013 mole) of bromobenzene. A solution of 1.13 g. (0.0065 mole) of *N*,*N*-dimethylcinnamamide in ether was added, stirring was continued for 3 hr., and 15 ml. of water was added to hydrolyze the lithium salts.

On removal of the solvent 3.75 g. of product was obtained. The method of Iddles *et al.*[12] was used for determination of the benzalacetophenone present. Since the reaction product was not completely soluble in 2*N* HCl, small quantities of alcohol were added. In order to test the effect of the added ethanol, three determinations were carried out on a standard solution of benzalacetophenone by adding 2-, 4- and 6-ml. portions of alcohol. The precipitates represented 96, 97.8, and 98.3% of the expected 2,4-dinitrophenylhydrazone, respectively.

Duplicate ketone determinations on the product obtained above indicated 64 and 67% yield of benzalacetophenone. The dinitrophenylhydrazones were combined, treated with glacial acetic acid, filtered, and allowed to crystallize, m.p. 245–7°. A mixture melting point with an authentic sample of benzalacetophenone 2,4-dinitrophenylhydrazone showed no depression.

A standard ultraviolet absorption curve of benzalacetophenone was prepared and compared with the spectrum of the crude reaction product. The yield calculated by this method was 72%.

Condensation of phenylmagnesium bromide with crotonylpiperidine. Phenylmagnesium bromide prepared from 25.2 g. (0.157 mole) of bromobenzene was treated with 15 g.

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(11) S. P. Mulliken, *Identification of Pure Organic Compounds*, John Wiley and Sons, New York, 1916, p. 165.

(12) H. A. Iddles *et al.*, *Ind. Eng. Chem.*, *Anal. Ed.*, 11, 102 (1939).

(0.098 mole) of crotonylpiperidine[13] in ether and the mixture was stirred for 30 min. Hydrolysis with dilute HCl, followed by fractionation yielded 11.6 g. (51%) of β-phenylbutyryl piperidine, b.p. 145–50° (0.3 mm.), n_D^{25} 1.5399.

Anal. Calcd. for $C_{15}H_{21}ON$: C, 77.88; H, 9.16. Found: C, 78.24; H, 8.95.

The ultraviolet absorption spectrum of the crude reaction product showed no peak in the region expected for phenyl propenyl ketone.

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[13] H. Staudinger and H. Schneider, *Ber.*, **56**, 699 (1923).

[CONTRIBUTION FROM MATERIALS LABORATORY, WRIGHT AIR DEVELOPMENT CENTER]

Derivatives of Ferrocene. III. The Preparation of Some Acylferrocenes and Alkylferrocenes[1]

MARTIN VOGEL, MARVIN RAUSCH, AND HAROLD ROSENBERG

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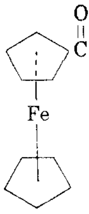
Several new acylferrocenes and 1,1′-diacylferrocenes have been prepared and reduced to the corresponding alkylferrocenes and 1,1′-dialkylferrocenes. Attempts to directly alkylate ferrocene resulted in mixtures of polyalkylated products.

One of the first reactions of ferrocene[2,3] to be investigated was the Friedel-Crafts acylation with acid chlorides and anhydrides in the presence of a suitable Lewis acid catalyst[4] under conditions similar to those used for preparing acylbenzenes. However, at the time of the inception of the present investigation, no successful attempts to directly alkylate ferrocene had been reported in the literature.[5,6]

In order to prepare a series of alkylferrocenes, the direct alkylation of ferrocene was first investigated and found to be an unsatisfactory synthetic method. The acylation of ferrocene and subsequent reduction was then studied and many new acylferrocenes and alkylferrocenes synthesized.

It has been found that both acylferrocenes (I) and 1,1′-diacylferrocenes (II) can be prepared in satisfactory yield by varying the ratio of ferrocene, acid chloride, and aluminum chloride, and also the mode of addition. Compounds of type I were prepared by the dropwise addition of the acid chloride-aluminum chloride complex to the ferrocene solution, using equimolar amounts of acid chloride, catalyst, and ferrocene. The disubstituted derivatives, II, were prepared by adding the ferrocene solution to the complex, using a molar ratio of both the acid chloride and the aluminum chloride to ferrocene of greater than 2:1.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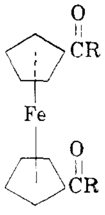
II

The preparation of both I and II by these procedures appears to be a very satisfactory synthetic method. Using the appropriate procedure, either was obtained uncontaminated by the other or by unreacted ferrocene. The unaccounted ferrocene was present in the form of tars. If the reaction was carried out at room temperature instead of at reflux, the amount of tar produced was considerably decreased. The yields of the diketones tended to decrease with increasing molecular weight, probably due to steric factors as well as decreased reactivity of the acid chlorides. The properties and analyses of the acylferrocenes and 1,1′-diacylferrocenes are summarized in Table I.

The catalytic hydrogenation of 1,1′-diacetylferrocene to 1,1′-diethylferrocene was successfully carried out by Rosenblum.[7] However, it was not possible to extend this reaction to the higher homologues under similar as well as stronger conditions, although it was possible to duplicate Rosenblum's work. This is in marked contrast to aryl alkyl ketones which in general are readily hydrogenated to hydrocarbons.[8] Consequently, the Clemmensen reduction was used for the reduction of the higher homologs. Recently, Nesmeyanov and Vol'kenau[9] have used this same method for the reduction of

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[1] Presented in part at the 131st Meeting of the American Chemical Society, Miami, Fla., April 7 to 12, 1957; see Abstracts of Papers, pp. 47–0.

[2] T. J. Kealy and P. L. Pauson, *Nature*, **168**, 1039 (1951).

[3] S. A. Miller, J. A. Tebboth, and J. F. Tremaine, *J. Chem. Soc.*, 632 (1952).

[4] R. B. Woodward, M. Rosenblum, and M. C. Whiting, *J. Am. Chem. Soc.*, **74**, 3458 (1952).

[5] V. Weinmayr, *J. Am. Chem. Soc.*, **77**, 3009 (1955).

[6] P. L. Pauson, *Quart. Revs.*, **9**, 391 (1955).

[7] M. Rosenblum, Ph.D. Thesis, Harvard University, 1953.

[8] W. H. Hartung and R. Simonoff, *Org. Reactions, VII*, 263–326 (1953).

[9] A. N. Nesmeyanov and N. A. Vol'kenau, *Doklady Akad. Nauk SSSR*, **107**, 262 (1956).