[Contribution from the Chemical Laboratory of Harvard University]

THE RELATIVE EASE OF 1,4 AND 1,6 ADDITION

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In the twenty-five years that have elapsed since Thiele[1] first drew attention to the peculiarities of substances which have "conjugated systems of double linkages," 1,4 addition has become one of the commonest reactions of unsaturated compounds. Meanwhile, the number and variety of substances with conjugated systems sufficiently long for 1,6 and 1,8 addition have multiplied, but the number of products that can reasonably be ascribed to these modes of addition has remained small. Moreover, in comparison with 1,4 addition even 1,6 addition not only is infrequent; it also appears to be restricted to very few types of reaction. The present investigation was undertaken for the purpose of securing facts that might help to explain this apparently great disparity in the relative ease of 1,4 and 1,6 addition.

Conspicuous among the processes that can reasonably be interpreted as 1,6 addition is reduction. Thiele[2] pointed out that substances with systems in which the conjugation is unbroken and ends in oxygen are invariably reduced with uncommon ease—a conclusion that is supported by the results of recent studies in reduction which are both extensive and exact.[3] He interpreted these reductions as addition of hydrogen to the oxygen at the ends of the conjugated system. In the acids of the fumaric series, the unsaturated γ-diketones, *o*-phthalic acid, the quinones, and most vat dyes, this implies 1,6 addition; in muconic and terephthalic acids, it implies 1,8 addition of hydrogen. Thiele also assumed 1,6 addition in the hydrogenation of substances like sorbic and cinnamylidene-malonic acids.

Similar additions have been reported in a few cases of reduction in which the final result is not hydrogenation but removal of oxygen. Of these the most noteworthy were obtained with the dinitro benzenes. Here the relation between the isomers is the same as that between the phthalic acids; in the *ortho* and *para* compounds the conjugation is unbroken, in the *meta* it is interrupted: O:N.C:C.N:O; O:N.C:C.C:C.N:O; O:N.C:C.C.N:O. In accordance with Thiele's ideas, Meisenheimer[4] found that the behavior of these isomers towards reducing agents is similar to that of the phthalic acids, the *ortho* and *para* derivatives being reduced by such mild reducing

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[1] Thiele, *Ann.*, **306**, 87 (1899).

[2] Ref. 1, p. 131.

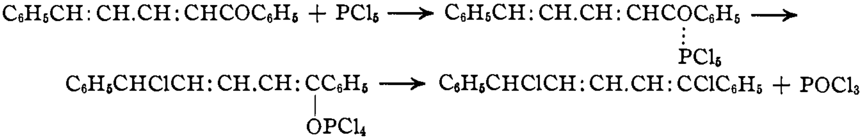
[3] Conant and Lutz, This Journal, **45**, 1047 (1923); **46**, 1254 (1924). Conant and Cutter, *J. Phys. Chem.*, **28**, 1096 (1924).

[4] Meisenheimer, *Ber.*, **36**, 4174 (1903). Meisenheimer and Patzig, *Ber.*, **39**, 2526 (1906).

agents as stannous chloride and hydroxylamine, which have no effect on the *meta* isomer. They also secured convincing evidence that this reduction starts with the addition of hydrogen at the extremities of the conjugated system.

Meisenheimer and his collaborators[5] secured good evidence also that aromatic nitro compounds form 1,6 addition products with alcoholates. They isolated addition products of this type from the red solutions of picric acid and its esters in sodium and potassium alcoholate, and they showed that the rearrangement of 9-nitro-anthracene into anthraquinone oxime, which occurs under the influence of alcoholates, is not a simple case of intramolecular oxidation, but is the result of a series of 1,6 addition and elimination reactions in which all intermediate compounds can be isolated.

Probably the most peculiar case of 1,6 addition, or something closely akin to it, occurs in the formation of "keto chlorides" from unsaturated ketones. By means of a series of carefully planned experiments Straus and his collaborators[6] proved that in the dichloro compounds formed by the action of phosphorus pentachloride, oxalyl chloride, or phosgene on unsaturated ketones, the two chlorine atoms are in the 1,3 or 1,5 positions, the distance between them depending on the length of the conjugated system in the ketone. Straus assumes that the first step in the process is the formation of a complex which is held together by secondary valences, and that this then undergoes rearrangement into a 1,4 or 1,6 addition product:



$$C_6H_5CH{:}CH.CH{:}CHCOC_6H_5 + PCl_5 \longrightarrow C_6H_5CH{:}CH.CH{:}CHC\underset{\underset{PCl_5}{\vdots}}{O}C_6H_5 \longrightarrow$$

$$C_6H_5CHClCH{:}CH.CH{:}\underset{\underset{OPCl_4}{|}}{C}C_6H_5 \longrightarrow C_6H_5CHClCH{:}CH.CH{:}CClC_6H_5 + POCl_3$$

The foregoing summary includes almost every case of 1,6 addition that has been reported. It creates the impression that this mode of addition is confined to reactions which are peculiar; the unsaturated compounds which participate in these reactions are mainly those in which the conjugated systems are bounded by oxygen, and the addition products contain atoms or groups of extraordinary mobility. The impression is strengthened by the fact that of the many substances which are capable of reacting with an unconjugated carbonyl group, nearly all form 1,4 addition products, not only when the carbonyl group is a part of a short conjugated system but also when the system is sufficiently long for 1,6 addition. Thus, cinnamylidene-acetophenone is known to combine more or less freely with hydroxyl amine,[7] ethyl mercaptan,[8] *p*-toluenesulfinic

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[5] Meisenheimer, *Ann.*, **323**, 221 (1902).

[6] Straus, *Ann.*, **393**, 235 (1912).

[7] Minunni, *Gazz. chim. ital.*, **27** (ii), 263 (1897); **29** (ii), 387 (1900) Minunni and Ciusa, *ibid.*, **34** (ii), 373 (1904).

[8] Ruhemann, *J. Chem. Soc.*, **87**, 461 (1905).

acid,[9] phosphorus trichloride,[10] phosphenyl chloride,[11] diphenyl-chlorophosphine,[12] malonic ester and other esters of this type,[13] organic magnesium compounds,[14] and organic zinc compounds;[15] and in this long list there is not a single reagent that does not add in the same way in which it would add if the second ethylene linkage were missing.

The doubly unsaturated esters behave, in the main, like the corresponding ketones; but here there is one notable exception. Vorländer[16] found that the mixture obtained by digesting sorbic ester with sodium malonic ester in benzene contains a 1,6 addition product. This is noteworthy not only because it is the only case in which any product of this type has been obtained in the Michael reaction, but also because Vorländer found no evidence of this mode of addition to the analogously constituted cinnamylidene acetic ester.

We repeated this condensation for the purpose of determining whether the reaction is reversible and whether there is 1,4 as well as 1,6 addition. We also added dimethyl malonate to methyl vinyl acrylate, and attempted to add it to methyl β-phenylcinnamylidene-acetate: the former should offer the least possible hindrance to 1,6 addition, the latter great hindrance to 1,4 addition.

We found that the Michael reaction in this as in other cases is reversible. In order to be able to compare the products with those formed in a reaction that is not reversible we decided to study the action of phenylmagnesium bromide on some compounds with long conjugated systems. Judging

TABLE I

RESULTS

Substance	Addition product	Yield
$\mathrm{CH_2:CHCH:CHCO_2CH_3}$	$\mathrm{CH(CO_2CH_3)_2CH_2CH:CHCH_2CO_2CH_3}$	75
$\mathrm{CH_3CH:CHCH:CHCO_2CH_3}$	$\mathrm{CH(CO_2CH_3)_2CH(CH_3)CH:CHCH_2CO_2CH_3}$	63
$\mathrm{C_6H_5CH:CHCH:CHCO_2CH_3}$	$\mathrm{C_6H_5CH:CHCH[CH(CO_2CH_3)_2]CH_2CO_2CH_3}$	45[17]
$\mathrm{C_6H_5CH:CHC(C_6H_5):CHCO_2CH_3}$	No addition	0
$\mathrm{CH_2:CHCH:CHCOC_6H_5}$	$\mathrm{CH_2:CHCH(C_6H_5)CH_2COC_6H_5}$	75
$\mathrm{C_6H_5CH:CHCH:CHCOC_6H_5}$	$\mathrm{C_6H_5CH:CHCH(C_6H_5)CH_2COC_6H_5}$	100[14]
$\mathrm{C_6H_5CH:CHC(C_6H_5):CHCOC_6H_5}$	$\mathrm{C_6H_5CH:CHC(C_6H_5):CHC(C_6H_5)_2OH}$	40
$\mathrm{C_6H_5CH:CHCO_2CH_3}$	$\mathrm{C_6H_5CH[CH(CO_2CH_3)_2]CH_2CO_2CH_3}$	95
$\mathrm{C_6H_5CH:CHCOC_6H_5}$	$\mathrm{C_6H_5CH[CH(CO_2CH_3)_2]CH_2COC_6H_5}$	98
$\mathrm{C_6H_5CH:CHCOC_6H_5}$	$\mathrm{(C_6H_5)_2CHCH_2COC_6H_5}$	100

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[9] Kohler and Reimer, *Am. Chem. J.*, **31**, 184 (1904).

[10] Conant, Bump and Holt, THIS JOURNAL, **43**, 1678 (1921).

[11] Conant and Pollack, *ibid.*, **43**, 1665 (1921).

[12] Conant, Braverman and Hussey, *ibid.*, **45**, 165 (1923).

[13] Vorländer and Staudinger, *Ann.*, **345**, 219 (1906).

[14] Kohler, *Am. Chem. J.*, **31**, 642 (1904).

[15] Kohler and Heritage, *ibid.*, **43**, 488 (1910).

[16] Vorländer, Weissheimer and Sponnagel, *Ann.*, **345**, 227 (1906).

[17] Vorländer and Groebel, *Ann.*, **345**, 206 (1906).

by the behavior of ethylenic compounds, the ideal substance for this purpose would be $CH_2:CH.CH:CHCOC_6H_5$. All our efforts to prepare either this ketone or its δ-methyl derivative in sufficient purity were unsuccessful. We therefore used vinyl acrylic ester and its β,δ-diphenyl derivative, because these—judging again by the behavior of the corresponding ethylenic compounds—would be expected to form ketones as the first step in the reaction with the Grignard reagent. Our results are summarized in Table I which, for comparison, contains some others already known.

The yields, given in this table, represent the amounts of pure products isolated. The reactions with sodium malonic ester are slow and never reach any real equilibrium because both the reacting substances and the addition products undergo secondary reactions. In our experiments the process was interrupted when the development of color indicated that these secondary reactions became significant. We found no indication of 1,4 addition; but inasmuch as a number of operations were necessary in order to separate the addition product from the unchanged esters, and to prove its structure, small quantities of 1,4 addition products might easily have escaped detection.

An examination of the table shows that the number, arrangement and character of substituents affect the mode of addition of sodium malonic ester as well as that of Grignard reagents. The most striking fact shown, however, is the difference in the mode of addition of these two types of substances; in favorable cases 1,6 addition products can evidently be formed with sodium malonic ester while such products are apparently never formed with a Grignard reagent. It is possible of course that, as some have believed, these malonic ester additions do not involve the carbonyl group; but since malonic ester itself does not combine even with such actively unsaturated compounds as ketenes,[18] and sodium malonic ester does not combine with any unsaturated compounds which do not have either carbonyl or some equivalent group, this view seems no longer tenable.

One might also attempt to account for the difference in the mode of addition of these two types of reagents by assuming with Straus[19] and Posner,[20] that the final addition products are preceded by the formation of complexes that are held together by secondary valences, and in which the distribution of the affinities of the conjugated system is quite different from that in the unsaturated compound itself. This is an attractive hypothesis. More or less highly colored intermediates appear and disappear in almost every reaction between an unsaturated compound and a Grignard reagent, and our knowledge of the distribution of affinities in such complexes is still so slight that it is difficult to estimate their signifi-

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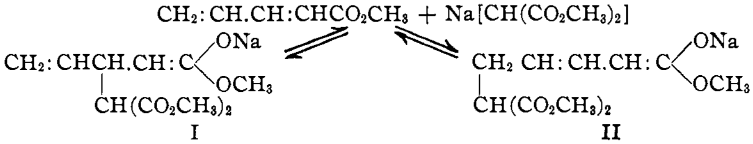
[18] Staudinger, *Ann.*, **356,** 93 (1907).

[19] Straus, *Ber.*, **42,** 2873 (1909). Ref. 6, p. 243.

[20] Posner, *Ann.*, **389,** 1 (1912).

cance. An examination of the results obtained with a long series of related ethylenic ketones,[21] shows, however, that the relative amounts of 1,2 and 1,4 addition are so largely determined by the number and arrangement of substituents that all other factors appear almost negligible. Complex formation may slightly influence the course of the reaction; it does not appear to control its outcome.

Although complex formation cannot be excluded entirely as a possible reason for the divergent results obtained with sodium malonic ester and phenylmagnesium bromide we think the explanation must be sought elsewhere, and we believe that it is to be found in the fact that the reaction with the ester is reversible while that with the organic magnesium compound is not. The reaction between sodium malonic ester and vinylacrylic ester, for example, is probably represented as follows.



$$CH_2{:}CH.CH{:}CHCO_2CH_3 + Na[CH(CO_2CH_3)_2]$$

$$\underset{\text{I}}{\begin{array}{l}CH_2{:}CHCH.CH{:}C\left\langle\begin{array}{l}ONa\\ OCH_3\end{array}\right.\\ \quad | \\ CH(CO_2CH_3)_2\end{array}} \rightleftharpoons \rightleftharpoons \underset{\text{II}}{\begin{array}{l}CH_2\ CH{:}CH.CH{:}C\left\langle\begin{array}{l}ONa\\ OCH_3\end{array}\right.\\ | \\ CH(CO_2CH_3)_2\end{array}}$$

The relative amounts of Products I and II that are finally obtained after the prolonged heating necessary to establish anything approaching equilibrium in this system, bear no simple relation to the relative rates at which they are formed. The relative amounts of 1,4 and 1,2 addition products obtained in the irreversible Grignard reaction, on the other hand, represent the relative rates of these two modes of addition. Since no 1,6 addition product is obtained in this most favorable case, we conclude that for some reason, inherent in the nature of conjugated systems, 1,4 addition is easier than 1,6 addition.

Experimental Part

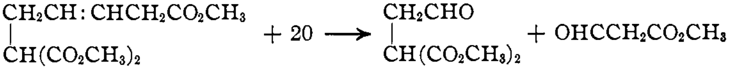
I. Addition of Dimethyl Malonate to Methyl Vinylacrylate

Our experiments indicate that this reaction gives no 1,4 addition, that the total yield of addition product is about 75%, and that at least 95% of this is formed in accordance with the reaction

$$\underset{\text{III}}{CH_2{:}CH.CH{:}CHCO_2CH_3} + CH_2(CO_2CH_3)_2 \rightleftharpoons \underset{\text{IV}}{CH_2[CH(CO_2CH_3)_2]CH{:}CHCH_2CO_2CH_3}$$

These facts were established by ozonizing both the principal product and the small quantity (about 5%) of higher-boiling or non-volatile residue.

The addition product IV would be expected to form an ozonide which, on decomposition with water, would give a mixture of aldehyde esters



$$\underset{\text{IV}}{\begin{array}{l}CH_2CH{:}CHCH_2CO_2CH_3\\ | \\ CH(CO_2CH_3)_2\end{array}} + 2O \longrightarrow \underset{\text{V}}{\begin{array}{l}CH_2CHO\\ | \\ CH(CO_2CH_3)_2\end{array}} + \underset{\text{VI}}{OHCCH_2CO_2CH_3}$$

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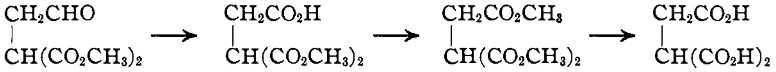
[21] Kohler, *Am. Chem. J.*, **38**, 511 (1907).

The decomposition of the pasty ozonide required protracted boiling with water. It was accompanied by partial hydrolysis of the esters and by evolution of acetaldehyde, which arose from the decomposition of the hydrolysis product of VI, and was identified by its solid nitrophenyl hydrazone VII.

$$\underset{\text{VI}}{OHCCH_2CO_2CH_3} \longrightarrow CHOCH_2CO_2H \longrightarrow CH_3CHO \longrightarrow \underset{\text{VII}}{CH_3CH{:}N.NHC_6H_4NO_2}$$

The separation of the mixture of aldehyde acids and esters formed in the decomposition of the ozonide did not appear to be feasible. The aldehydes were, therefore, oxidized to acids, the acids esterified and the resulting mixture of esters was separated by distillation. The lowest-boiling component was dimethyl malonate, formed from VI and identified by means of its solid addition product with benzal-acetophenone; the remainder was the trimethyl ester of ethane-tricarbonic acid which was formed from V. This was identified by hydrolyzing it to the acid and ultimately converting this into succinic acid and its anhydride:



$$\begin{matrix} CH_2CHO \\ | \\ CH(CO_2CH_3)_2 \end{matrix} \longrightarrow \begin{matrix} CH_2CO_2H \\ | \\ CH(CO_2CH_3)_2 \end{matrix} \longrightarrow \begin{matrix} CH_2CO_2CH_3 \\ | \\ CH(CO_2CH_3)_2 \end{matrix} \longrightarrow \begin{matrix} CH_2CO_2H \\ | \\ CH(CO_2H)_2 \end{matrix}$$

V VIII

A 1,4 addition product, on similar treatment, would be expected to give formaldehyde and tricarballylic acid; neither of these substances could be detected.

Methyl Vinylacrylate (III).—Vinylacrylic acid, although known for a long time, is still hard to prepare in any but small quantities. Doebner's original method of preparation gives a moderate yield of crude product but this contains a large quantity of the polymerized acid. Nottbohm's more recent method gives a still lower yield of pure acid—15–20%. The following modification of Doebner's method gave about 30% of pure acid.

To a solution of 90 g. of malonic acid in 200 g. of pyridine which was cooled in a freezing mixture, 60 g. of acrolein was added gradually while the solution was stirred vigorously with a mechanical stirrer. The mixture became yellow and deposited a very viscous oil. After three hours the temperature was raised to 35–40° where it was kept for five hours during which the oil dissolved with evolution of carbon dioxide. The solution was acidified and extracted with ether. The residue, after evaporating the ethereal solution, partially crystallized in a freezing mixture. The oil was removed by rapid filtration with suction, and the solid washed with cold ether and petroleum ether. This gave 45 g. of crude acid from which 30 g. of pure acid was obtained by recrystallization from petroleum ether. The acid was colorless and melted at 72°.

THE METHYL ESTER.—The methyl ester was made through the silver salt. Probably owing to polymerization, the yield was only 64%. The ester is a colorless liquid that boils at 77–80° under 25 mm.

Addition of Dimethyl Malonate.—A solution of sodium methylate obtained by dissolving 0.75 g. of sodium in the minimum quantity of dry methyl alcohol was added to 55 g. of dimethyl malonate. The mixture was diluted with absolute ether until the sodium malonate barely dissolved on vigorous shaking. After the addition of 25 g. of the unsaturated ester to this solution, it was boiled for four hours during which a small quantity of white solid was deposited. This proved to be sodium malonate. The filtered solution was further diluted with ether, washed and dried in the usual manner, and freed from ether. This left a yellow oil which was fractionated under diminished pressure. It gave a low-boiling fraction composed of unaltered esters, 36 g. of a colorless liquid boiling at 147–150° under 11 mm. and 1.5 g. boiling at 151–160°. There was practically no residue.

Trimethyl-pentene-3-tricarboxylate-1,1,5.—The fraction distilling at 147–150° was analyzed.

Anal. Calcd. for $C_{11}H_{16}O_6$: C, 54.1; H, 6.6. Found: C, 54.1; H, 6.4.

Oxidation.—A slow current of ozonized oxygen containing about 6% of ozone was passed through a solution of 36 g. of the addition product in carbon tetrachloride for 20 hours. The ozone was absorbed completely for 17 hours and the solution remained clear to the end. By evaporating the solvent under diminished pressure, the ozonide was obtained as a clear, colorless paste. This was digested with water. The reaction started near the boiling point of water and was accompanied by evolution of a gas with the pungent odor of acetaldehyde. The gas was swept into a solution of *p*-nitrophenylhydrazine hydrochloride. It precipitated a solid that melted at 126° and was identified as the *p*-nitrophenylhydrazone of acetaldehyde (VII) by comparison with a sample made from the aldehyde.

The ozonide-water mixture was boiled for five hours, then cooled, treated with 20 cc. of hydrogen peroxide, and set aside until it gave only a faint test for aldehydes with fuchsin reagent. From the solution obtained in this manner, most of the water was removed by evaporation under diminished pressure, the remainder by several evaporations with absolute alcohol. This left a colored residue composed of ester acids. These were esterified with methyl alcohol and sulfuric acid. The resulting mixture of esters was subjected to distillation under 23 mm.

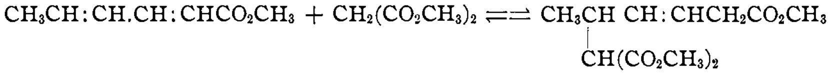
The first fraction—5 g.—contained only dimethyl malonate; with benzal-acetophenone it gave, quantitatively, a solid addition product melting at 106° and identified by comparison with a specimen on hand.

The remaining mixture was collected in 3 fractions, and a small quantity of higher-boiling residue that was not distilled. In order to improve the chance of detecting any tricarballylic ester, each of these fractions as well as the residue was hydrolyzed separately. The largest fraction, on hydrolysis with alcoholic potassium hydroxide, gave an acid that, without purification, melted with decomposition at 154°—evidently ethanetricarbonic acid (VIII) which, when pure, melts with decomposition at 160°. The acid was heated at 170° until evolution of carbon dioxide ceased. A part of the product sublimed and collected on the walls of the flask in long needles melting at 117°. This was succinic anhydride. The remainder of the product was succinic acid. This, like the anhydride, was identified by comparing its melting point with that of a mixture with samples of known origin. The other fractions and the residue were hydrolyzed with boiling hydrochloric acid. Each gave only succinic acid.

The small quantity of higher-boiling liquid obtained in the addition reaction was likewise ozonized. The ozonide, treated like that of the principal fraction, also gave only succinic acid; it probably contained some polymerized vinylacrylic ester.

II. Addition of Dimethyl Malonate to Methyl Sorbate

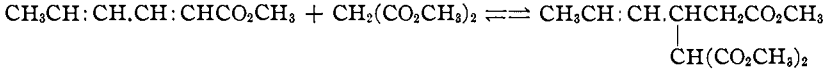
Our results show that dimethyl malonate does not combine as readily with methyl sorbate as it does with methyl vinylacrylate, and that at least 90% of the addition product is formed in accordance with the equation



$$\mathrm{CH_3CH{:}CH.CH{:}CHCO_2CH_3 + CH_2(CO_2CH_3)_2 \rightleftharpoons \underset{\displaystyle CH(CO_2CH_3)_2}{CH_3CH}\ CH{:}CHCH_2CO_2CH_3}$$

IX X

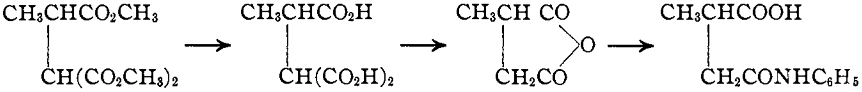
There is also some indication that there may be a small amount of 1,4 addition in accordance with the equation



$$\mathrm{CH_3CH{:}CH.CH{:}CHCO_2CH_3 + CH_2(CO_2CH_3)_2 \rightleftharpoons CH_3CH{:}CH.\underset{\displaystyle CH(CO_2CH_3)_2}{CH}CH_2CO_2CH_3}$$

X

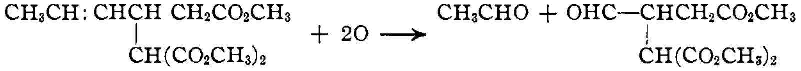
The procedure employed for determining the structure of the addition product was the same as that used with the addition product of the vinylacrylic ester. By this procedure the addition product (IX) would be expected to give acetaldehyde, dimethyl malonate and the trimethyl ester of propane-1,1,2-tricarbonic acid. All these products were obtained. The structure of tricarbonic ester was established by converting it into methylsuccinic acid, methylsuccinic anhydride and methylsuccinanilic acid, and comparing these with the corresponding compounds made in another manner.



$$\mathrm{\begin{array}{l}CH_3CHCO_2CH_3\\ |\\ CH(CO_2CH_3)_2\end{array} \longrightarrow \begin{array}{l}CH_3CHCO_2H\\ |\\ CH(CO_2H)_2\end{array} \longrightarrow \begin{array}{l}CH_3CH\ CO\\ |\qquad\quad >O\\ CH_2CO\end{array} \longrightarrow \begin{array}{l}CH_3CHCOOH\\ |\\ CH_2CONHC_6H_5\end{array}}$$

XI XII XIII XIV

The highest-boiling fraction of the esterified oxidation product gave a small quantity of a substance whose composition and molecular weight agreed closely with those of the aldehyde (XV) which would be obtained by oxidation of the 1,4 addition product.



$$\mathrm{CH_3CH{:}CH\underset{\displaystyle CH(CO_2CH_3)_2}{CH}\ CH_2CO_2CH_3 + 2O \longrightarrow CH_3CHO + OHC{-}\underset{\displaystyle CH(CO_2CH_3)_2}{CH}CH_2CO_2CH_3}$$

X XV

This substance reduced ammoniacal silver nitrate but formed neither phenylhydrazone nor semicarbazone. It may be the aldehyde (XIII), but it seems quite as likely that it is some condensation product formed from malonic aldehyde and malonic ester.

Methyl Sorbate.—The methyl ester was made from the acid through the silver salt. It is a colorless liquid that boils at 83–85° (20 mm.); yield, 85%.

Addition of Dimethyl Malonate.—The addition was first attempted, without success, in dry methyl alcohol containing enough sodium methylate to produce permanent alkalinity. It was then carried out successfully by the same procedure that was used with vinylacrylic ester. Distillation under 23 mm. pressure first gave a fraction boiling at 84–90° composed of unaltered esters; then the temperature rose rapidly to 184° and most of the product distilled at 184–186°.

Anal. Calcd. for $C_{12}H_{18}O_6$: C, 55.8; H, 7.2. Found: C, 55.4; H, 7.2.

Trimethyl Ester of 2-Methylpentane-1,1,5-tricarboxylic Acid.—The trimethyl ester of 2-methylpentane-1,1,5-tricarboxylic acid is a colorless liquid that boils at 185° (23 mm.), or at 155° (10 mm.); yield, 62%.

Reversibility of the Addition Reaction.—A solution of 0.2 g. of sodium in a small quantity of methyl alcohol was added to an ethereal solution of 10 g. of the addition product. The pale yellow solution was boiled for two hours, then washed, dried and distilled as before. It gave a low-boiling fraction in which sorbic ester was readily detected by its characteristic odor. This fraction was added to a boiling methyl alcoholic solution of 2 g. of benzal-acetophenone and a small quantity of sodium methylate. The solution on cooling deposited the solid methyl malonate addition product of benzal-acetophenone. The malonic ester addition reaction is, therefore, reversible.

Oxidation of the Addition Product.—The addition product was ozonized and the ozonide treated as described in previous cases. The reaction between the ozonide and water was accompanied by the evolution of acetaldehyde which was identified by its solid *p*-nitrophenylhydrazone. The mixture of esters obtained by esterifying the oxidation products was separated by distillation under 7 mm. pressure. It gave a low-boiling fraction composed mainly of dimethyl malonate which was identified by its solid addition product with benzal-acetophenone. The remainder was collected in 2 fractions—the principal product, which boiled at 127–131°, and a very viscous oil which distilled around 155°.

Methylpropane-1,1,2-tricarboxylate, (X).—The fraction which distilled at 127–131° was a colorless, mobile liquid.

Anal. Calcd. for $C_9H_{14}O_6$: C, 49.5; H, 6.4. Found: C, 50.0; H, 6.5.

The substance is evidently a trimethyl ester of a propane tricarbonic acid. Since the acetaldehyde, in this case, would be formed both from a 1,4 and from a 1,6 addition product, this ester might be either the trimethyl ester of tricarballylic acid or that of propane-1,1,2-tricarbonic acid. For the purpose of distinguishing between these, both tricarballylic ester and the ester in question were converted into the corresponding solid trihydrazides.

The Trihydrazide of Carballylic Acid.—Tricarballylic acid was made by the method of Auwers, and turned into the methyl ester as directed by Emery. The trimethyl ester boiled at 130–135° (10 mm.). It was treated at the ordinary temperature with excess of hydrazine hydrate in methyl alcohol and set aside. The clear solution gradually deposited a bulky, white precipitate, which was recrystallized from dil. methyl alcohol. The hydrazide crystallizes in needles and melts, without decomposition, at 183–186°.

Hydrazide of Propane-1,1,2-tricarbonic Acid.—An excess of hydrazine hydrate (0.6 g.) was added to a solution of 0.5 g. of the ester, boiling at 127–131°, in 4 cc. of dry methyl alcohol. During 48 hours at the ordinary temperature this solution deposited a bulky, white precipitate which was readily soluble in water, insoluble in methyl alcohol and ether. This was purified by solution in water and reprecipitation with methyl alcohol.

Anal. Calcd. for $C_6H_{14}O_3N_6$: N, 38.5. Found: 39.1.

The new hydrazide melted with decomposition at 208°, and a mixture of the two hydrazides melted at 167–170°. The methyl ester, therefore, is not trimethyl carballylate.

Hydrolysis.—A hot, concentrated aqueous solution containing 2 g. of potassium hydroxide was added to a hot solution of 2 g. of the ester boiling at 127–131° in methyl alcohol. After four days the methyl alcohol was removed by evaporation under diminished pressure, and the aqueous solution acidified. From the acidified solution ether extracted an oily acid that began to lose carbon dioxide at about 120°. This was heated to 160° under diminished pressure. It gave a distillate, presumably composed largely of methylsuccinic anhydride (m. p., 31°) which did not solidify. A small quantity of this liquid when boiled with water gave an acid that melted at 109°. The remainder was divided into 2 portions; one of these was treated with a benzene solution of aniline, the other with a similar solution of *p*-toluidine. The anilido acid melted at 144°, the *p*-toluido acid at 160°.

For the purpose of comparison, methylsuccinic acid was prepared by reducing itaconic anhydride with sodium amalgam. This gave an acid that melted at 110°, an anilido acid melting at 147°, and a toluido acid melting at 162°. The melting points of mixtures of the two preparations were: the acid 110°, the anilido acid 143°, the toluido acid 160°. The ester is, therefore, derived from propane-1,1,2-tricarbonic acid, which can be formed only from the 1,6 addition product (IX).

The high-boiling residues of the esterified oxidation product were combined and refractioned under a pressure of 7 mm. They were composed mainly of the ester which has been described, but gave between 1 g. and 2 g. of another liquid boiling at 164–167°.

Anal. Calcd. for $C_{10}H_{14}O_7$: C, 48.8; H, 5.7. Found: C, 49.2; H, 5.9.

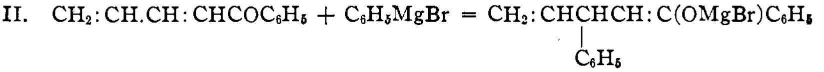
Mol. wt. Calcd. for $C_{10}H_{14}O_7$: mol. wt., 246. Found: 258.5.

Analyses and molecular weight agree fairly well for the aldehyde ester (XV) which would be formed as the primary oxidation product of the 1,4 addition product (X). It seems little likely, however, that such an aldehyde could have survived both the prolonged action of hydrogen peroxide and the subsequent esterification. The substance reduced ammoniacal silver nitrate but not fuchsin. It gave neither phenylhydrazone nor semicarbazone.

III. Addition of Phenylmagnesium Bromide to Vinylacrylic Ester

In order to avoid the formation of complex products, this reaction was carried out in the presence of a large excess of the Grignard reagent. It gave two substances which were separated by distillation under diminished pressure. The structure of the principal product, which constituted about 75% of the whole, was readily established by oxidation with permanganate. The oxidation products—formic acid and α-phenyl-β-benzoylpropionic acid—show that this product was formed in accordance with the following equations:

I. $CH_2{:}CH.CH{:}CHCO_2C_2H_5 + C_6H_5MgBr = CH_2{:}CH.CH{:}CHCOC_6H_5 + Mg(OC_2H_5)Br$



II. $$CH_2{:}CH.CH{:}CHCOC_6H_5 + C_6H_5MgBr = CH_2{:}CH\underset{\displaystyle C_6H_5}{\underset{|}{C}}HCH{:}C(OMgBr)C_6H_5$$

In addition to the 1,4 addition product, the reaction gave a considerable quantity (25%) of another substance which could not be distilled without change and, therefore, was not obtained in a pure state. The substance did not reduce permanganate. When oxidized with chromic acid it gave carbon dioxide, benzophenone, and a small quantity of benzoic acid. The nature of this substance is not known, but since it does not reduce permanganate and is oxidized to benzophenone by chromic acid it is probably a polymer of the 1,2 addition product, $CH_2{:}CH.CH{:}CHC(C_6H_5)_2OH$.

Vinylacrylic Ester.—The ethyl ester used in these experiments was made by way of the silver salt and purified by distillation, under diminished pressure, in a current of dry hydrogen. In agreement with Auwers[22] we found the boiling point 79–81° (35

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[22] Auwers, *J. prakt. Chem.*, **105**, 361 (1923).

mm.). The esterification was accompanied by polymerization and the yield of pure ester was only 65%.

The Grignard Reaction.—A solution of 22 g. of the ester in dry ether was added drop by drop to a cooled solution of phenylmagnesium bromide which contained four equivalents of magnesium. The solution remained clear but turned slightly yellow. It was poured into iced ammonium chloride. The ethereal layer after the customary washing and drying was concentrated, and since it gave no indication of crystallizing, finally distilled in a current of hydrogen under a pressure of 8–10 mm. By several fractional distillations under this pressure it was separated into three portions— a low-boiling fraction composed mainly of bromobenzene and diphenyl, the main product which distilled at about 190°, and a red residue which could not be distilled under this pressure.

β-Phenyl-β-vinyl-propiophenone, $CH_2:CH.CH(C_6H_5)CH_2COC_6H_5$.—The fraction boiling at 190° was analyzed.

Anal. Calcd. for $C_{17}H_{16}O$: C, 86.4; H, 6.9. Found: C, 86.5; H, 7.1.

Mol. wt. Calcd. for $C_{17}H_{16}O$: mol. wt., 236. Found: 237.

Oxidation.—The ketone was oxidized with permanganate in acetone. A minute quantity of solid melting at about 158°, the only neutral oxidation product found, was discarded without further investigation. The acid products were collected in ether. The washed and dried ethereal solution, on evaporation, left a solid immersed in a small quantity of liquid which was easily identified as formic acid by its characteristic pungent odor. The liquid was evaporated under diminished pressure and the solid recrystallized from dil. alcohol.

Anal. Calcd. for $C_{16}H_{14}O_3$: C, 75.5; H, 5.5. Found: C, 75.3; H, 5.5.

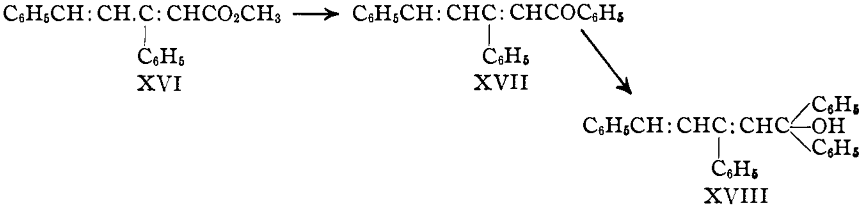
The composition and the melting point (150°) indicated α-phenyl-β-benzoylpropionic acid (m. p., 153°). This acid was made by adding hydrocyanic acid to benzalacetophenone and hydrolyzing the product. It melted at 151°, and a mixture of the two acids melted at 150°.

The non-volatile residue (5 g.) did not reduce permanganate in acetone. It was, therefore, oxidized with chromic acid in glacial acetic acid. Complete oxidation required 10 g. of chromic acid. The oxidation products were collected in ether in the usual manner. From the ethereal solution sodium carbonate removed a small quantity of a solid which was identified as benzoic acid. The ether on evaporation left an oil. This was purified by distillation with steam. It then solidified when inoculated with benzophenone. The solid melted at 45°; when mixed with pure benzophenone the melting point was likewise 45°.

IV. Addition of Phenylmagnesium Bromide to Methyl-β-phenyl-cinnamylidene-acetate

The experiments with the methyl ester of β-phenyl-cinnamylidene-acetic acid turned out to be the most troublesome of all, partly because the volatility of the products was too small for successful distillation at any pressure available to us, partly also because in addition to other complications, stereoisomerism enters as a disturbing factor. Although the ester could not be made to combine with dimethyl malonate, it reacted quite readily with phenylmagnesium bromide. We ultimately succeeded in getting one of the products as a solid melting at 121°.

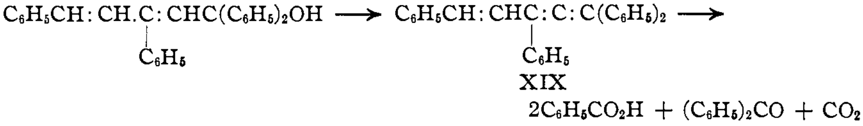
The formula of the solid, $C_{29}H_{24}O$, shows that two molecules of the Grignard reagent participate in the reaction and also that the first step is the replacement of methoxyl by phenyl. When the substance was oxidized with ozone, it gave only benzoic acid and benzophenone. This indicates that it is a tertiary alcohol and that the conjugated system is not involved in the reaction.



$$C_6H_5CH{:}CH.\underset{\substack{|\\ C_6H_5}}{C}{:}CHCO_2CH_3 \longrightarrow C_6H_5CH{:}CH\underset{\substack{|\\ C_6H_5}}{C}{:}CHCOC_6H_5 \searrow C_6H_5CH{:}CH\underset{\substack{|\\ C_6H_5}}{C}{:}CHC\!\left<\begin{matrix}C_6H_5\\ OH\\ C_6H_5\end{matrix}\right.$$

XVI XVII XVIII

The behavior of the substance confirms this conclusion; it reacts vigorously with ethylmagnesium bromide and liberates a gas; in absolute ether it is attacked by sodium with evolution of hydrogen, and when its solution in methyl alcohol is saturated with dry hydrogen chloride, it forms a solid chloride which readily loses hydrogen chloride and passes into an unsaturated hydrocarbon. This hydrocarbon, when oxidized with ozone, likewise gave only benzoic acid and benzophenone.



$$C_6H_5CH{:}CH.\underset{\substack{|\\ C_6H_5}}{C}{:}CHC(C_6H_5)_2OH \longrightarrow C_6H_5CH{:}CH\underset{\substack{|\\ C_6H_5}}{C}{:}C{:}C(C_6H_5)_2 \longrightarrow 2C_6H_5CO_2H + (C_6H_5)_2CO + CO_2$$

XIX

Only 40% of the product was composed of this solid tertiary alcohol; the remainder was an oil which either held a considerable quantity of the solid in solution or, more probably, consisted of a mixture of stereoisomeric carbinols.

Methyl β-Phenyl-cinnamylidene-acetate, (XVI).—The ester was made by eliminating water from the methyl ester of γ-benzal-β-phenyl-β-hydroxybutyric acid. The ester of the hydroxy acid was obtained without difficulty by the method described in an earlier paper,[23] and we also found a fairly satisfactory procedure for converting the hydroxy ester into a solid unsaturated acid; but all methods of esterifying this acid gave oily esters which in turn gave only oily products in the Grignard reaction. We finally succeeded in getting a small quantity of a solid ester, and with this available for inoculation it was possible to get a moderate yield of solid ester directly from the hydroxy ester. The procedure was as follows.

To a solution of the hydroxy ester in the minimum quantity of hot methyl alcohol, concd. hydrochloric acid was added in the proportion of 5 cc. for 10 g. of ester. The mixture was boiled for four hours. The alcohol was then evaporated, the residue dissolved in ether, and the ethereal solution washed with dilute sodium carbonate and dried with calcium chloride. The residue from evaporation of the ether was dissolved at the ordinary temperature in the minimum quantity of dry methyl alcohol. This solution was cooled slowly and inoculated with the solid ester. After crystalli-

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[23] Ref. 15, p. 479.

zation started, the cooling was continued down to —20°. The solid was recrystallized once more from methyl alcohol. It is colorless and melts at 49°.

Anal. Calcd. for $C_{18}H_{16}O_2$: C, 81.8; H, 6.1. Found: C, 81.5; H, 6.1.

Addition of Phenylmagnesium Bromide.—An ethereal solution containing 5 g. of the solid ester was added to a solution of phenylmagnesium bromide made from 1.8 g. of magnesium. The solution turned yellow and the temperature rose to the boiling point. The solution was boiled for 20 minutes during which a solid magnesium compound deposited. It was cooled and diluted with ether until further dilution no longer increased the amount of solid. The magnesium compound was collected on a filter, washed with absolute ether and then decomposed with ice and ammonium chloride. It gave a solid product but the ethereal filtrate gave only oils. The solid was purified by recrystallization from ether and petroleum ether. The best yield was 40%.

Anal. Calcd. for $C_{29}H_{24}O$: C, 89.7; H, 6.2. Found: C, 89.6; H, 6.0.

1,3,5,5-Tetraphenyl-pentadiene-(1,3)-ol-5 (XVIII).—1,3,5,5-Tetraphenyl-pentadiene-(1,3)-ol-5 crystallizes in needles and melts at 121°. It is readily soluble in ether, alcohol and chloroform. Its solution in concentrated sulfuric acid is red by transmitted, deep blue by reflected light.

Triphenyl-styryl-allene (XIX).—A solution of the tertiary alcohol in methyl alcohol was cooled in ice water and saturated with dry hydrogen chloride. The solution first turned to a deep blue color, then began to deposit a colorless, crystalline solid which melted at approximately 64°. An attempt to recrystallize the solid from ether and petroleum ether resulted in an oil. When the solid was moistened with a small quantity of dry methyl alcohol it gave off hydrogen chloride vigorously and changed to another solid product. This was purified by recrystallization from methyl alcohol.

Anal. Calcd. for $C_{29}H_{22}$: C, 94.0; H, 6.0. Found: C, 93.2; H, 6.2.

The unsaturated hydrocarbon is readily soluble in benzene and in ether, sparingly soluble in alcohol and in petroleum ether. It melts at 158°. When it was oxidized with ozone in the usual manner it gave benzoic acid and benzophenone.

Summary

1. Sodium malonic ester combines fairly readily with the esters of vinylacrylic and sorbic acids; the reaction is reversible and leads to the formation of 1,6 addition products.

2. With the same esters phenylmagnesium bromide first forms the corresponding phenylketones—presumably as a result of 1,2 addition; it then combines with the ketones to form 1,4 addition products.

3. β-Phenyl-cinamylidene-acetic acid, which offers a hindrance to both 1,4 and 1,6 addition, does not combine with sodium malonic ester but gives a tertiary alcohol with phenylmagnesium bromide.

4. For some reason inherent in the nature of long conjugated systems 1,6 addition does not take place as easily as 1,4 addition.

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