increase in the speed of the reduction in those cases where it was possible to estimate this speed with any degree of accuracy.

Cambridge 38, Massachusetts

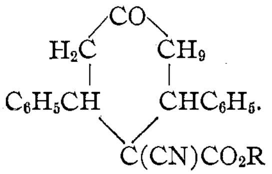
[Contribution from the Chemical Laboratory of Harvard University]

THE ADDITION REACTIONS OF CERTAIN PENTADIENONES
II. ADDITION OF MALONIC ESTERS

By E. P. Kohler and C. S. Dewey

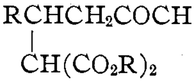
Received February 2, 1924

In the first paper[1] it was shown that in the presence of a little sodium methylate the esters of cyano-acetic acid combine very rapidly both with dibenzal acetone and with dianisal acetone. The products are saturated cyclohexanone derivatives formed by the addition of one molecule of ester to one of ketone: RCH:CHCOCH:CHR + $CNCH_2CO_2R$ =



. No open-chained addition products of any sort could be detected and no appreciable difference was observed in the relative ease of the reaction with the two ketones.

This result is quite different from that which Borsche[2] reported after he had studied the addition of malonic ester, aceto-acetic ester and other substances containing active hydrogen to these same ketones and to others constituted like them. Thus, on condensing malonic ester and dibenzal acetone in the presence of piperidine he obtained only an unsaturated open-chained addition product: RCH:CHCOCH:CHR + $CH_2(CO_2C_2H_5)_2$ =



$$\underset{\displaystyle CH(CO_2R)_2}{RCH}CH_2COCH{:}CHR$$

. Moreover, Borsche found that neither malonic ester nor aceto-acetic ester combines at all with dianisal acetone under conditions under which both combine with dibenzal acetone with the greatest ease. Since in these experiments both the ester and the condensing agent were different from those used in the work with the esters of cyano-acetic acid, it now became desirable to determine which of these was responsible for the marked difference in the results. We have, therefore, studied the addition of malonic esters to a number of unsaturated ketones of this type, and have employed both alcoholates and piperidine as condensing agents.

We have found that with dimethyl malonate as the substance to be added and sodium methylate as condensing agent the results are similar

---

[1] Kohler and Helmkamp, This Journal, **46**, 1018 (1924).

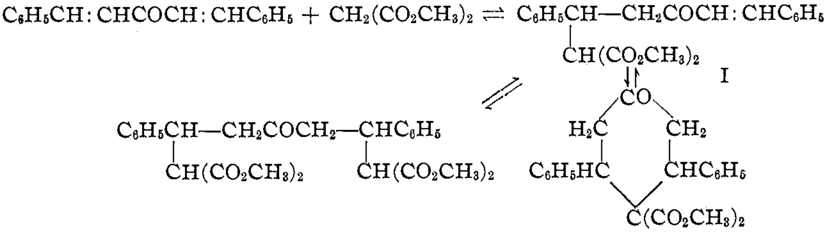
[2] Borsche, *Ann.*, **375**, 145 (1910).

to those obtained with methyl cyano-acetate. The addition does not proceed quite so rapidly; hence, in order to get a homogeneous product it is necessary to warm the mixture a little longer or, better, to use a little more condensing agent, but unless special precautions are taken the cyclohexanone derivative is usually the only substance that can be isolated. With piperidine as condensing agent the results are much more like those reported by Borsche; the substance most easily obtained is usually the unsaturated open-chained addition product, I.

It is evident from these results that in these reactions sodium methylate is a much more active condensing agent than piperidine. The difference between the two is, however, merely one of degree. Thus it is possible to get a very fair yield of the open-chained addition product by shaking a solution of dibenzal acetone and dimethyl malonate with a little sodium methylate at the ordinary temperature and inoculating it from time to time with a trace of the open-chained compound until this begins to separate from the solution. The product obtained with piperidine, on the other hand, always contains some of the cyclic compound even though it be heated for but a third of the time employed by Borsche. By keeping the reacting mixture at a temperature above that at which the readily soluble, low-melting, open-chained compound separates, and inoculating it from time to time with the cyclic compound, this can be made the principal product, and the result then becomes identical with that obtained with sodium methylate.

In all these reactions there is also formed along with the unsaturated and cyclic compounds the only other possible addition product, namely, the one that contains two molecules of the ester to one of the ketone. It is easiest to get this in the first instance by adding more methyl malonate to the unsaturated addition product at a low temperature; but once a sample is available for use in inoculation, it can be obtained without difficulty directly from dibenzal acetone.

It is evident, from the facts cited, that the reaction between dimethyl malonate and dibenzal acetone, in the presence of alkaline condensing agents, must be represented as follows.



II III

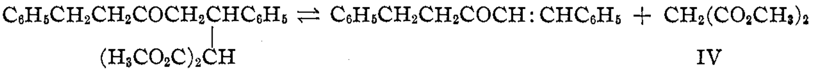
This scheme, doubtless, represents also the reaction between malonic esters and all other pentadienones that are constituted like dibenzal acetone.

We tried the reaction with the symmetrical ketones dianisal acetone and dicinnamal acetone, and also with the unsymmetrical benzal anisal acetone, benzal cinnamal acetone, and anisal cinnamal acetone. In all these cases we obtained the cyclic compounds corresponding to Type III without difficulty, both with sodium methylate and with piperidine. In nearly all cases we also isolated the intermediate unsaturated addition products of Type 1.

In the paper cited,[2] Borsche strongly emphasized the difference in combining power of various ketones of this type, and proposed several hypotheses based on "the partition of affinity in unsaturated organic compounds" to account for it. In systems so complicated as these are it is extremely difficult to get reliable evidence as to the relative activity of the various ketones. Borsche's conclusions were based upon an examination of the substances that separated slowly from solutions containing the condensing agent as well as the reactants and their products. From results obtained in this way he decided, among other things, that while dibenzal acetone is exceedingly active, dianisal acetone has so little combining power that no evidence of addition was obtained after a concentrated solution of this ketone had been boiled for a day with malonic ester and the usual amount of piperidine. It is, however, to a considerable extent a matter of accident as to what substances separate from such solutions. Thus from a liquid that was obtained by first boiling for five hours, and then slowly cooling a solution containing 10 g. each of dibenzal acetone and dimethyl malonate, 10 drops of piperidine and 60 cc. of dry methyl alcohol, it was possible to get almost at will either unchanged ketone or any one of the three addition products by inoculating it with one of these and carefully preventing infection with others.

We have tried an equally crude but more trustworthy method for gaining some idea of the relative activity of these ketones. This consisted in boiling corresponding solutions of the ketones, dimethyl malonate, and piperidine for the same length of time, removing the catalyst, and then separating the resulting mixtures as completely as possible by fractional crystallization. In this manner a solution obtained by boiling for five hours a solution containing 10 g. each of dibenzal acetone and dimethyl malonate, 10 drops of piperidine, and 60 cc. of methyl alcohol, gave about 20% of unchanged ketone, 52% of the unsaturated addition product I, 9% of the saturated addition product II and 7% of the cyclic compound III. The corresponding solution with dianisal acetone gave 40% of unchanged ketone, 3% of the cyclic compound and 45% of an oil which, although it failed to solidify, doubtless was composed largely of the unsaturated addition product, because a little cold sodium methylate transformed it into nearly an equal weight of cyclic compound. Dicinnamal acetone and anisal cinnamal acetone gave results similar to those obtained with dianisal acetone. There seems to be no doubt, therefore, that the order in which Borsche arranged the ketones is correct; but the difference between the combining power of dibenzal acetone and that of the others is not nearly so great as he assumed. Indeed, it appears to be small and it seems to us unprofitable to attempt to represent these fine gradations in properties by means of a series of variants to our present structural formulas.

The saturated, open-chained compound II is of particular interest because addition products of this type have been obtained so seldom.[1] It is evidently formed in all cases, because it could invariably be detected by inoculating the filtrates from the unsaturated and cyclic compounds. The amount of it is very small, however, even when the malonic ester is used in large excess, except when the condensation is carried out at a low temperature. It is the most sensitive of all the addition products. While stable in boiling methyl alcohol when the solution is entirely free from base, addition of a few drops of piperidine soon leads to an equilibrium mixture containing approximately 75% of the unsaturated product, and addition of a little sodium methylate to the boiling solution produces an entirely different equilibrium mixture which contains nearly 90% of the cyclic compound. The reaction expressed by the equation,



$$C_6H_5CH_2CH_2COCH_2\underset{\underset{(H_3CO_2C)_2CH}{|}}{C}HC_6H_5 \rightleftharpoons C_6H_5CH_2CH_2COCH{:}CHC_6H_5 + CH_2(CO_2CH_3)_2$$

IV

which was studied for comparison, proceeds somewhat more slowly at the boiling point of methyl alcohol, but the amount of addition product left after equilibrium has been established is not much greater than that left in the case of the saturated malonic ester addition of dibenzal acetone.

Experimental Part

Dibenzal Acetone and Methyl Malonate

The experiments in which sodium methylate was used as the condensing agent were carried out both at the boiling point of the solutions and at the ordinary temperature. The result was the same; when the solutions were not inoculated with one of the open-chained addition products, the only substance obtained was the cyclohexanone derivative.

Dimethyl 2,6-Diphenyl-4-keto-cyclohexane Dicarboxylate, III.—Two cc. of a 5% solution of sodium methylate was added to a solution of 10 g. of dibenzal acetone, and 5 cc. of methyl malonate in 150 cc. of methyl alcohol. The mixture was boiled for five minutes and then set aside. The solution remained clear for several days but crystallized rapidly after inoculation with some of the cyclic compound which had meanwhile been obtained in another way. The great rapidity with which this condensation takes place is shown by another experiment in which a solution containing 5 g. of the ketone, 3 cc. of dimethyl malonate and 1 cc. of 5% sodium methylate in 75 cc. of commercial methyl alcohol was shaken at the ordinary temperature. Separation of the cyclic compound began almost immediately and in the first ten minutes the solution deposited 3.5 g. of this product. The substance was recrystallized from boiling methyl alcohol. It separates in irregular white prisms and melts at 135°. As the analyses show that it contains the components in the ratio of 1:1, and as it neither reduces permanganate nor combines with bromine it must be the cyclohexanone derivative.

Analyses. Calc. for $C_{22}H_{22}O_5$: C, 72.1; H, 6.0. Found: C, 71.9; H, 6.1.

HYDROLYSIS.—A solution of 10 g. of potassium hydroxide in 30 cc. of methyl alcohol was poured into a warm solution containing 5 g. of the cyclic ester in 40 cc. of the same solvent. The pale yellow color of the mixture gradually became red and a crystalline potassium salt slowly separated from the solution. This was filtered off after 48 hours, washed, first with cold, dry methyl alcohol until colorless, and then with ether; yield, 3.8 g. The filtrate was evaporated in a current of dry air but it contained only a small quantity of water-soluble substances, the residue being composed largely of substances with very high melting points—evidently complex condensation products.

From the aqueous solution of the potassium salt, hydrochloric acid precipitated a colorless acid which was purified by several recrystallizations from boiling water from which it separated in transparent needles.

Analyses. Calc. for $C_{20}H_{18}O_5.2H_2O$: C, 64.5; H, 5.9; H_2O, 9.7. Found: C, 64.7; H, 5.9; H_2O, 9.9.

The air-dried acid contains 2 molecules of water of crystallization. It is stable in a vacuum desiccator but loses all of its water between 75° and 100°. When it is heated rapidly it melts at about 100°, then resolidifies after the water has been expelled, and finally melts with effervescence at about 150°. The anhydrous acid is moderately soluble in ether and in boiling water, very slightly soluble in cold water.

Methyl 2,6-Diphenyl-4-keto-cyclohexanoate.—The dibasic acid was heated to 170° under diminished pressure until effervescence ceased. This left a yellow melt that solidified when digested with ether. After one recrystallization from ether in which it is moderately soluble the resulting monobasic acid melted sharply at 162°. When it was esterified with a 3% solution of hydrochloric acid it gave a methyl ester which melted at 107°, identical with the ester of the cyclic monobasic acid whose structure was established in an earlier paper.[1]

Piperidine as Condensing Agent.—When piperidine is used as condensing agent the addition takes place too slowly at the ordinary temperature, but the protracted heating employed by Borsche is inadvisable because when the boiling is prolonged beyond six or seven hours the yield of open-chained addition products falls off and the by-products interfere with their crystallization.

Dimethyl β-Phenyl-γ-cinnamoyl Ethylmalonate, I.—A solution containing 30 g. of dibenzal acetone, 20 cc. of methyl malonate, and 30 drops of piperidine in 200 cc. of dry methyl alcohol was boiled for 5 hours. On cooling, it slowly solidified to a pasty solid, which was filtered off after the mixture had remained overnight. After recrystallization from methyl alcohol from which it separated in long, silky needles it melted at 108°; yield, 25.5 g.

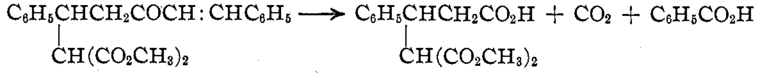
Analyses. Calc. for $C_{22}H_{22}O_5$: C, 72.1; H, 6.1. Found: C, 71.8; H, 6.2.

OXIDATION.—Finely ground permanganate was added to a solution of 9.5 g. of the addition product in 200 cc. of acetone. The solution was constantly shaken and frequently cooled under the tap. It required about 14 g. of permanganate, equivalent to 5 atoms of oxygen per molecule, to produce a permanent color in the solution. The mixture was then boiled for a short time, and filtered. The oxides of manganese were digested with boiling acetone and again filtered and washed before they were finally extracted with boiling water. The cooled aqueous extract, on acidification, yielded a sparingly soluble acid which separated as a solid, and benzoic acid which was extracted from the acid solution.

The solid acid was dissolved in ether, the solution dried, diluted to faint cloudiness with petroleum ether and allowed to evaporate slowly. It deposited colorless prisms which after recrystallization from the same mixture melted at 101°.

Analyses. Calc. for $C_{13}H_{14}O_6$: C, 58.6; H, 5.3. Found: C, 58.7; H, 5.7.

Oxidation of the open-chained addition product would be expected to give the dimethyl ester of a tribasic acid, $C_{14}H_{16}O_8$.



$$\underset{\mathrm{CH(CO_2CH_3)_2}}{\mathrm{C_6H_5CH}}\mathrm{CH_2COCH{:}CHC_6H_5} \longrightarrow \underset{\mathrm{CH(CO_2CH_3)_2}}{\mathrm{C_6H_5CH}}\mathrm{CH_2CO_2H} + \mathrm{CO_2} + \mathrm{C_6H_5CO_2H}$$

The composition of the acid obtained corresponds to that of a monomethyl ester of such an acid, and a titration of the substance with standard base showed that it was a dibasic acid. It was, therefore, heated on a steam-bath for two hours with excess of concd. potassium hydroxide solution. This gave an acid that was difficult to handle, and therefore the mixture was heated at 170–185° until all evolution of carbon dioxide ceased. The residue crystallized from a mixture of ether and petroleum ether in needles and melted at 136°. The substance was completely identified as phenylglutaric acid by comparison with a specimen made according to the directions of Meerwein.[3] There can be no doubt, therefore, that the addition product is the unsaturated open-chained compound.

ISOMERIZATION TO THE CYCLIC COMPOUND.—When the solid unsaturated addition product is dropped into a cold 5% solution of sodium methylate in methyl alcohol it dissolves at once and in a short time the cyclohexanone derivative crystallizes from the solution. There is no production of color and the weight of cyclic compound is practically the same as that of the substance used. The same change can be brought about with piperidine but it then requires prolonged boiling and the yield is smaller. Thus a solution containing 5 g. of the substance and 10 drops of piperidine in 60 cc. of dry methyl alcohol was boiled for five hours, then cooled and inoculated with the cyclic compound. Only a small quantity separated. The boiling was continued for ten hours longer during which the liquid turned to a paler yellow color. On cooling the mixture in ice water it deposited 3.8 g. of the cyclic compound. The filtrate was concentrated under diminished pressure and the residue poured into iced hydrochloric acid. This precipitated an oil which was extracted with ether. The dried ethereal solution yielded small quantities of unsaturated addition product and unsaturated ketone, showing that the reaction in which the addition product is formed from the unsaturated ketone is reversible in the presence of bases.

THE SATURATED ADDITION PRODUCT, II.—This substance was first obtained by dissolving 5 g. of the unsaturated addition product in a hot mixture of 5 g. of dimethyl malonate and an equal weight of dry methyl alcohol, carefully cooling the resulting solution and adding to it 5 drops of a 5% solution of sodium methylate. A white solid began to separate after the solution had stood in an ice box for several days. By the end of a week the entire mixture had solidified. It was filtered with suction, the solid was washed with cold dil. methyl alcoholic hydrochloric acid, and then recrystallized from methyl alcohol containing a trace of acid. It is very readily soluble in methyl alcohol, separates from solution very slowly, crystallizes in long, silky needles not unlike those of the unsaturated addition product, and melts at 109–112°.

Analyses. Calc. for $C_{27}H_{30}O_9$: C, 65.0; H, 6.1. Found: C, 65.1; H, 6.0.

Dimethyl β-Phenyl-γ-hydrocinnamoyl Ethylmalonate, IV.—A solution of 8 g. of

---

[3] Meerwein, *Ann.*, **360**, 344 (1908).

benzyl benzal acetone in a hot mixture of 8 g. each of dimethyl malonate and dry methyl alcohol was cooled, treated with 5 drops of 10% sodium methylate, and placed in an ice chest. It began to deposit crystals in two days and it solidified in the course of a week. The solid was filtered with suction, washed with dil. methyl alcoholic hydrochloric acid, and recrystallized from methyl alcohol.

Analyses. Calc. for $C_{22}H_{24}O_9$: C, 71.7; H, 6.6. Found: C, 71.0; H, 6.5.

The addition product is readily soluble in the common organic solvents and crystallizes very poorly from all of them. The purest product melted at 57°. Like the saturated addition product II, it readily loses malonic ester when its methyl alcoholic solution is boiled in the presence of a small quantity of base.

Dibenzal Acetone and Ethyl Malonate

Sodium Methylate as Condensing Agent.—A solution containing 25 g. of dibenzal acetone, 15 cc. of diethyl malonate, and 5 cc. of 5% sodium ethylate in 500 cc. of dry ethyl alcohol was boiled for five minutes and then set aside. It crystallized very slowly but deposited 23 g. of colorless solid in the course of four days. The product was recrystallized from alcohol from which it separated in very thin, white needles melting at 79°.

Analyses. Calc. for $C_{24}H_{26}O_5$: C, 73.1; H, 6.7. Found: C, 72.4; H, 6.7.

Since the substance does not reduce permanganate, and is formed by the action of sodium alcoholate upon the unsaturated open-chained addition product it is evidently the cyclohexanone derivative.

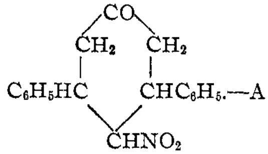
With Piperidine as Condensing Agent.—The condensation was carried out as directed by Borsche but the boiling was stopped after six hours. The yield of unsaturated addition product was about 65%. The filtrate deposited about 5% of the cyclohexanone derivative after inoculation with this substance.

Dibenzal Acetone and Methyl Cyano-acetate

In the first paper of this series attention was drawn to the remarkable rapidity with which methyl cyano-acetate combines with dibenzal acetone in the presence of sodium methylate, and forms a cyclohexanone derivative. In order to compare the ease of addition of this ester with that of dimethyl malonate we carried out the reaction in the presence of piperidine. To this end we dissolved 12 g. of dibenzal acetone, and 6 g. of methyl cyano-acetate in 30 cc. of dry methyl alcohol, added 10 drops of piperidine, boiled the mixture for an hour, and cooled it. The resulting liquid solidified promptly. It was diluted with ether, acidified with glacial acetic acid and filtered. The solid was recrystallized from acetone and petroleum ether, was compared with the product previously obtained by condensing with sodium methylate and the two were found to be identical. The yield was 12.8 g.; no unsaturated ketone was found in the filtrate. The cyano ester, therefore, combines with the ketone far more rapidly than the malonic ester does, and the addition product is also far more rapidly rearranged to the cyclic compound.

Dibenzal Acetone and Nitromethane

Nitromethane can be condensed with dibenzal acetone in the presence of piperidine, but the process is very slow even at the temperature of boiling alcohol, and as the nitro compound itself undergoes condensation under these conditions, the result is an unpromising mixture of colored, oily products. In the presence of an equivalent quantity of sodium methylate, however, the addition takes place readily and gives a satisfactory yield of a nitrocyclohexanone derivative.



4-Nitro-3,5-diphenyl Cyclohexanone, $\mathrm{C_6H_5HC}\langle(\mathrm{CH_2})\mathrm{CO}(\mathrm{CH_2})\rangle\mathrm{CHC_6H_5}$, $\mathrm{CHNO_2}$ ring.—A pasty suspension of sodium nitromethane, obtained by adding 5 g. of nitromethane to a solution of 1.5 g. of sodium in 20 cc. of dry methyl alcohol was poured into a mixture of 12 g. of finely ground dibenzal acetone and 100 cc. of dry methyl alcohol. The mixture was shaken vigorously until the ketone had completely disappeared (15 minutes), set aside for an hour, and then cooled in ice and acidified with glacial acetic acid which was added very slowly while the solution was stirred with a rapid mechanical stirrer. The result was a mass of crystals coated with a gummy, red oil. The oil was removed with ether and the solid recrystallized from dry methyl alcohol. It was thus obtained in colorless, prismatic crystals, melting at 93–94°.

Analyses. Calc. for $C_{18}H_{17}O_3N$: C, 73.2; H, 5.8. Found: C, 73.1; H, 6.

The substance neither combines with bromine nor reduces permanganate and is, therefore, a cyclohexanone derivative. Like open-chained nitroparaffins, it readily forms a sodium compound when it is treated with sodium methylate.

THE BROMO COMPOUND.[4]—4-Bromo-4-nitro-3,5-diphenyl cylcohexanone was obtained by treating the sodium derivative of the nitro compound with bromine. It crystallized in small prisms and melted at 156–157°.

Analysis. Calc. for $C_{18}H_{16}O_3NBr$: Br, 21.4. Found: 21.2.

Benzal Anisal Acetone and Dimethyl Malonate

Sodium Methylate as Condensing Agent.—The condensation was carried out like that with dibenzal acetone, and no difference could be detected in the relative ease of the reaction of these two ketones. The only product was a cyclohexanone derivative analogous to that obtained with dibenzal acetone. It is sparingly soluble in ether and in cold alcohol, readily in boiling alcohol and in acetone. It crystallizes in very fine, white needles and melts at 145–146°.

Analyses. Calc. for $C_{23}H_{24}O_6$: C, 69.7; H, 6.1. Found: C, 69.4; H, 6.3.

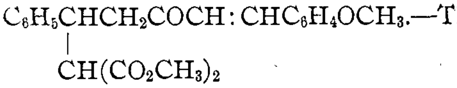
Piperidine as Condensing Agent.—The condensation seems to take place somewhat more slowly than that with dibenzal acetone, for when a solution containing 6 g. of the ketone, 4 cc. of dimethyl malonate and 10 drops of piperidine was boiled for six hours, and then cooled, it still deposited some unchanged ketone while no unsaturated ketone could be

---

[4] Made and analyzed by N. L. Drake.

detected after an equivalent solution of dibenzal acetone had been boiled for the same length of time. After the solution had been boiled for 14 hours it was free from unsaturated ketone, but during this prolonged action nearly half of the unsaturated primary addition product was changed into the cyclohexanone derivative. The reaction mixture, as it cooled, solidified to a pasty mass in which the only solid was an unsaturated compound. After this had been removed, the filtrate slowly deposited an equal amount of the same cyclic compound, that was obtained by condensation with sodium methylate.

Dimethyl β-Phenyl-γ-(p-methoxycinnamoyl) Ethyl Malonate,



$\underset{\displaystyle CH(CO_2CH_3)_2}{C_6H_5CH}CH_2COCH:CHC_6H_4OCH_3$.—The unsaturated compound was recrystallized from methyl alcohol from which it separated as a mass of indistinct, white needles. It is moderately soluble and melts at 124°.

Analyses. Calc. for $C_{23}H_{24}O_6$: C, 69.7; H, 6.1. Found: C, 69.3; H, 6.2.

When the substance was oxidized in acetone with potassium permanganate it gave anisic acid and the same ester acid that was obtained by oxidizing the addition product from dibenzal acetone. The substance is, therefore, an open-chained compound formed by addition to the benzal end of the ketone.

Benzal Cinnamal Acetone and Dimethyl Malonate

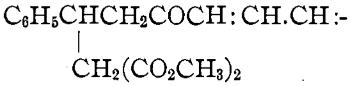
Sodium Methylate as Condensing Agent.—The condensation appears to take place readily enough but inasmuch as the unsaturated ketone is very sparingly soluble and the product sensitive to bases as well as capable of existing in a number of stereoisomeric forms it is more difficult to find the conditions under which it gives a satisfactory yield.

The best results were obtained when a solution of 6 g. of the ketone, 4 cc. of the ester, and 5 cc. of 5% sodium methylate solution in 100 cc. of dry methyl was refluxed for ten minutes. This solution as it cooled deposited 6 g. of colorless prisms. The substance is only very slightly soluble even in boiling alcohol, but crystallizes well from acetone from which it separates in lustrous, transparent prisms; m. p., 156°.

Analyses. Calc. for $C_{24}H_{24}O_5$: C, 73.4; H, 6.2. Found: C, 73.3; H, 6.2.

The addition product does not reduce permanganate in dry acetone even at the boiling point of the solution but it is slowly oxidized in pyridine or acetone containing a small quantity of water. The oxidation product was not obtained in a form suitable for analysis but as the condensation product is also readily formed by the action of the methylate on the open-chained addition product there is no doubt that it is the cyclohexanone derivative.

The Open-Chained Addition Product,



$\underset{\displaystyle CH_2(CO_2CH_3)_2}{C_6H_5CH}CH_2COCH:CH.CH:CHC_6H_5$.—When the concentration of condensing agent is less than that given above, or when the reacting mixture is heated for a shorter time, the result is a mixture of cyclic and open-chained compounds. Thus a solution containing 15 g. of the ketone, 10 cc. of dimethyl malonate, and 5 cc. of 5% sodium methylate in 300 cc. of dry methyl alcohol was boiled for five minutes. As it cooled it deposited 8.3 g. of the prismatic cyclic compound, but an entirely different product separated from the filtrate in fluffy needles. The yield of this new product can be increased by diminishing the concentration of the methylate still more; but it then becomes contaminated with unchanged ketone. It was recrystallized from methyl alcohol from which it separated in white needles; m. p., 112°.

Analyses. Calc. for $C_{24}H_{24}O_5$: C, 73.4; H, 6.2. Found: C, 73.5; H, 6.3.

The substance readily reduces permanganate in acetone and combines with bromine in chloroform. It is, therefore, an open-chained addition product. The mode of addition was established by oxidizing it with permanganate in acetone and separating the acid products with petroleum ether. These were found to be benzoic acid and the same ester acid that had been obtained previously by oxidizing the addition product obtained with dibenzal acetone. The addition is, therefore, to the benzal end of the ketone. This open-chained compound is converted into the cyclohexanone derivative with the greatest ease. It is sufficient to add a few cubic centimeters of 5% sodium methylate to a concd. methyl alcoholic solution, boil for a few minutes and cool.

Piperidine as Condensing Agent.—The condensation takes place more slowly even than that of benzal anisal acetone. After a solution containing 5 g. of the ketone, 3 cc. of methyl malonate, and 5 drops of piperidine in 30 cc. of methyl alcohol had been boiled for 18 hours and then allowed to cool, nearly half of the ketone was recovered unchanged. The rest of it had combined with an equivalent amount of the ester, and formed the same open-chained addition product (112°) that was obtained with sodium methylate.

Dianisal Acetone and Dimethyl Malonate

Sodium Methylate as Condensing Agent.—A solution containing 3 g. of the ketone, 1.3 cc. of the ester and 1.5 cc. of 5% sodium methylate in 50 cc. of dry methyl alcohol was boiled for five minutes. Colorless crystals began to separate from the boiling solution and by the time this was cold 3.5 g. of the cyclohexanone derivative had been deposited. This was the only product. It is almost insoluble in boiling alcohol but is readily recrystallized from acetone from which it separates in brilliant prisms that melt at 194°. It does not reduce permanganate but like other anisyl derivatives it is readily attacked by bromine.

Analyses. Calc. for $C_{24}H_{26}O_7$: C, 67.6; H, 6.2. Found: C, 67.6; H, 6.4.

Piperidine as Condensing Agent.—All attempts to get the unsaturated open-chained addition product were unsuccessful. When the usual solutions of unsaturated ketone, ester and piperidine were boiled for six to ten hours and allowed to cool they deposited variable amounts of unchanged ketone. The filtrates from which this had been removed as completely as possible contained an oil which must have been composed mainly of the unsaturated compound because, while it deposited no cyclic compound when inoculated with this substance, it gave nearly the same weight of cyclic compound on addition of sodium methylate. When the solutions containing piperidine were boiled for a longer period they gradually began to deposit the sparingly soluble cyclic compound. The behavior of dianisal acetone is, therefore, exactly like that of dibenzal acetone but addition takes place somewhat less rapidly.

Anisal Cinnamal Acetone and Dicinnamal Acetone

Our results with these ketones were exactly like those obtained with dianisal acetone. When the usual solutions of ketone and ester were boiled with a small quantity of sodium methylate, the ketone disappeared rapidly and the sparingly soluble cyclohexanone derivatives crystallized from the boiling solutions. When piperidine was used as condensing agent, the ketones disappeared slowly, the open-chained unsaturated compounds could not be obtained in solid form but the cyclohexanone derivative gradually separated from the solution, and in the end the result was the same as that obtained with sodium methylate.

Dimethyl 2-Anisyl-4-keto-6-cinnamyl-cyclohexane Dicarboxylate.—The cyclohexanone derivative obtained by adding dimethyl malonate to anisal cinnamal acetone is very sparingly soluble in methyl alcohol, and readily soluble in boiling acetone. It crystallizes in lustrous tables or prisms and melts at 170°.

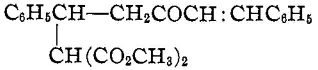
Analyses. Calc. for $C_{25}H_{26}O_6$: C, 71.2; H, 6.0. Found: C, 70.7; H, 6.2.

Dimethyl 2,6-Dicinnamyl-4-keto-cyclohexane Dicarboxylate.—The product obtained from dicinnamal acetone is very sparingly soluble in alcohol, moderately soluble in acetone. It crystallizes in small lustrous prisms and melts at 112°.

Analyses. Calc. for $C_{26}H_{26}O_5$: C, 74.6; H, 6.3. Found: C, 74.4; H, 6.2.

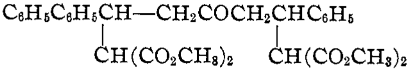
Summary

1. Under the influence of basic condensing agents dimethyl malonate and dibenzal acetone combine to form the three products.



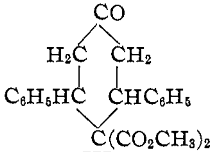
$C_6H_5\underset{\underset{CH(CO_2CH_3)_2}{|}}{CH}-CH_2COCH:CHC_6H_5$

I



$C_6H_5C_6H_5\underset{\underset{CH(CO_2CH_3)_2}{|}}{CH}-CH_2COCH_2\underset{\underset{CH(CO_2CH_3)_2}{|}}{C}HC_6H_5$

II



III

2. As the reactions by which these addition products are formed are reversible, the result of operating in dilute solution is an equilibrium mixture containing all three as well as their components.
3. By selecting suitable conditions it is possible to get any one of the three at will.
4. Pentadienones containing substituted phenyl groups combine with the ester less rapidly than dibenzal acetone but the difference is not pronounced.
5. The hindrance of the malonic ester residue in I, to the addition of another molecule of the ester is not conspicuously greater than that of hydrogen in the same position.

CAMBRIDGE 38, MASSACHUSETTS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMICAL RESEARCH, PARKE, DAVIS AND COMPANY, NO. 24]

ALKYLCHLOROMALONAMIDES. THE INFLUENCE OF HOMOLOGY ON TASTE

BY ARTHUR W. DOX AND BRUCE HOUSTON

RECEIVED FEBRUARY 8, 1924

In an attempt to prepare a cyclic derivative by condensation of sulfuryl chloride with ethylmalonamide, a white crystalline substance was obtained which was found to possess a decidedly sweet taste. The substance was later identified as ethylchloromalonamide. Instead of the expected condensation a simple chlorination had occurred. A search through the literature convinced us that only three chloromalonamides had previously been described, namely, chloromalonamide,[1] dichloromalonamide[2] and benzylchloromalonamide.[3] In the description of these derivatives no mention is made of taste. Having found that dichloromalonamide also has a decidedly sweet taste, we undertook to prepare a number of homologs to ascertain whether a constant variation in sweetness would occur with increasing size of alkyl groups. The unchlorinated alkylmalonamides were for the most part available as preparations obtained in previous work. These were all practically tasteless.

In addition to the three known derivatives already mentioned, chloromalonamides containing the methyl, ethyl, *n*-propyl, *iso*propyl, *n*-butyl, *iso*butyl, *iso*amyl and *n*-hexyl groups, were prepared and identified and their tastes noted in accordance with the test of sweetness proposed by Mulliken.[4]

[1] Conrad and Bischoff, *Ann.*, **209**, 231 (1882).

[2] Conrad and Bischoff, *Ber.*, **24**, 2994 (1891).

[3] Bischoff and Emmert, *Ber.*, **15**, 1113 (1882).

[4] Mulliken, "Identification of Pure Organic Compounds," John Wiley and Sons. **1916**, vol. II, p. 43.