CCIX.—*Properties of Conjugated Compounds. Part X. Variability in the Mode of Ester Addition to Butadiene Esters and Ketones.*

By ERNEST HAROLD FARMER and THAKORBHAI NARANJI MEHTA.

AN examination of the additive behaviour of butadienoid compounds with bromine and hydrogen has established that the mode of addition varies from member to member of a conjugated series for the same addendum, the variation being apparently directly related to (although, so far as has been definitely proved, possibly not entirely dependent on) the nature and position of the substituents in the butadiene chain. There is no reason to suppose that dependence of additive mode on the constitution of the conjugated compound does not hold for all the common dividing addenda and consequently it would be expected that the union of sodio-esters with butadiene esters would yield αβ-, αδ-, or *both* αβ- and αδ-addition products in different instances. Yet, although the separate occurrence of αβ- and of αδ-addition to butadiene esters (δ-phenylated and δ-alkylated respectively) * has been known for more than twenty years (Vorländer, *Annalen*, 1906, **345**, 227), no single instance has been discovered in which *both* αβ- and αδ-addition compounds are simultaneously produced from the same reactants.

Kohler and Butler (*J. Amer. Chem. Soc.*, 1926, **48**, 1036) and Farmer and Healey (J., 1927, 1060) independently subjected the malonic ester addition products of methyl β-vinylacrylate and methyl sorbate to ozonolytic degradation in order to discover whether αδ-products were indeed the only ones formed, and in 1924, before ozone was available as a reagent in the laboratory, one of the present authors oxidised large quantities of the latter product with permanganate in the hope of isolating tricarballylic acid, the expected degradation product of an αβ-additive compound (unpublished work). The result of these efforts made it appear probable that only αδ-derivatives were formed in these instances, although, in connexion with the compound from methyl sorbate, Kohler and Butler (*loc. cit.*, p. 1045) mention a small fraction of the major degradation product which, differing slightly in boiling point from the remainder, could possibly be derived from the αβ-compound.

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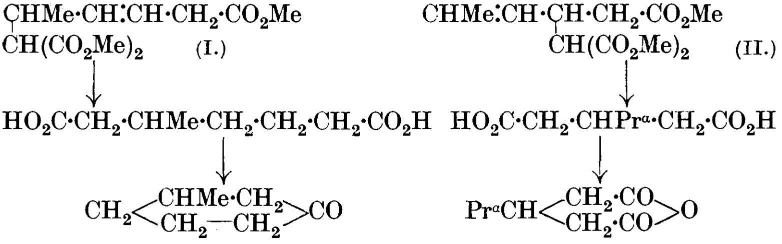
* Indirect evidence as to the possibility of bringing about αδ-ester addition to a phenylated butadiene ester is furnished by Meerwein's production of a double addition product $Ph{\cdot}CHX{\cdot}CH_2{\cdot}CHX{\cdot}CH(CO_2R)_2$ [$X = CH(CO_2R)_2$] from cinnamylidenemalonic ester and sodiomalonic ester, or directly from cinnamaldehyde and sodiomalonic ester (*Annalen*, 1908, **360**, 324). Here presumably the αδ-addition to the conjugated ester which is first effected is rapidly followed by βγ,αβ-double bond displacement and αβ-addition.

Similarly the same two conjugated esters appeared to yield only αδ-addition products with methylcyanoacetic ester (Farmer and Healey, *loc. cit.*). Since that time the addition of malonic ester to two conjugated ketones has been studied by one of the authors, but in neither case was the simultaneous formation of both αβ- and αδ-products proved.

Now, the ozonolytic degradation of unsaturated ester-addition products usually proceeds so smoothly that the failure to detect thereby the formation of more than one type of additive compound in each instance has suggested that a second type, if produced at all, could represent only an extremely small fraction of the addition product. Yet it appeared quite certain from experience gained with other addenda that, if simultaneous formation of αβ- and αδ-compounds could occur at all, then, in some examples at least, the minor component of the addition product should be present to the extent of considerably more than a mere trace. Therefore, whilst the investigation of a sufficiently large number of examples by the degradation methods hitherto employed might ultimately be expected to disclose instances of multiple-type addition (instances in which the αβ-, αδ-ratio approached unity), there seemed to be no question as to the desirability of re-examining some of the older examples by supplementary experimental methods. The authors have therefore returned to the investigation of the product derived by the interaction of methyl sorbate and methyl sodiomalonate, substituting a reduction process for the degradative methods previously employed.

When this product is successively reduced, hydrolysed, and partly decarboxylated, an oily mixture of acids is obtained which is partly separable into its components by distillation. The higher-boiling portion, which quickly solidifies, is β-methylpimelic acid derived from the preponderating αδ-product (I). The lower-boiling portion, which remains liquid, is a mixture of β-methylpimelic acid and β-propylglutaric acid, the latter derived from an αβ-product (II).

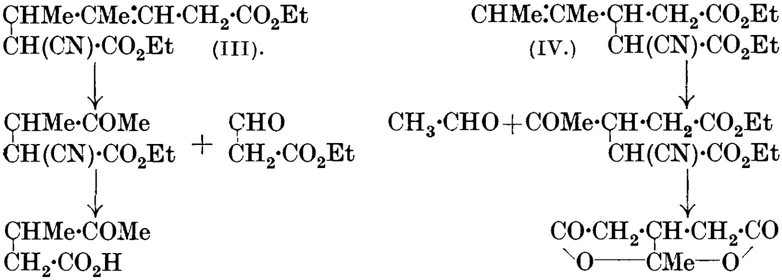


$$\begin{array}{ll} \mathrm{CHMe{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CO_2Me} & \mathrm{CHMe{:}CH{\cdot}CH{\cdot}CH_2{\cdot}CO_2Me} \\ \mathrm{CH(CO_2Me)_2} \quad \text{(I.)} & \qquad\quad \mathrm{CH(CO_2Me)_2} \quad \text{(II.)} \\ \downarrow & \downarrow \\ \mathrm{HO_2C{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H} & \mathrm{HO_2C{\cdot}CH_2{\cdot}CHPr^{\alpha}{\cdot}CH_2{\cdot}CO_2H} \\ \downarrow & \downarrow \\ \mathrm{CH_2}{<}{\begin{smallmatrix}\mathrm{CHMe{\cdot}CH_2}\\ \mathrm{CH_2{-}CH_2}\end{smallmatrix}}{>}\mathrm{CO} & \mathrm{Pr^{\alpha}CH}{<}{\begin{smallmatrix}\mathrm{CH_2{\cdot}CO}\\ \mathrm{CH_2{\cdot}CO}\end{smallmatrix}}{>}\mathrm{O} \end{array}$$

The components of this mixture may be readily separated by taking advantage of the dissimilar character of their anhydrides;

the unimolecular anhydride of the propylglutaric acid distils at a temperature lower than that at which the polymolecular anhydride of its isomeride begins to suffer degradation to β-methyl*cyclo*hexanone. Since the propylglutaric anhydride is a liquid and the corresponding acid very difficult to recrystallise, the former is converted into its anilic acid for the purpose of estimating the yield. From the yields so determined with fairly large quantities of material, it appears that αβ-addition accompanies αδ-addition to the extent of at least 7% but improbably more than 10%.

Ethyl γ-methylsorbate also gives both αβ- and αδ-addition products with ethyl sodiocyanoacetate. In this, the latest instance studied, the authors were quite unable to bring about the catalytic reduction of the addition compounds (III and IV) or their closely related derivatives. But here degradation by ozonolysis yields definite evidence. The mixture of ester-addition products gives the appropriate fission products according to the scheme :



(III).

$$\begin{array}{l}\mathrm{CHMe{\cdot}CMe{:}CH{\cdot}CH_2{\cdot}CO_2Et}\\ \mathrm{CH(CN){\cdot}CO_2Et}\end{array} \longrightarrow \begin{array}{l}\mathrm{CHMe{\cdot}COMe}\\ \mathrm{CH(CN){\cdot}CO_2Et}\end{array} + \begin{array}{l}\mathrm{CHO}\\ \mathrm{CH_2{\cdot}CO_2Et}\end{array}$$

$$\begin{array}{l}\mathrm{CHMe{\cdot}COMe}\\ \mathrm{CH(CN){\cdot}CO_2Et}\end{array} \longrightarrow \begin{array}{l}\mathrm{CHMe{\cdot}COMe}\\ \mathrm{CH_2{\cdot}CO_2H}\end{array}$$

(IV.)

$$\begin{array}{r}\mathrm{CHMe{:}CMe{\cdot}CH{\cdot}CH_2{\cdot}CO_2Et}\\ \mathrm{CH(CN){\cdot}CO_2Et}\end{array} \longrightarrow \mathrm{CH_3{\cdot}CHO} + \begin{array}{r}\mathrm{COMe{\cdot}CH{\cdot}CH_2{\cdot}CO_2Et}\\ \mathrm{CH(CN){\cdot}CO_2Et}\end{array}$$

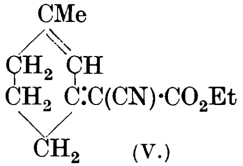
$$\begin{array}{r}\mathrm{COMe{\cdot}CH{\cdot}CH_2{\cdot}CO_2Et}\\ \mathrm{CH(CN){\cdot}CO_2Et}\end{array} \longrightarrow \begin{array}{c}\mathrm{CO{\cdot}CH_2{\cdot}CH{\cdot}CH_2{\cdot}CO}\\ \mathrm{\diagdown O{-\!\!-}CMe{-}O\diagup}\end{array}$$

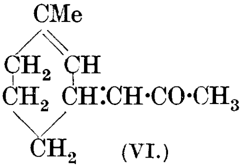
Owing to the failure of the reduction method a satisfactory estimate of the αβ, αδ-ratio could not be made, but it was clear from the amounts of the different degradation products isolable that the ratio approached unity far more closely than in the preceding example.

The addition of ethyl malonate and of ethyl cyanoacetate to ethyl βδ-dimethylsorbate has been attempted, but here, as with ester addition to ethyl crotylidenemalonate (Farmer and Healey, *loc. cit.*), conditions suitable for promoting reaction could not be found.

It appears from the experiments carried out that the reactivity of the differently substituted butadiene esters towards sodio-esters varies widely, but, on the other hand, slight changes in the experimental conditions have many times been found to have a profound effect in facilitating or inhibiting reaction. It is hoped later to furnish values of the αβ, αδ-ratio for a number of substituted butadiene esters, ketones and nitriles, distinguishing between the effect due to alkylation in the different positions of the chain and that (if any) due to modification of the activating group.

Whether or no the value of the αβ, αδ-ratio in a given instance is at all influenced by changes in the addendum (as, for instance, by alkylation or replacement of $\cdot CO_2Et$ by $\cdot CN$) remains to be shown, but the indications at present are that such changes affect only the ease of reaction. The influence on the αβ, αδ-ratio of cyclisation is also somewhat doubtful. Many αβ- and αδ-addition products readily undergo cyclisation in the presence of the condensing agent and in some instances it is difficult to find experimental conditions under which addition is promoted but intramolecular cyclisation excluded. For instance, from ethyl methyl*cyclo*hexenylidenecyanoacetate (V) and methyl*cyclo*hexenylideneacetone (VI) only


(V.)


(VI.)

cyclic αβ-addition products have so far been obtainable, but the legitimacy of concluding that the αβ,αδ-relationship which holds under the cyclising conditions employed is also the normal one is uncertain.

In view of the fact that the formation of a 7—10% yield of one of the ester-addition products of methyl sorbate previously escaped detection, although the search for evidence of such formation was the specific object of investigation, it may well be that the αδ-bromination of β-vinylacrylic acid (Farmer and Healey, *loc. cit.*) and of sorbic acid (Auwers and Heyna, *Annalen*, 1923, **434**, 140) is not quite so complete as ozonisation experiments have indicated. The conclusions of Farmer and Healey with respect to the bromination product of the former acid have recently been endorsed by Muskat, Becker, and Lowenstein (*J. Amer. Chem. Soc.*, 1930, **52**, 326), but the detection and the reasonably efficient isolation of ozone fission products are so much the more difficult of accomplishment when working with diolefin dibromides than when working with unsaturated acids (indeed experience with hydrocarbon dibromides and hydrobromides has clearly shown the danger of relying on ozonisation technique alone) that a supplementary examination of the bromination products of both acids is very desirable.

EXPERIMENTAL.

Addition of Methyl Malonate to Methyl Sorbate.—The yield of addition product previously recorded by Farmer and Healey (*loc. cit.*, p. 1064) was considerably improved by modifying slightly the experimental conditions. Methyl malonate (50 g.) was added to a solution of sodium (0·6 g.) in methyl alcohol (6 c.c.) and a quantity of ether *insufficient to produce a precipitate* (usually about 10 c.c.) was added. From the resulting solution, after being heated on a steam-bath for 6 hours, a mixture of unchanged reactants (b. p. 102—110°/20 mm.) and addition product (b. p. 172—178°/17 mm.) was isolated. Yield of addition product, 80%.

Hydrogenation of the Addition Product.—The addition product, dissolved in aqueous methyl alcohol, absorbed 2 atoms of hydrogen per molecule when shaken therewith in the presence of colloidal palladium for 4 hours. The reduction product, obtained in quantitative yield, was a colourless oil, b. p. 165—170°/14 mm., which yielded a granular sodium salt when boiled with alcoholic sodium hydroxide (excess of the latter was necessary to ensure complete hydrolysis). After the heating had been continued for 4 hours, the sodium salt was filtered off, freed from alcohol, and boiled with 25% hydrochloric acid until decarboxylation was complete (40 hours). The hydrolysis product, isolated with only small loss, was a colourless oily acid which would not solidify. It was distilled and collected in several fractions, of which those of higher boiling point partly or wholly solidified on standing.

The solid material, after being drained and washed with petroleum (recrystallisation operations proved extremely unsatisfactory), melted at 47° and corresponded in properties with the β-methylpimelic acid (m. p. 48—50°) of Einhorn and Ehret (*Annalen*, 1897, **295**, 179) [Found : *M*(dibasic), 174. Calc., 174]. It was readily convertible into β-methyl*cyclo*hexanone on heating with lime, and the ketone yielded a semicarbazone, m. p. 191°, identical with that derived from an authentic specimen.

The liquid acid, still containing a proportion of β-methylpimelic acid, could not be induced to solidify. It was therefore converted into its anhydride by boiling with acetic anhydride for 4 hours, after which the unimolecular anhydride of β-propylglutaric acid could be separated from the polymolecular anhydride of β-methylpimelic acid by distillation. The former compound was a colourless oil, b. p. 175°/20 mm., which yielded β-propylglutaric acid, m. p. 52°, on being heated with caustic alkali and then acidified (compare Day and Thorpe, J., 1920, **117**, 1471), and an anilic acid, m. p. 128°, on treatment with aniline (Day and Thorpe, *loc. cit.*) (Found : C, 67·3 ; H, 7·5. Calc. for $C_{14}H_{19}O_3N$: C, 67·45 ; H, 7·6%) ; the latter compound partly decomposed above 200°/17 mm. and was rapidly converted into β-methyl*cyclo*hexanone when heated at atmospheric pressure.

The weight of β-propylglutaric anhydride (estimated as the corresponding anilic acid) derivable from a known weight of the hydrolysed reduction product was ascertained. This figure showed the β-propylglutaric acid content of the acid mixture to be about 7%—improbably more than 10%—of the whole.

Addition of Esters to Ethyl γ-Methylsorbate.—The γ-methylsorbic ester was obtained from tiglic aldehyde in 50% yield (b. p. 99—100°/15 mm.) by the method of Auwers and Heyna (*Annalen*, 1923, **434**, 162). Since ethyl malonate could not be added to this compound under any of the conditions employed, ethyl cyanoacetate was used in its place.

The conjugated ester (22 g.) was added to a mixture prepared by adding ethyl cyanoacetate (33 g.) to a solution of sodium (0·4 g.) in the minimal quantity of absolute alcohol. No ether was added, since such addition at once precipitated the sodiocyanoacetic ester and subsequently inhibited the formation of an addition product. The reaction mixture, after being heated for 9 hours on a steam-bath, yielded (i) unchanged reactants (b. p. below 130°/18 mm.), (ii) an addition product, and (iii) a very small quantity of a dark-coloured viscous liquid. The addition product was a colourless oil, shown subsequently to be a mixture of *ethyl α-cyano-βγ-dimethyl-Δ^{γ}-pentene-αε-dicarboxylate* (III) and *ethyl α-cyano-β-*iso*butenylglutarate* (IV) (Found: C, 62·8; H, 7·95. $C_{14}H_{21}O_4N$ requires C, 62·9; H, 7·85%). Yield, 18—40%.

Ozonolysis of the Addition Product.—The addition product, dissolved in chloroform, was ozonised for 30 hours. The ozonide, from which the solvent was removed in the usual way, was decomposed by water, the containing vessel being gradually heated to 50° while a stream of carbon dioxide was passed through it. The escaping vapours were conducted into a solution of dimethyldihydroresorcinol, which rapidly deposited a bulky precipitate. The precipitate was the acetaldehyde derivative of dimethyldihydroresorcinol, 1 : 1-dimethyl-4-ethylidene-3 : 5-*cyclo*hexadione, m. p. 139° (mixed m. p. with an authentic specimen, 139°).

When the evolution of acetaldehyde had ceased, the reaction mixture, which gave an intense purple colour with ferric chloride (to be expected if either formylacetic ester or its polymeride, α-formylglutaconic ester, were present), was boiled on a sand-bath for about 3 hours to decompose the last trace of ozonide. The bulk of the resulting solution was considerably reduced by distilling off water at diminished pressure and the residue was boiled with 25% hydrochloric acid for 12 hours. After cooling, the acid solution was thoroughly extracted, first with ether and then with chloroform. The solvent was removed from the extracts and the united residues were distilled. Two principal fractions were collected, the first, b. p. 120—125°/10 mm., consisting of crude β-methyllævulic acid (compare Bischoff, *Annalen*, 1881, **206**, 331), the second, b. p. 205—210°/10 mm., the solid keto-dilactone of β-acetylglutaric acid (compare Emery, *Annalen*, 1897, **295**, 104).

The former of these was taken up in water at 0° to separate it from the dissolved dilactone and converted into its semicarbazone. When the precautions necessary to the formation of a normal semicarbazone were followed (Blaise, *Compt. rend.*, 1900, **130**, 1718), the product, after twice recrystallising from aqueous alcohol, decomposed at about 182° but melted at 197°, the temperature recorded by Blaise, when heated on the Maquenne block (Found : C, 44·7 ; H, 7·0. Calc. for $C_7H_{13}O_3N_3$: C, 44·9 ; H, 6·9%).

The solid keto-dilactone was sparingly soluble in ether but readily soluble in chloroform. It crystallised in colourless needles, m. p. 98—99°, from absolute alcohol (Fittig and Roth, *Annalen*, 1900, **314**, 16, give m. p. 99° ; Emery, *loc. cit.*, gives m. p. 101—102°) (Found : C, 53·7 ; H, 5·1. Calc. for $C_7H_8O_4$: C, 53·85 ; H, 5·1%).

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IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W. 7.

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