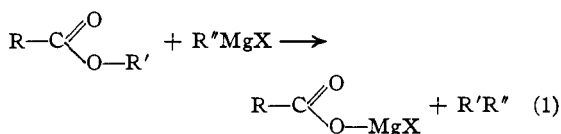


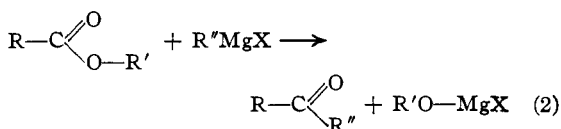
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Mechanism of the Reaction between Hindered Carbonyl Compounds and the Grignard Reagent. II¹BY RICHARD T. ARNOLD AND R. WINSTON LIGGETT²

In the first paper of this series¹ it was shown that esters of the type $R-C\begin{matrix} O \\ // \\ O-R' \end{matrix}$ are cleaved abnormally by the Grignard reagent if in R— there are substituents which sterically hinder additions to the carbonyl group of the ester, and if R'— is of such a nature that it has considerable thermodynamic stability as a cation (R'+). The general reaction between such an ester and the Grignard reagent can be expressed by the equation



If on the other hand, R'— has little tendency to form a cation and the group —OR' readily forms an anion (*i. e.*, Cl⁻, —OC₆H₅, or R₁CO₂⁻) then an entirely different reaction takes place and ketones are produced^{3,4,5,6}



The present paper deals with a study of the cleavage reaction (Eq. 1). As indicated earlier,¹ when the magnitude of the steric factors about the carbonyl group is small, then simple allyl esters of carboxylic acids react normally with the Grignard reagent to produce tertiary alcohols.⁷

If the steric factors in R— are sufficiently great to prevent or decidedly inhibit the addition of R''MgX to the carbonyl group, then allyl esters react entirely according to Equation (1). Obviously there must be some point between these two extremes where the rates of the normal ester-Grignard reaction and the cleavage reaction are alike. This midpoint has now been roughly de-

termined by a systematic study in which the steric effects in group R— have been varied over a wide range of values.

R = I	= triphenylmethyl
II	= diphenylmethylcarbonyl
III	= 2,3-dimethylnaphthyl
IV	= benzyloethylmethylcarbonyl
V	= 3-heptyl
VI	= 3-pentyl
VII	= cyclohexyl
VIII	= 1-ethylcyclohexyl

The element of steric hindrance is pronounced enough when R = I, II, III, or IV that the corresponding allyl esters undergo complete cleavage with phenylmagnesium bromide. When R = V or VI, the cleavage and normal reactions proceed simultaneously and at comparable rates. The marked increase in steric properties observed when one passes from a methyl to an ethyl group is usually attributed to the large effective volume swept out by the freely rotating methyl component of the ethyl group. We have found additional confirmation for this explanation in the fact that when R = VII or VIII only the normal reaction takes place between the allyl esters and phenylmagnesium bromide. In these two cases, free rotation is prevented by the rigidity of the ring structures.

A later report will discuss the effects of changes in the nature of groups R' and R'' on the allyl ester-Grignard reaction.

Experimental

1-Bromo-2,3-dimethylnaphthalene.—To a cooled solution of 200 g. of 2,3-dimethylnaphthalene in 500 cc. of chloroform in an ice-bath, 215 g. of bromine in 200 cc. of carbon tetrachloride was added over a two-hour interval with stirring. After three additional hours at room temperature the solution was thoroughly washed with dilute alkali, the solvent distilled off and the residue crystallized from 400 cc. of hot ethanol; yield, 250 g.; m. p. 62–63°; after recrystallization, m. p. 63–64°.

Anal. Calcd. for C₁₂H₁₁Br: C, 61.3; H, 4.72. Found: C, 60.4; H, 4.72.

2,3-Dimethyl-1-naphthoic Acid.—Fifty-seven grams of 1-bromo-2,3-dimethylnaphthalene in 150 cc. of ether was converted to the Grignard reagent with 11.8 g. of magnesium and two drops of ethylmagnesium bromide solution. Carbonation was effected by dropping the Grignard solution slowly into dry ether through which passed a vigorous stream of anhydrous carbon dioxide. After

(1) For paper I see *THIS JOURNAL*, **63**, 3444 (1941).

(2) DuPont Postdoctorate Fellow 1941–1942.

(3) Adams and Binder, *THIS JOURNAL*, **63**, 2773 (1941).

(4) Whitmore, *et al.*, *ibid.*, **64**, 1242, 1247, 1252 (1942).

(5) Fuson, Bottorff and Speck, *ibid.*, **64**, 1450 (1942).

(6) Fuson, Corse and Rabjohn, *ibid.*, **63**, 2852 (1941).

(7) The one general exception to this rule is the case in which group R' has an extreme tendency to form a cation (*i. e.*, triphenylmethyl acetate); here only cleavage occurs [Fieser and Heymann, *THIS JOURNAL*, **64**, 378 (1942)].

decomposition there was obtained 36–40 g. of crude acid. Recrystallization from methanol–water mixtures gave a product melting at 167–168°.

Anal. Calcd. for $C_{13}H_{12}O_2$: C, 78.0; H, 6.04. Found: C, 77.4; H, 6.13.

Allyl 2,3-Dimethyl-1-naphthoate.—Fifty grams of 2,3-dimethyl-1-naphthoic acid was treated with a sodium ethoxide solution prepared from 6 g. of sodium and 100 cc. of ethanol. The alcohol was removed by vacuum distillation and to the residue was added 32 cc. of allyl bromide in 200 cc. of xylene. The mixture was effectively stirred at the reflux temperature for eight hours. Extraction of the xylene solution with dilute alkali followed by drying and fractionation gave 37.5 g. of ester; b. p. 155–160° (2 mm.). The distillate was taken up in low boiling petroleum ether and cooled. The ester appeared as a white solid; m. p. 33–34°.

Anal. Calcd. for $C_{16}H_{16}O_2$: C, 79.78; H, 6.70. Found: C, 79.79; H, 6.13.

Reaction of Allyl 2,3-Dimethyl-1-naphthoate with Phenylmagnesium Bromide.—The Grignard solution was prepared from 13.0 cc. of bromobenzene and 3.2 g. of magnesium in 75 cc. of ether. To this in one portion was added 15.1 g. of the crystalline ester dissolved in 50 cc. of ether. Refluxing was continued for two hours and the solution stood at room temperature for an additional twenty-four hours. Alkali extraction of the ether layer after decomposition yielded 12.2 g. of 2,3-dimethyl-1-naphthoic acid (97%). Fractionation of the ether layer gave 6 g. of allylbenzene (82.4%); b. p. 155–157°.

Allyl Triphenylacetate.—The anhydrous salt from 6.4 g. of triphenylacetic acid was heated under reflux for ten hours with 20 cc. of allyl bromide and 50 cc. of toluene. After filtration, the toluene was removed by distillation and the oily residue taken up in ether and extracted with dilute alkali. Evaporation of the ether solution gave a solid ester which on recrystallization from alcohol melted at 85–85.5°.

Anal. Calcd. for $C_{23}H_{20}O_2$: C, 84.14; H, 6.14. Found: C, 84.18; H, 6.16.

Cleavage of Allyl Triphenylacetate.—To a solution of phenylmagnesium bromide prepared from 2.6 g. of bromobenzene was added 3.8 g. of the ester dissolved in 50 cc. of ether. After standing overnight the solution was decomposed with dilute hydrochloric acid in the usual way. There was obtained 3.1 g. (93%) of triphenylacetic acid.

Ethyl Benzylmethylethylacetate.—The enolate of ethyl methylethylacetate was formed by the use of triphenylmethylsodium according to the procedure of Hudson and Hauser.⁹ Because of the unexpected violent reaction which ensued during the benzylation with benzyl bromide, a slight accident occurred and only 44.5 g. of ethyl benzylmethylethylacetate was obtained from 61 g. of the starting ester. The product boiled at 127–130° (9–10 mm.).

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.47; H, 9.12.

Allyl Benzylmethylethylacetate.—The ethyl ester (28 g.) was saponified by refluxing for ten hours with 25 g. of potassium hydroxide in 50 cc. of absolute alcohol. After adding 250 cc. of water and extracting with ether, the

aqueous solution was neutralized to congo red with hydrochloric acid. The free acid was extracted with ether and purified by distillation; yield 24 g. From this acid the anhydrous sodium salt was prepared with sodium ethoxide and converted to the ester by heating with 20 cc. of allyl bromide and 150 cc. of xylene for ten hours. The allyl ester weighed 23 g. (80%) and distilled at 139–140° (8 mm.).

Anal. Calcd. for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.66; H, 8.51.

Cleavage of Allyl Benzylmethylethylacetate.—The ester (20 g.) was added in one portion to a Grignard solution prepared from 21 cc. of bromobenzene in the usual manner. After an induction period of a few minutes the reaction became quite violent and had to be cooled periodically. The reaction mixture was decomposed after standing two hours with dilute hydrochloric acid. There was obtained 14.5 g. (87%) of benzylmethylethylacetic acid and 7.0 g. (70%) of allylbenzene.

Allyl α,α -Diphenylpropionate.—Fifteen grams of α,α -diphenylpropionic acid⁹ was converted to its sodium salt by treatment with 1.7 g. of sodium in 50 cc. of absolute ethanol. The ethanol was removed by distillation under diminished pressure, and the residual salt refluxed with allyl bromide (10 cc.) in 100 cc. of dry xylene for thirty hours. The ester (b. p. 175–177° (8 mm.)) was isolated in the usual manner.

Anal. Calcd. for $C_{15}H_{18}O_2$: C, 81.11; H, 6.82. Found: C, 81.19; H, 6.75.

Reaction of Phenylmagnesium Bromide with Allyl α,α -Diphenylpropionate.—To a Grignard solution prepared from 5.25 cc. of bromobenzene in 50 cc. of ether there was added 5.07 g. of the allyl ester in one portion. The solution was refluxed gently for four hours. After decomposition of the reaction mixture there was obtained 3.8 g. (88%) of α,α -diphenylpropionic acid.

Allyl 2-Ethylcaproate.—One hundred grams of commercial 2-ethylhexanal was placed in a large gas drying tower with a trace of manganese dioxide. Air was bubbled through vigorously for four hours at 90°. Basic extraction of the acid from the mixture and purification by distillation resulted in a yield of 58 g.; b. p. 118–120° (8–10 mm.). The acid was converted to the pure acid chloride; yield 56 g. To a solution of 50 g. of pyridine and 25 g. of allyl alcohol in 100 cc. of chloroform, the acid chloride dissolved in 50 cc. of chloroform was added slowly. The mixture was cooled at all times to prevent the temperature from rising above 15°. After addition, the solution was kept at 4° overnight.¹⁰ The mixture was washed once with normal hydrochloric acid, twice with water, and then extracted with dilute sodium bicarbonate solution. The chloroform layer was dried and distilled. The allyl ester (45 g.) boiled at 79–79.5° (8 mm.).

Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.67; H, 10.94. Found: C, 71.44; H, 10.87.

Phenylmagnesium Bromide Reaction with Allyl 2-Ethylcaproate.—Treatment of the allyl ester (31.5 g.) with a Grignard solution prepared from 36.6 g. of bromobenzene in 100 cc. of ether yielded after decomposition 2-

(8) Hudson and Hauser, *THIS JOURNAL*, **63**, 2457 (1940).

(9) Batemann and Marvel, *ibid.*, **49**, 2917 (1927).

(10) Schving and Sabetay, *Bull. soc. chim.*, **43**, 857 (1928).

ethylcaproic acid (30%), allylbenzene (26%) and a mixture recognized as carbinol (about 49%) containing the olefin as impurity.

Allyl Diethylacetate.—This ester was prepared from the dry sodium salt (from 160 g. of acid), allyl bromide and xylene as described above. The reflux time employed was forty-eight hours; yield 65 g.; b. p. 165–167°.

Anal. Calcd. for $C_9H_{16}O_2$: C, 69.3; H, 10.3. Found: C, 69.9; H, 10.3.

Reaction of Allyl Diethylacetate with Phenylmagnesium Bromide.—The Grignard solution was prepared from 45 cc. of bromobenzene in 200 cc. of ether. To this was added slowly 25.3 g. of allyl diethylacetate in 50 cc. of ether. A violent reaction ensued and the mixture was decomposed after thirty minutes. There were obtained 4.5 g. of diethylacetic acid, 9.0 g. of allylbenzene, and 10.3 g. of carbinol boiling at 170–175° (8 mm.). The carbinol was identified by dehydration with formic acid to an olefin having the correct composition for 1,1-diphenyl-2-ethylbutene-1.

Anal. Calcd. for $C_{18}H_{20}$: C, 91.5; H, 8.5. Found: C, 91.3; H, 8.5.

Allyl Hexahydrobenzoate.—This ester was prepared from 50 g. of the acid chloride, 25 g. of allyl alcohol, 100 cc. of chloroform and 40 g. of pyridine by the method described above; yield 44 g.; b. p. 103–104° (18 mm.).

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.35; H, 9.58. Found: C, 71.15; H, 9.48.

Diphenylcyclohexylidenemethane.—Treatment of allyl hexahydrobenzoate with two moles of phenylmagnesium bromide in the usual manner gave a carbinol as the sole product. Dehydration of the carbinol with formic acid (85%) gave the expected olefin; m. p. 82–83°. ¹¹

Ethyl 1-Ethyl-2-ketocyclohexanecarboxylate.—Dry sodium ethoxide was prepared in xylene solution from sodium (13.5 g.) and ethanol. The excess ethanol was removed by distillation. To this suspension was added 100 g. of ethyl 2-ketocyclohexanecarboxylate in 100 cc. of xylene. After stirring at reflux temperature for three hours, 110 g. of ethyl benzenesulfonate was added and the mixture was refluxed for fifteen hours. The precipitate was filtered and the filtrate was carefully fractionated. The desired alkylated β -ketoester (86 g.) was obtained; b. p. 125–130°

(15–18 mm.). Its semicarbazone melted at 156.5–157°.

Anal. Calcd. for $C_{12}H_{21}O_3N_3$: C, 56.44; H, 8.30. Found: C, 56.69; H, 8.05.

Allyl 1-Ethylcyclohexanecarboxylate.—As preliminary tests at each stage showed that purification of the intermediates was unnecessary and wasteful, the following series of reaction was carried out without purifying at each step. Forty-one grams of ethyl 1-ethyl-2-ketocyclohexanecarboxylate was reduced with Raney nickel at 175–200° and 2000 lb. pressure of hydrogen. The product after removing the catalyst was dissolved in dry benzene and 30 g. of phosphorus pentoxide was cautiously added. The solution was refluxed for two hours. The benzene solution was poured from the tarry residue and the solvent was removed; 25 g. of oil remained. The oil was reduced with Raney nickel at 150° and 1800 pounds pressure of hydrogen. The reduced material (12 g.) distilled at 100–110° (10–15 mm.). Saponification with methanolic potassium hydroxide yielded 7.5 g. of crude acid. This was converted through its acid chloride and allyl alcohol to the allyl ester; yield 4.7 g.; b. p. 97–98° (8 mm.).

Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.4; H, 10.3. Found: C, 73.4; H, 10.7.

Reaction of Allyl 1-Ethylcyclohexanecarboxylate with Phenylmagnesium Bromide.—A Grignard solution (30 cc.) prepared from 5 cc. of bromobenzene was treated with 3 g. of the allyl ester. A rather violent reaction ensued and after standing overnight the mixture was decomposed with dilute acid. No fatty acid or allylbenzene could be detected. The highly viscous product was obviously the normally expected carbinol.

Summary

1. A number of allyl esters have been prepared which have varying degrees of steric hindrance about the carbonyl group.
2. It has been shown that the magnitude of these steric factors determines very largely whether the allyl esters are cleaved by the Grignard reagent or undergo the well-known reaction to produce tertiary alcohols.

(11) Schmidlin and Escher, *Ber.*, **45**, 893 (1912).