CCLVIII.—*Properties of Conjugated Compounds. Part XII. The Addition of Esters to Butadiene Esters and Ketones: the Effect of Constitution on the αβ,αδ-Ratio.*

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THE study of ester addition is a useful means of determining the extent to which the additive mode of butadienoid compounds is dependent on constitutive factors. The Michael reaction affords the advantages of fairly constant conditions of operation over a wide range of examples, and a high degree of stability in the end products; consequently it seemed possible to follow experimentally the variation in additive mode with (1) change in the alkyl (or other) substituent in the butadiene chain, (2) modification of the activating group attached to the α-carbon atom of the butadiene chain, and (3) graduated modification of the addendum. The utility of the process as a source of accurate comparative data has, in practice, been greatly diminished by the difficulty of separating, estimating, or even recognising the presence of the isomeric compounds which should result from the simultaneous occurrence of different additive modes; indeed, owing to this difficulty, the concurrent production of both αβ- and αδ-ester-addition products has only recently been demonstrated (Farmer and Mehta, J., 1930, 1610). The compounds which should arise by interaction of the simpler butadiene esters and ketones with common ester- or keto-addenda are for the most part unknown and difficult of synthesis; consequently, separative methods offer at present the only practicable means of computing the ratio of isomeric addition products. The present paper describes an attempt to overcome the experimental difficulties (compare Farmer and Mehta, *loc. cit.*) sufficiently to obtain reasonably accurate estimates of the αβ,αδ-ratio holding for a number of alkylated butadiene esters and ketones.

Of the two methods previously employed in computing the ratio, *viz.*, (*a*) the quantitative estimation of the proportion in which acids of the glutaric and pimelic series can be obtained from the catalytically reduced addition products, and (*b*) the separation of suitable derivatives of the ozonolytic degradation products of the respective additive compounds, only the first could be successfully applied to the product from methyl sorbate and methyl malonate. The same method, however, proved unsuitable when applied to the product from ethyl γ-methylsorbate and ethyl cyanoacetate, the presence of the γ-methyl group in the addition product appearing effectively to inhibit the catalytic reduction of βγ- and γδ-double-bonded addition products under conveniently accessible conditions of temperature and pressure. A similar resistance to catalytic reduction appears from recent work to characterise the presence of a β-methyl group in the addition product; therefore, as no type of simple derivative *generally* suited to the separation of isomeric addition products has been discovered, it has been necessary, in order to deal with instances in which the reductive method fails, to improve the ozonolytic method.

This method of estimation, being degradative, requires the employment of much larger quantities of starting material than the reductive method; moreover, the αβ-addition products of the series yield ultimately by degradation, acids of the tricarballylic group which are extremely liable to escape isolation. By improving the method of extracting these acids, whilst employing larger quantities of addition product than formerly, it has been possible to increase the total yield of separated degradation products, but this yield does not exceed 63%. There is a possibility, therefore, that the figures obtained by the two methods are not comparable, *i.e.*, that the losses incurred by employing the ozonolytic method apply unequally to the respective degradation products of αβ- and αδ-forms. This does not appear, however, to be generally or seriously the case, since the values of the αβ,αδ-ratio determined by the two methods for the additions of methyl malonate to methyl sorbate and to crotylideneacetone are almost identical in each case. The table shows the effect on the percentage of the αβ-addition product of (*a*) methyl substitution at the β- and γ-atoms of the butadiene chain in sorbic ester * and (*b*) change of the activating group from carbomethoxyl to acetyl.

Reaction.	Method of treatment.	Yield of isolated material, %.	Proportion of αβ-form.
1. Methyl sorbate + methyl malonate	(i) Ozonolysis	60	9
	(ii) Hydrogenation	90	7—10
2. Ethyl β-methylsorbate + ethyl malonate	Ozonolysis	62	<7*
3. Ethyl γ-methylsorbate + ethyl cyanoacetate	(i) Hydrolysis and ozonolysis	64	74·5
	(ii) Ozonolysis	76	70
4. Crotylideneacetone + methyl malonate	(i) Ozonolysis	67	27
	(ii) Hydrogenation	90	29

* Farmer and Mehta, *loc. cit.*

The numerical values appear to have a well-defined constitutional significance. At present, however, it is difficult to correlate the low ratios found for the δ-methyl and βδ-dimethylbutadiene esters, and the high ratios for the analogous γδ-dimethyl compound, with such detailed views on the relative activating and modifying powers of groups situated at the different carbon atoms of the three-carbon system as have been expressed in connexion with the principle of mobile ion tautomerism (see Ingold, *Ann. Reports*, 1928, **25**, 127). Further comment on this question is, therefore, postponed pending investigation of the way in which the ratio varies with changes in the activating group attached to the butadiene system. It is clear

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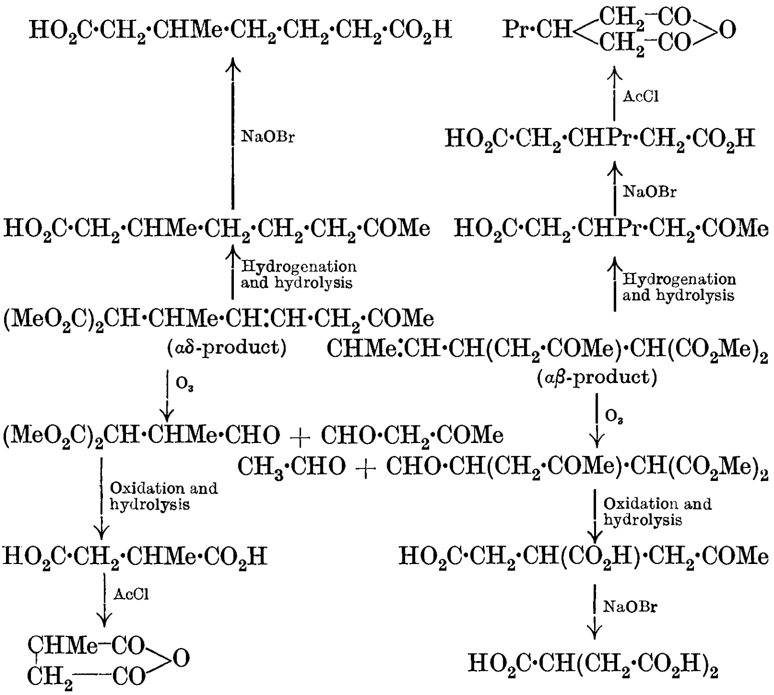
* Methyl substitution at both β- and δ-carbon atoms of sorbic ester totally inhibits addition, so that the joint effect of β- and δ-alkyl substituents has been unascertainable. It seems probable from recorded observations (Kohler and Butler, *J. Amer. Chem. Soc.*, 1926, **48**, 1036; Farmer and Healey, J., 1927, 1060) that the amount of the αβ-isomeride from the parent butadiene ester (β-vinylacrylic ester) amounts at most to one or two units %.

that the nature of the activating group is not without some effect in determining the proportion between isomeric forms of the addition product; indeed, the alteration in the ratio consequent on change from CO_2Et to COMe is so great that comparisons between different types of butadienoid compounds (esters, ketones, nitriles, etc.) would seem to be invalidated.

It should be noted that the addendum in the instance of ethyl γ-methylsorbate was ethyl cyanoacetate and not ethyl malonate. Presumably the αβ,αδ-ratio of an alkylated sorbic ester is independent of the constitution of the particular ester- or keto-addendum employed in its determination, but the point is being tested experimentally. It should also be noted that the ester additions described in this series of papers have all been carried out under " catalytic " conditions of operation, *i.e.*, with only a small proportion of sodium alkoxide as condensing agent.



$$HO_2C\cdot CH_2\cdot CHMe\cdot CH_2\cdot CH_2\cdot CH_2\cdot CO_2H \xleftarrow{NaOBr} HO_2C\cdot CH_2\cdot CHMe\cdot CH_2\cdot CH_2\cdot CH_2\cdot COMe \xleftarrow{\text{Hydrogenation and hydrolysis}} (MeO_2C)_2CH\cdot CHMe\cdot CH{:}CH\cdot CH_2\cdot COMe$$

(αδ-product)

$$(MeO_2C)_2CH\cdot CHMe\cdot CH{:}CH\cdot CH_2\cdot COMe \xrightarrow{O_3} (MeO_2C)_2CH\cdot CHMe\cdot CHO + CHO\cdot CH_2\cdot COMe$$

$$(MeO_2C)_2CH\cdot CHMe\cdot CHO \xrightarrow{\text{Oxidation and hydrolysis}} HO_2C\cdot CH_2\cdot CHMe\cdot CO_2H \xrightarrow{AcCl} \begin{matrix} CHMe-CO \\ CH_2-\!\!-CO \end{matrix}\!\!>\!O$$

$$Pr\cdot CH\!<\!\begin{matrix} CH_2-CO \\ CH_2-CO \end{matrix}\!>\!O \xleftarrow{AcCl} HO_2C\cdot CH_2\cdot CHPr\cdot CH_2\cdot CO_2H \xleftarrow{NaOBr} HO_2C\cdot CH_2\cdot CHPr\cdot CH_2\cdot COMe \xleftarrow{\text{Hydrogenation and hydrolysis}} CHMe{:}CH\cdot CH(CH_2\cdot COMe)\cdot CH(CO_2Me)_2$$

(αβ-product)

$$CHMe{:}CH\cdot CH(CH_2\cdot COMe)\cdot CH(CO_2Me)_2 \xrightarrow{O_3} CH_3\cdot CHO + CHO\cdot CH(CH_2\cdot COMe)\cdot CH(CO_2Me)_2$$

$$CHO\cdot CH(CH_2\cdot COMe)\cdot CH(CO_2Me)_2 \xrightarrow{\text{Oxidation and hydrolysis}} HO_2C\cdot CH_2\cdot CH(CO_2H)\cdot CH_2\cdot COMe \xrightarrow{NaOBr} HO_2C\cdot CH(CH_2\cdot CO_2H)_2$$

Since the more important details connected with the reduction and degradation of the addition products from methyl sorbate and ethyl γ-methylsorbate have already been described, it is only necessary to refer to the method of dealing with the products from crotylideneacetone and ethyl β-methylsorbate. The αβ,αδ-ratio for the former was determined (*a*) by weighing the amount of β-propylglutaric acid (isolated from its mixture with β-methylpimelic acid) derivable from a weighed amount of the catalytically reduced addition product, and (*b*) by estimating the proportions of tricarballylic acid and methylsuccinic anhydride obtainable by the decomposition of a weighed amount of the addition product. The stages passed through in attaining the end products are indicated in the scheme on p. 1907.

The addition products from ethyl β-methylsorbate should yield by degradation β-methyltricarballylic acid and methylsuccinic acid. The latter was readily isolated, but the presence of β-methyltricarballylic acid remained undetected. This acid is doubtless produced in very small amount, since its complementary degradation product, acetaldehyde, is detectable, but in view of the fact that it should be more readily extracted from the oxidation residues than tricarballylic acid and that the latter has been isolated in a proportion corresponding to 7% of an αβ-addition product, there is every reason to believe that the proportion of αβ-addition product in this instance does not exceed, and is probably considerably less than, 7%.

EXPERIMENTAL.

Addition of Methyl Malonate to Methyl Sorbate.—The mixture of addition products (compare Farmer and Mehta, *loc. cit.*) (32 g.), dissolved in chloroform, was ozonised at 0° until no more ozone was absorbed. Removal of the solvent from the product yielded a viscous ozonide which was gently heated with water (40 c.c.) to about 70°, the vapours generated in the reaction vessel being swept by a slow stream of carbon dioxide into a saturated solution of 5 : 5-dimethyl*cyclo*hexane-1 : 3-dione. After a few minutes a precipitate began to form in the latter solution; this, after being washed with water, melted at 139° and was found to be the acetaldehyde derivative of dimethyl*cyclo*hexanedione (mixed m. p. 139°).

The aqueous reaction product, which gave an intense colour with ferric chloride, indicating the presence of formylacetic ester or its polymeride, γ-formylglutaconic ester, was ultimately heated for 2 hours on a sand-bath in order to decompose any residual ozonide. The aldehydic esters contained in the product were oxidised with 30% hydrogen peroxide (40 c.c.), the mixture being kept at room temperature with occasional shaking until the product no longer gave a coloration with Schiff's reagent (2 days). The acid reaction product, when made alkaline with sodium carbonate and shaken with ether, yielded no neutral (unoxidised) material. The dissolved acid esters were hydrolysed by heating with the calculated quantity of caustic soda solution and then decarboxylated by refluxing for

12 hours with approximately 20% hydrochloric acid. The resulting liquor was extracted 10 times with ether, evaporated to dryness, and the residue exhaustively extracted with ether. The final residue was heated for some time at 180° to convert any polybasic acids into their anhydrides, and then thoroughly extracted with ether. The first and second of these extracts yielded crude methylsuccinic acid; the third contained no dissolved material. Since in none of the degradations of the sorbic ester addition product previously carried out had separation of even a small quantity of tricarballylic acid from the crude methylsuccinic acid been achieved by fractional crystallisation, the whole of the acid material was heated with acetyl chloride for 3 hours. Removal of excess acetyl chloride by distillation, and of acetic acid by keeping the residue over caustic soda in a vacuum desiccator, yielded an anhydride which was separated by distillation into two portions, (i) b. p. 112—115°/7 mm. and (ii) b. p. 220—225°/7 mm. The first fraction yielded methylsuccinic acid on boiling with water (m. p. and mixed m. p. 111°; equiv., 66), and the second, which solidified in the receiver (m. p. 131° after recrystallisation from acetic acid–chloroform), gave tricarballylic acid (m. p. and mixed m. p. 160°; equiv., 58·3) on boiling with water. Yields: methylsuccinic acid, 9 g.; tricarballylic acid, 1·2 g.

Addition of Methyl Malonate to Crotylideneacetone.—The additive process. The addition product was obtained by warming gently on a steam-bath for 7 hours the mixture obtained by adding successively methyl malonate (50 g.), sufficient dry ether to produce turbidity (about 10 c.c.), and crotylideneacetone (24 g.) to a solution of sodium (0·6 g.) in the minimal quantity of methyl alcohol (about 6 c.c.). The product was cooled, poured into water, and extracted with ether. The dried ethereal extract yielded (i) unchanged reactants which distilled below 100°/18 mm., (ii) the addition product, a colourless oil, b. p. 170—175°/18 mm., and (iii) high-boiling material which constituted only a small proportion of the whole except when the additive process was unduly prolonged. The addition product, obtained in 66% yield, was shown as described below to be a mixture of the isomeric substances *methyl* β-*acetonyl*-Δ^γ-*pentene*-αα-*dicarboxylate* and *methyl* β-*methyl*-ε-*acetyl*-Δ^γ-*pentene*-αα-*dicarboxylate* (Found: C, 59·3; H, 7·3. $C_{12}H_{18}O_5$ requires C, 59·5; H, 7·4%).

Hydrogenation of addition products. The addition product (24 g.) was dissolved in aqueous methyl alcohol and shaken with hydrogen in the presence of colloidal palladium and gum arabic: it was necessary to renew the catalyst several times in order to ensure the absorption of a molecular proportion of hydrogen. The reduction product, worked up in the usual way, was a colourless oil, b. p. 158—163°/12 mm.; yield quantitative.

Acids derived from the hydrogenation product. The reduction product was boiled for 12 hours with 4 times its volume of 20% hydrochloric acid. The resulting solution was first extracted 6 times with ether and then evaporated to dryness, the residue being taken up in ether. From the ethereal liquors an almost quantitative yield of syrupy ketonic acid was obtained.

Since the ketonic hydrolysis product could not be directly resolved into its component acids, it was oxidised by dissolving it (17 g.) in cold dilute potash solution and gradually adding it with shaking to a hypobromite solution (bromine, 20 c.c.; potassium hydroxide, 45 g.; water 250 c.c.). The resulting solution, from which bromoform soon separated, was kept over-night, treated with sodium sulphite, evaporated to dryness, acidified with hydrochloric acid, and extracted thoroughly with ether. From the ethereal extract a syrupy mixture of isomeric acids was obtained in about 90% yield. Separation of the acids was achieved by distillation, the portion distilling at 163—165°/10 mm. consisting of β-propylglutaric anhydride admixed with a little β-methylpimelic acid, and that distilling at 195—200°/10 mm. consisting of β-methylpimelic acid, m. p. 47° (mixed m. p. 47°); the calcium salt of the latter readily yielded, on heating, 3-methyl*cyclo*hexan-1-one, b. p. 160—165° (semicarbazone, m. p. 191°). The β-propylglutaric acid was purified by converting it into its anhydride by means of acetyl chloride and boiling the pure anhydride (b. p. 181—183°/23 mm.) with water; the regenerated acid, after recrystallisation from dilute hydrochloric acid, melted at 52° (mixed m. p. 52°), and its anilic acid at 128° (mixed m. p. 128°). The total yield of β-propylglutaric acid from 15 g. of the mixed acids was 4·4 g., corresponding to a proportion of αβ-addition products of 29·3%.

Ozonolysis of the addition product. A further portion of the addition product (37 g.) was ozonised as described above. Considerable acetaldehyde was generated (dimethone, m. p. and mixed m. p. 139°), and the aqueous reaction product gave, as would be expected if an αδ-addition product were present originally, a deep colour with ferric chloride. The aldehydic esters were oxidised with hydrogen peroxide as described above, and then heated with 15% hydrochloric acid for 24 hours. The aqueous acid liquor was thoroughly extracted with ether, and then evaporated to dryness, and the residue taken up in ether. The dried ethereal liquors yielded an acid syrup which was heated with acetyl chloride for 3 hours, and then, after removal of the reagent and aceticacid, distilled, giving methylsuccinic anhydride, b. p. 113—120°/10 mm., and acetonylsuccinic anhydride, b. p. 200—210°/10 mm., as colourless oils. The former was identified by conversion into the anilic acid (white crystalline powder, m. p. 156°;

Kohler and Butler, *J. Amer. Chem. Soc.*, 1926, **48**, give m. p. 147°. Found : C, 63·55 ; H, 6·1. Calc. for $C_{11}H_{13}O_3N$: C, 63·3 ; H, 6·3%) and into methylsuccinic acid (colourless prisms, m. p. and mixed m. p. 111° ; equiv., 66) ; the acetonylsuccinic anhydride, which could not be induced to crystallise, or give a semicarbazone, a nitrophenylhydrazone, or a crystalline specimen of its acid (Emery, *J. pr. Chem.*, 1896, **53**, 305, describes the anhydride and the acid as solids melting at 95° and 107—109° respectively), was identified by conversion into tricarballylic acid (m. p. and mixed m. p. 160°). This conversion was accomplished by the action of potassium hypobromite, the tricarballylic acid being precipitated as the lead salt and regenerated by means of hydrogen sulphide.

Addition of Ethyl Malonate to Ethyl β-*Methylsorbate.—Ethyl* β-*methylsorbate.* The preparation of this substance in pure condition and good yield is difficult. Our experiments showed that, in the usual method of preparation from ethylideneacetone and ethyl bromoacetate (compare Burton and Ingold, J., 1929, 2029), (1) it is not advantageous to employ excess of the ketone in the preliminary Reformatski reaction, and (2) of the numerous methods which have been applied to dehydration of Reformatski products, the action of thionyl chloride is preferable in this instance. The hydroxy-ester (85 g.) (ethyl β-hydroxy-β-methyl-Δ^{γ}-hexenoate) is dissolved in pyridine (40 g.), and into the solution, cooled in a freezing mixture, thionyl chloride (35·4 c.c.) is dropped slowly with shaking ; the product is kept at room temperature for 3 hours, then poured into water, and worked up in the usual way. The conjugated ester, b. p. 115—116°/36 mm., is thus obtained in 64% yield (Found : C, 63·7 ; H, 8·9. Calc. for $C_9H_{14}O_2$: C, 63·6 ; H, 9·1%).

The additive reaction. Ethyl malonate (50 g.) was added to a solution of sodium (0·5 g.) in ethyl alcohol (7 c.c.). Ether (about 10 c.c.) and the conjugated ester (23 g.) were then added, and the mixture heated in a steam-bath for 7 hours. The reaction product, worked up in the usual way, gave unchanged reactants and a colourless oil, b. p. 170—175°/10 mm. The latter proved to be a mixture of *ethyl* β-*methyl*-Δ^{γ}-*hexenoate*-β-*malonate* and *ethyl* βδ-*dimethyl*-Δ^{β}-*pentene*-αεε-*tricarboxylate* (Found : C, 61·0 ; H, 8·3. $C_{16}H_{26}O_6$ requires C, 61·1 ; H, 8·3%). Yield, 39—42%. The reduction of this mixture (in the presence of colloidal palladium or platinum) was attempted, but at room temperature only very small amounts of hydrogen were absorbed under 1 or 2 atm.

Ozonolysis of the addition product. The operation was conducted as previously described. The addition product (36 g.) gave a very viscous ozonide which decomposed to form acetaldehyde (dimethone, m. p. 139°) and a mixture of aldehydic esters. The latter, which gave the expected deep colour with ferric chloride due to the presence of acetoacetic ester, were further oxidised with hydrogen peroxide (see above) and subsequently hydrolysed with alkali and decarboxylated by boiling with 20% hydrochloric acid for 12 hours (direct hydrolysis with hydrochloric acid caused gross decomposition through charring). From the hydrolysis product an acid syrup was obtained which was immediately converted by acetyl chloride into a mixture of anhydrides. This distilled, with the exception of a few drops of high-boiling material, at 115—120°/10 mm. and consisted almost entirely of methylsuccinic anhydride. The anhydride was converted into methylsuccinic acid (m. p. and mixed m. p. 111°), the total yield being 9·4 g. (62% yield); no β-methyltricarballylic acid derived from an αβ-addition product was isolated, and repetition of this experiment, with careful examination of the methylsuccinic acid, failed to establish the presence of the former acid.

The αβ,αδ-Ratio of the Addition Products from Ethyl Cyanoacetate and Ethyl γ-Methylsorbate.—The method previously employed in attempting to determine the composition of the addition product from ethyl γ-methylsorbate (Farmer and Mehta, *loc. cit.*) was modified as described in (*a*) and (*b*) below. By this means independent approximate estimates of the αβ,αδ-ratio were obtained.

(*a*) The addition product, b. p. 190—195°/18 mm. (20 g.), was dissolved in concentrated sulphuric acid (50 g.) and kept over-night. The solution was diluted with water (120 c.c.) and then refluxed for 9 hours on a sand-bath. The hydrolysis product, a mixture of βγ-dimethyl-Δ^{γ}-pentene-αε-dicarboxylic acid and β-*iso*butenylglutaric acid, was extracted with ether and worked up in the usual way. Yield 90%. This acid mixture was ozonised, and the ozonide decomposed as previously described. The decomposition products were extracted with ether and distilled, giving (1) β-methyllævulic acid (2 g.), b. p. 140—150°/20 mm., and (2) the dilactone of β-acetylglutaric acid (7 g.), b. p. 200—210°/20 mm. (compare Farmer and Mehta, *loc. cit.*, p. 1615). The proportions of these substances corresponded to the presence initially of 25·5% of the αδ- and 74·5% of the αβ-addition product. On this basis the total yield of the pure decomposition products was 64·3%.

(*b*) Ozonolytic decomposition of the original addition product (15 g.) was carried out as described above. The subsequent procedure differed from that formerly employed by the authors (*loc. cit.*) in that the ketonic esters first produced (ethyl α-cyano-β-methyllævulate from the αδ- and ethyl α-cyano-β-acetylglutarate from the αβ-addition product) were not converted for purposes of estimation into substances (1) and (2) [see (*a*) above] respectively. The esters differed sufficiently in b. p. from one another and from the original addition product to allow of reasonably good fractionation. It being assumed that these fractions were homogeneous, the αβ, αδ-ratio of the original addition products was 7 : 3; on this basis the yield of isolated decomposition products was 76%. The ketonic esters were subsequently shown to be respectively convertible into the acid and dilactone named above.

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