531. *Experiments on the Synthesis of the Pyrethrins. Part XIII.* Total Synthesis of* (±)-cis- *and* -trans-*Chrysanthemumdicarboxylic Acid,* (±)-cis- *and* -trans-*Pyrethric Acid, and Rethrins II.*

By L. Crombie, S. H. Harper, and K. C. Sleep.

(±)-*cis*- and -*trans*-Chrysanthemumdicarboxylic acids † are synthesised by treating *trans*-2 : 5-dimethylsorbic ester with diazoacetic ester. Their structures are established by ozonolysis to *meso-cis*- and (±)-*trans*-caronic acids respectively. The -*trans*-dicarboxylic acid is equated with the natural (+)-acid by infrared solution spectra. It follows that the natural acid has a *trans*-side-chain, and, from our previous work, can be correlated with glyceraldehyde.

Routes to 2 : 5-dimethylsorbic acid are investigated and a convenient synthesis from acetoacetaldehyde dimethylacetal is described. It is shown to be the *trans*-acid.

Dimethyl (±)-*cis*-, (±)-*trans*-, and (+)-*trans*-chrysanthemumdicarboxylate are converted into pyrethric acids by partial hydrolysis, and the structure of the (+)-*trans*-compound established by oxidative degradation and biological evidence. Esterification of allylrethrolone with pyrethric acids leads to the first totally synthetic rethrins II.

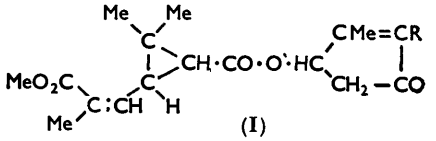
Hydrolysis of pyrethrin II (Ia) and cinerin II (Ib), which occur in natural pyrethrum extract, gives a substituted *cyclo*propane, chrysanthemumdicarboxylic acid (II; R = R′ = H). Staudinger and Ruzicka [1] established its structure as (+)-*trans*-3-(2-carboxyprop-1-enyl)-2 : 2-dimethyl*cyclo*propane-1-carboxylic acid by ozonising it to (−)-*trans*-caronic acid and pyruvic acid. On controlled alkaline hydrolysis of a crude semicarbazone they isolated the half methyl ester of chrysanthemumdicarboxylic acid (pyrethric acid) (II; R = H, R′ = Me) from which methyl pyruvate was obtained on ozonolysis. This

* Part XII, *J.*, 1957, 1083.

† As all the compounds mentioned in this paper have *trans*-side-chains, the prefix *cis* or *trans* used with chrysanthemumdicarboxylic acid and related substances refers only to the configuration about the *cyclo*propane ring. If differentiation is needed, $trans_c$- may be used to indicate the arrangement of the ring substituents and $trans_o$ to indicate the stereochemistry of the olefinic linkage, *e.g.*, (III; R = R′ = H) is $trans_o$: cis_c-chrysanthemumdicarboxylic acid.

[1] Staudinger and Ruzicka, *Helv. Chim. Acta*, 1924, **7**, 201.

established that it is the acidic function attached to the *cyclo*propane ring which is involved in ester formation with the rethrolone fragment. Staudinger and Ruzicka's work left two stereochemical points unsettled: first, the configurative correlation with (+)-glyceraldehyde and, secondly, the stereochemistry of the side-chain double bond. Crombie and

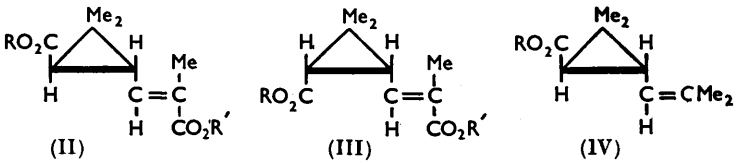


(I)

(Ia): R = $CH_2 \cdot CH{=}\overset{c}{C}H \cdot CH{=}CH_2$

(Ib): R = $CH_2 \cdot CH{=}\overset{c}{C}HMe$

Harper [2] established the configurative correlation for (+)-*trans*-chrysanthemic acid (IV), which also gives (−)-*trans*-caronic acid on ozonolysis, and it follows that the same relation must hold for (+)-*trans*-pyrethric acid and its rethrins II (cf. footnote on p. 2747). The structures are represented spatially in (II)—(IV). The stereochemistry of the side-chain double bond is clarified below.



(II) (III) (IV)

This paper is concerned with the synthesis of the chrysanthemumdicarboxylic acids, and a summary has appeared elsewhere.[3] Experiments on model compounds indicated that diazoacetic ester attacks the 4 : 5-double bond in sorbic and 2-methylsorbic ester, though yields are low, and, because of the number of stereoisomers possible, it is difficult to isolate crystalline products.[4] From the addition of diazoacetic ester to 2 : 5-dimethylsorbic ester only two geometrical arrangements of the substituents on the *cyclo*propane ring are possible, (II) and (III), and this route was pursued.

2 : 5-Dimethylsorbic acid had not previously been described and various preparations were investigated. Reformatski reaction between *iso*valeraldehyde and ethyl α-bromopropionate gave the expected ethyl 3-hydroxy-2 : 5-dimethylhexanoate, which resisted dehydration with phosphorus oxychloride, potassium hydrogen sulphate, or thionyl chloride in pyridine, but was dehydrated by phosphoric oxide. The product showed no high-intensity absorption between 215 and 300 mμ and only a weak double-bond stretching vibration, suggesting that it is (V) and not (VI). Dehydrogenation with *N*-bromo-

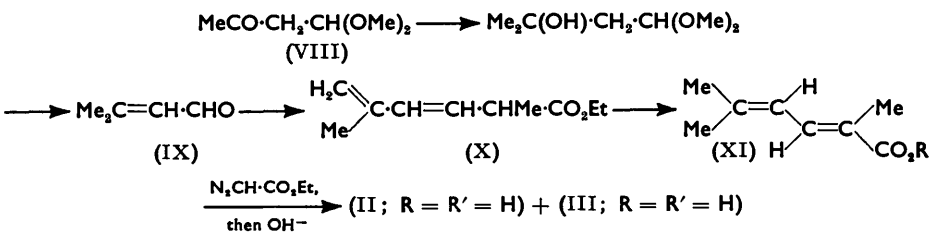
(V) $Me_2CH \cdot CH{:}CH \cdot CHMe \cdot CO_2Et$ $Me_2CH \cdot CH_2 \cdot CH{:}CMe \cdot CO_2Et$ (VI)

succinimide and pyridine gave a mixture having maxima at 225—227 and 269—276 mμ which probably contained ethyl 2 : 5-dimethylhexa-3 : 5- and -2 : 4-dienoate. When this was treated with phosphorus oxychloride (see below) and then hydrolysed, low yields of 2 : 5-dimethylsorbic acid were obtained. This result parallels the experience of Reid and Sause [5] who obtained only poor yields of 5-methylsorbic acid from a similar dehydrogenation procedure. As an alternative route, 1-bromo-3-methylbut-2-ene was converted into 2 : 5-dimethylhex-4-enoic acid by methylmalonic ester synthesis. The acid obtained from the decarboxylation step was contaminated with lactone produced by self-addition (cf. 5-methylhex-4-enoic acid, which, prepared by similar route,[6] is contaminated with 12% of lactone), and was freed from this, and esterified. Dehydrogenation with *N*-bromosuccinimide and pyridine gave discouraging results and the method was abandoned.

An obvious route to 2 : 5-dimethylsorbic acid is the Reformatski reaction between

[2] Crombie and Harper, *J.*, 1954, 470.
[3] Harper, Sleep, and Crombie, *Chem. and Ind.*, 1954, 1538.
[4] Harper and Reed, *J.*, 1955, 779.
[5] Reid and Sause, *J.*, 1954, 516.
[6] Linstead and Rydon, *J.*, 1933, 580.

β-methylcrotonaldehyde and α-bromopropionic ester but the relative inaccessibility of the aldehyde seemed a source of difficulty. Although a number of preparations are described,[7] none seemed suitable and we adapted a procedure for α-unsaturated aldehydes described by Price and Pappalardo.[8] These authors used acylacetaldehyde acetals prepared from chlorovinyl ketones, but Franke *et al.*[9] have made acetoacetaldehyde dimethyl acetal (VIII) readily available from diacetylene, and we used material from this source. This acetal with methylmagnesium bromide gave β-hydroxy*iso*valeraldehyde dimethyl acetal in 60% yield. Distillation with oxalic acid then gave β-methylcrotonaldehyde in 35—37% yield. A restriction on the method is that yields decline when the scale of the last step is above 0·3 mol. Fresh β-methylcrotonaldehyde was treated with activated zinc and ethyl α-bromopropionate under the usual Reformatski conditions, and, since the product was expected to be the hydroxy-ester, it was treated with phosphorus oxychloride. This procedure gave the expected ethyl 2 : 5-dimethylsorbate but treatment with phosphorus oxychloride has other significance and this is dealt with later.



Hydrolysis of ethyl 2 : 5-dimethylsorbate gave the crystalline acid, ultraviolet max. 274 mμ (ε 22,700), which absorbed two mols. of hydrogen over a platinum catalyst. Though the mother-liquors were searched, only one form, m. p. 137°, could be isolated. The resistance of 2 : 5-dimethylsorbic acid to cyclisation by mineral acid strongly supports the *trans*-configuration, for 5-methylhex-4-enoic acid is lactonised extremely easily under these conditions [6] and, structurally, *cis*-2 : 5-dimethylsorbic acid is still more favourably disposed for cyclisation. Esterification with diazomethane gave pure methyl *trans*-2 : 5-dimethylsorbate.

Addition of ethyl diazoacetate to ethyl 2 : 5-dimethylsorbate at 110—115° in the presence of copper bronze gave an ester $C_{14}H_{22}O_4$ in 41% yield, together with substantial amounts of unchanged sorbate. When hydrolysed, the new ester gave a mixture of two acids, the less soluble of which was isolated pure by crystallisation from dilute acetic acid. On ozonolysis it yielded (±)-*trans*-caronic acid and pyruvic acid (2 : 4-dinitrophenylhydrazone), showing that addition had occurred at the 4 : 5-double bond. On the reasonable assumption that the configuration of the 2 : 3-double bond is unaltered by the reaction, the less soluble acid is (±)-*trans*-3-(2-carboxyprop-*trans*-1-enyl)-2 : 2-dimethyl-*cyclo*propane-1-carboxylic acid (II; R = R′ = H). Its light absorption (max. 235—236 mμ; ε 14,900) agreed with that of natural (+)-chrysanthemumdicarboxylic acid (max. 235—236 mμ; ε 14,200). The synthetic acid was converted into the crystalline dimethyl ester and its infrared spectrum (in carbon tetrachloride solution) compared with that of natural dimethyl (+)-chrysanthemumdicarboxylate. The two spectra were identical (for the full curves see our note [3]) : the ultraviolet absorption was also identical within experimental error. Staudinger and Ruzicka's structure [1] is thus confirmed synthetically, and the side-chain configuration shown to be *trans*.

[7] *Inter al.*, Fischer, Ertel, and Löwenberg, *Ber.*, 1931, **64**, 30; Fischer and Löwenberg, *Annalen*, 1932, **494**, 263; Burkhardt, Heilbron, and Aldersley, B.P. 512,465; Jones and Weedon, *J.*, 1946, 937; Young and Linden, *J. Amer. Chem. Soc.*, 1947, **69**, 2912; Wendler and Slates, *ibid.*, 1950, **72**, 5341; Inouye and Shinohara, *Botyu-Kagaku*, 1954, **19**, 102; Julia and Surzur, *Compt. rend.*, 1954, **238**, 2426; Braude and Evans, *J.*, 1955, 3334.

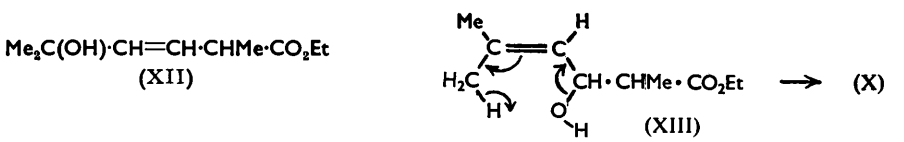
[8] Price and Pappalardo, *J. Amer. Chem. Soc.*, 1950, **72**, 2613.

[9] Franke, Kraft, Tietjen, and Weber, *Chem. Ber.*, 1953, **86**, 793; Franke and Kraft, *Angew. Chem.*, 1955, **67**, 395.

The mixed acids from hydrolysis of the diazoacetic ester reaction product were converted into their dimethyl esters to facilitate separation of the second acid. Crystalline dimethyl (±)-*trans*-chrysanthemumdicarboxylate was removed from a liquid ester, and the latter distilled. The crystalline and the liquid ester were isomeric and both absorbed at 235 mμ. The infrared spectrum of the liquid ester was different from that of dimethyl (+)chrysanthemumdicarboxylate (liquid films) especially between 1030 and 715 cm.$^{-1}$ and on hydrolysis gave a dibasic acid, m. p. 208—210°, which depressed the melting point of (±)-*trans*-chrysanthemumdicarboxylic acid (m. p. 207—208°). When ozonised, the liquid ester gave *meso-cis*-caronic acid so it must be methyl (±)-*cis*-3-(2-methoxycarbonylprop-*trans*-1-enyl)-2 : 2-dimethyl*cyclo*propane-1-carboxylate, and the acid (±)-*cis*-chrysanthemumdicarboxylic acid (III; R = R′ = H).

We now return to the Reformatski reaction between β-methylcrotonaldehyde and ethyl α-bromopropionate. If, from this reaction, ethyl 3-hydroxy-2 : 5-dimethylhex-4-enoate were isolated, and reaction with ethyl diazoacetate carried out, followed by dehydration, an alternative route to chrysanthemumdicarboxylic acid would be available. Inouye, Shinohara, and Ohno [10] claimed to have done this and obtained a chrysanthemumdicarboxylic acid, m. p. 180° (later revised to m. p. 185—186°) : no spectroscopic data were given. In our hands, the product from the Reformatski reaction was, after distillation, not the hydroxy-ester ($C_{10}H_{18}O_3$) but a mixture of two isomeric esters ($C_{10}H_{16}O_2$). All the fractions had maxima at 227—228 and 276—277 mμ and absorbed two mols. of hydrogen over a catalyst. This indicates that they were mixtures of the retro-diene ethyl 2 : 5-dimethylhexa-3 : 5-dienoate (X) and the expected product, ethyl 2 : 5-dimethylhexa-2 : 4-dienoate (XI; R = Et) : extinction data show that the lower-boiling fractions contained > 90% of the former and the higher-boiling ones about equal amounts of the two components. Infrared absorption confirmed the presence of a substance containing the groupings RR′C=CH_2 (888 cm.$^{-1}$), and R·CH=CHR′ (968 cm.$^{-1}$) in the low-boiling material, and the position of the ester-carbonyl absorption (1736 cm.$^{-1}$) indicated that it was α-saturated. When treated with phosphorus oxychloride, the ester (X) was readily isomerised into (XI). The formation of ethyl 2 : 5-dimethylhexa-3 : 5-dienoate by dehydration of the hydroxy-ester (XIII) might be due to prior anionotropic rearrangement, followed by dehydration of the tertiary alcohol (XII), or to a cyclic concerted process as indicated.

Addition of ethyl diazoacetate to mixtures of ethyl 2 : 5-dimethylhexa-2 : 4- and -3 : 5-dienoate (containing mostly the latter) gave a product $C_{14}H_{22}O_4$. This was not a stereoisomer of diethyl chrysanthemumdicarboxylate for it showed no maximum above 210 mμ (ε 17,800 at 210 mμ) and absorbed 1·2 mols. of hydrogen on hydrogenation. The latter figure suggests that either the ester is a mixture or else it contains a grouping which is partially cleaved by hydrogenation. The ester was stable to phosphorus oxychloride and

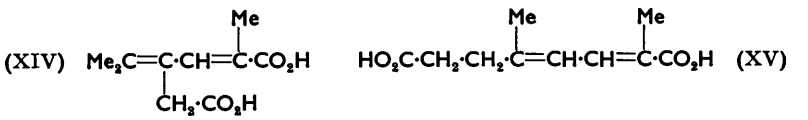


on alkaline hydrolysis gave, in low yield, an acid, of m. p. 187° which was identical (mixed m. p.) with the substance originally claimed by Inouye and his co-workers [10] to be chrysanthemumdicarboxylic acid. The acid absorbed 2 mols. of hydrogen and had an ultraviolet maximum at 274 mμ, indicating the chromophore R·CMe:CH·CH:CMe·CO_2H. Infrared evidence is in agreement.

After publication of our note,[3] Inouye, Takeshita, and Ohno [11] confirmed our synthesis

[10] Inouye, Shinohara, and Ohno, *Botyu-Kagaku*, 1954, **19**, 35.
[11] Inouye, Takeshita, and Ohno, *ibid.*, 1955, **20**, 102; *Bull. Inst. Chem. Res. Kyoto Univ.*, 1955, **33**, 73.

of (±)-chrysanthemumdicarboxylic acid and now agree that the acid of m. p. 187° is not a stereoisomer of that system but a substituted sorbic acid. They claim to have obtained the latter by adding ethyl diazoacetate to ethyl 3-hydroxy-2 : 5-dimethylhex-4-enoate but this was not analysed and light absorption data, which would indicate that it had not dehydrated, appear to have been omitted. The acid of m. p. 187° is now formulated by them as (XIV) but it is difficult to explain its formation from our retrodiene (X). Our diene ester precursor cannot, on light-absorption grounds, be merely the ester derived from this acid. Since the acid gives lævulic acid on ozonolysis, structure (XV) is a reasonable



alternative. A speculative mode of formation is by attack of ethyl diazoacetate at the 5 : 6-double bond of (X) with the formation of an olefinic rather than a *cyclo*propane linkage (analogies for this exist [12]). Alkaline isomerisation of the intermediate unconjugated diene could then give the acid (XV) by prototropic shifts.[13] The by-product, and its origin, are being examined more closely.

In order to make totally synthetic rethrins II it was necessary to devise a procedure for preparing (±)-*trans*-pyrethric acid (II; R = H, R′ = Me). As the side-chain methoxycarbonyl group is tertiary and α-unsaturated, whereas the ring methoxycarbonyl group is secondary, it seemed possible that half-hydrolysis of the dimethyl ester might be successful. The procedure was tested on natural dimethyl (+)-*trans*-chrysanthemumdicarboxylate, and, when distilled, the product had $[\alpha]_D^{16}$ +103·4°, in good agreement with Staudinger and Ruzicka's value [1] of $[\alpha]_D^{18}$ +103·9° for natural pyrethric acid.* Confirmation of its structure was obtained by ozonising it to methyl pyruvate, and, when esterified with allylrethrolone, it gave a partially synthetic rethrin II with high insecticidal activity. The procedure was then applied to the preparation of totally synthetic (±)-*trans*-pyrethric acid: its infrared spectrum (liquid film) was identical with that of natural (+)-*trans*-pyrethric acid. If the partial hydrolysis was carried out in ethanol, the ethyl (±)-*trans*-half ester, resulting from ester interchange, could be isolated as a crystalline solid. (±)-*cis*-Pyrethric acid was also prepared. The pyrethric acids were converted into their acid chlorides and then esterified with (±)-allyl-rethrolones to give the first totally synthetic rethrins II. Biological data are summarised in the experimental section and it is material that (±)-allylrethronyl (+)-*trans*-chrysanthemate is **4·1** times as toxic as the (+)-*trans*-pyrethrate made by the partial hydrolysis procedure, for LaForge and his co-workers [14] found a ratio of 4·4 using (±)-allylrethronyl (+)-*trans*-pyrethrate prepared from natural pyrethric acid.

Natural (+)-*trans*-pyrethric acid has previously been re-esterified with natural (+)-*cis*-cinerolone and (+)-*cis*-pyrethrolone to give cinerin II and pyrethrin II. Since we have previously synthesised (±)-*cis*-cinerolone [15] and (±)-*cis*-pyrethrolone,[16] the problem of making the natural rethrins-II with the correct geometrical form at the two olefinic and the *cyclo*propane centres is now solved. Attention may be directed to improvements in

* This completes a total synthesis of natural (+)-pyrethric acid for Matsui, Miyano, and Yamashita (*Proc. Japan. Acad.*, 1956, **32**, 353) find that natural (+)-chrysanthemic acid (first synthesised by Campbell and Harper, *J.*, 1945, 283) can be converted into (+)-chrysanthemumdicarboxylic acid by oxidation with selenium dioxide, followed by treatment with silver oxide.

[12] von Auwers and Ungemach, *Ber.*, 1933, **66**, 1198; D'yakonov, *Zhur. obshchei Khim.*, 1949, **19**, 1891.

[13] Goldberg and Linstead, *J.*, 1928, 2343.

[14] LaForge, Gersdorff, Green, and Schechter, *J. Org. Chem.*, 1952, **17**, 381.

[15] Crombie and Harper, *Nature*, 1949, **164**, 534; *J.*, 1950, 1152; Crombie, Harper, Stedman, and Thompson, *J.*, 1951, 2445.

[16] Crombie, Harper, and Newman, *Chem. and Ind.*, 1954, 1109; *J.*, 1956, 3963.

the synthetic methods and optical resolution of *cis*-pyrethrolone and *trans*-pyrethric acid. Information on the latter aspect has recently appeared.[17]

Experimental

Ultraviolet measurements were made in ethanol with a Unicam SP.500 instrument, and infrared measurements with Grubb-Parsons single- and double-beam spectrometers (rock-salt optics).

β-*Hydroxyisovaleraldehyde Dimethyl Acetal*.—Acetoacetaldehyde dimethyl acetal (132 g., 1 mole; b. p. 67—68°/15 mm., n_D^{20} 1·4138) was added slowly to a Grignard reagent prepared from magnesium (34 g., 1·4 g.-atoms) and methyl bromide in dry ether (400 ml.), at 20°. When reaction was complete, ammonium acetate solution was cautiously added, and the ethereal layer separated. The aqueous phase was extracted with ether (2 × 100 ml.), and the united ethereal solutions were dried ($MgSO_4$), evaporated, and distilled. After elimination of a fore-run, b. p. to 72°/14 mm., n_D^{20} 1·4228 (12·6 g.), β-hydroxy*iso*valeraldehyde dimethyl acetal (89 g., 60%), b. p. 72—79°/14 mm., n_D^{20} 1·4196, was obtained. A total of 850 g. of material was prepared (n_D^{20} 1·4190—1·4196), in yields varying from 48 to 60%.

β-*Methylcrotonaldehyde*.—β-Hydroxy*iso*valeraldehyde (39·7 g.), anhydrous oxalic acid (7·5 g.; prepared by azeotropic distillation with carbon tetrachloride), and quinol (0·5 g.) were distilled together at 10 mm., the still-head temperature being kept below 50° and the receiver at −30°. The distillate was fractionated to give, after removal of the methanol, β-methylcrotonaldehyde (8·3 g., 37%), b. p. 40—46°/13 mm., n_D^{20} 1·4550. The 2 : 4-dinitrophenylhydrazone had m. p. 184—185° (lit.,[7] b. p. 68—72°/95 mm.; 2 : 4-dinitrophenylhydrazone, m. p. 184—185°). Each batch was used immediately in the Reformatski reaction below. When the scale of the reaction was increased, yields diminished. A modification in which the acetal (44 g.) was added dropwise to anhydrous oxalic acid (8 g.) and quinol (0·8 g.) contained in a 50 ml. Claisen flask at 85—90°/2 mm. gave 35 g. of crude product. On redistillation through a short column, this yielded β-methylcrotonaldehyde (8·8 g., 35%), but the material was less pure than that from the first method (b. p. 44—60°/17 mm., n_D^{20} 1·4520).

Ethyl 2 : 5-*Dimethylhexa*-2 : 5-*dienoate* (2 : 5-*Dimethylsorbate*).—A few ml. of a mixture of β-methylcrotonaldehyde (11·0 g.), ethyl α-bromopropionate (25 g.), and dry benzene (30 ml.) was added to zinc wool (8·5 g.; activated by immersion in 2N-hydrochloric acid for 20 sec., followed by washing with water, acetone and ether, and drying under a vacuum) and dry benzene (10 ml.) containing a crystal of iodine. Reaction commenced, with vigorous refluxing, after warming and stirring, and the remainder of the aldehyde mixture was added dropwise so as to maintain steady refluxing. The product was heated on a water-bath for 2 hr., cooled, and stirred with ice-cold 2N-sulphuric acid (100 ml.). The benzene layer was isolated and washed with 10% sodium hydrogen carbonate solution, N-sulphuric acid (25 ml.), and water (2 × 25 ml.). The acidic washing was added to the 2N-acid used for decomposition and extracted with ether (2 × 25 ml.): these extracts were added to the benzene solution, the whole was dried, and the ether evaporated. Phosphorus oxychloride (8 g.) was added to the benzene solution, and the mixture heated under reflux for 20 min. The product was washed with water (2 × 50 ml.), then dried ($MgSO_4$), and the benzene distilled. Distillation of the residue yielded ethyl 2 : 5-dimethylsorbate (12·5 g., 57%), b. p. 112—114°/22 mm., n_D^{20} 1·5029. Light absorption: max. 276—277 mμ (ε 24,400). Replacement of benzene as solvent by tetrahydrofuran gave similar yields, but the working up was less convenient.

2 : 5-*Dimethylsorbic Acid*.—Ethyl 2 : 5-dimethylsorbate (9·3 g.) was heated under reflux with potassium hydroxide (9·3 g.) in ethanol (100 ml.) for 1 hr. The ethanol was distilled, water (50 ml.) added, and the product acidified to Congo-red. The precipitated 2 : 5-*dimethylsorbic acid* (6·4 g., 83%) had m. p. 132—134°. It was recrystallised from light petroleum (b. p. 80—100°) to m. p. 137° (5·5 g., 71%) and formed colourless needles (Found: C, 68·5; H, 8·5. $C_8H_{12}O_2$ requires C, 68·5; H, 8·6%). Light absorption: max. 274 mμ (ε 22,700). The infrared spectrum showed bands at 1677 (unsatd. CO_2H) and 1630 and 1597 $cm.^{-1}$ (conj. diene). When it was hydrogenated in ethyl acetate with Adams catalyst 1·98 mols. of hydrogen were absorbed. Its methyl ester, prepared by use of diazomethane, had b. p. 100—102°/14 mm., n_D^{20} 1·5167 (yield 87%), absorption max. 276 mμ (ε 24,200).

[17] Inouye and Ohno, *Bull. Inst. Chem. Res. Kyoto Univ.*, 1956, **34**, 90.

2 : 5-Dimethylsorbic acid (27 mg.) was heated under reflux for 40 min. with 2N-sulphuric acid. The acid was somewhat volatile in steam. After being set aside overnight, the solution was thoroughly extracted with ether, and the extracts were dried and evaporated. The infrared spectrum of the crude solid product (Nujol mull) was identical with that of 2 : 5-dimethylsorbic acid, and no lactone band was present.

Ethyl 2 : 5-Dimethylhexa-3 : 5-dienoate.—A Reformatski reaction was carried out as above with zinc wool (7·5 g.), β-methylcrotonaldehyde (8·5 g.), ethyl α-bromopropionate (21 g.), and dry tetrahydrofuran (40 ml.). Phosphorus oxychloride treatment was omitted and the *product*, when distilled at 0·2 mm., was separated into five fractions: (i) b. p. 52—53°, n_D^{20} 1·4587 (0·96 g.); (ii) b. p. 53—54°, n_D^{20} 1·4633 (3·99 g.); (iii) b. p. 54—59°, n_D^{20} 1·4655 (0·63 g.); (iv) b. p. 59—64°, n_D^{20} 1·4721 (1·63 g.); (v) b. p. 64—66°, n_D^{20} 1·4864 (3·70 g.) [Found, in fraction (ii) C, 71·2; H, 9·7. In fraction (iv): C, 69·8; H, 9·7. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·6. $C_{10}H_{18}O_3$ requires C, 64·5; H, 9·8%]. Light absorption of fraction (ii), max. 228—229 mμ (ε 18,500) and 275—276 mμ (ε 2400).

A similar reaction was carried out with benzene as solvent and two main fractions taken: (*a*) b. p. 64—66°/0·5 mm., n_D^{20} 1·4611; (*b*) b. p. 74—80°/0·5 mm., n_D^{20} 1·4829. Light absorptions: (*a*) max. 229 mμ (ε 16,400) and 276—277 mμ (ε 2300); (*b*) max. 228—229 mμ (ε 8700) and 276—277 mμ (ε 10,900). On hydrogenation over 5% palladium–charcoal in ethyl acetate, (*a*) absorbed 2·08, and (*b*) 2·07 mols. of hydrogen. It was necessary to add a little Adams catalyst to complete the hydrogenation of (*a*). The light absorption data show that (ii) and (*a*) contain less than 10% of ethyl 2 : 5-dimethylsorbate. The composition of successive fractions can easily be followed by their infrared spectra using, in particular, bands at 1736 (α-saturated ester), 1705 (α-unsaturated ester), 968 (*trans*-CH=CH) and 888 (CH_2=CRR′) cm.$^{-1}$.

Isomerisation of Ethyl 2 : 5-Dimethylhexa-3 : 5-dienoate to Ethyl 2 : 5-Dimethylsorbate.—Fraction (*a*) above (1·0 g.; n_D^{20} 1·4611) was heated under reflux with phosphorus oxychloride (0·35 g.) in benzene (7 ml.) for 25 min. The product was washed with water (2 × 5 ml.), dried, evaporated, and distilled to give ethyl 2 : 5-dimethylsorbate (0·60 g.), b. p. 109—111°/16 mm., n_D^{20} 1·5030. On hydrolysis this gave a good yield of 2 : 5-dimethylsorbic acid, m. p. 133—135°, which when recrystallised had m. p. 137°, undepressed on admixture with the specimen prepared as above.

Ethyl 3-Hydroxy-2 : 5-dimethylhexanoate.—A Reformatski reaction[18] was carried out as described above with *iso*valeraldehyde (20 g.), ethyl α-bromopropionate (45 g.), zinc wool (20 g.), and benzene (40 ml.), a benzene solution of the product being treated under reflux (20 min.) with phosphorus oxychloride (12 g.). Working up and distillation gave *ethyl 3-hydroxy-2 : 5-dimethylhexanoate* (13·7 g., 31%), b. p. 104—108°/8 mm., n_D^{20} 1·4304, no dehydration having occurred. On redistillation the product had b. p. 113—114°/15 mm., n_D^{20} 1·4305 (Found: C, 64·3; H, 10·8. $C_{10}H_{20}O_3$ requires C, 63·8; H, 10·7. $C_{10}H_{18}O_2$ requires C, 70·55; H, 10·65%). It did not decolorise bromine in carbon tetrachloride, could not be hydrogenated over Adams catalyst, and was transparent in the region 213—300 mμ but showed strong hydroxyl absorption at 3435 cm.$^{-1}$.

A Reformatski reaction in which the phosphorus oxychloride treatment was omitted gave the same product, b. p. 104—108°/8 mm., n_D^{20} 1·4305, in 57% yield.

Ethyl 2 : 5-Dimethylhex-3-enoate.—Ethyl 3-hydroxy-2 : 5-dimethylhexanoate (5·0 g.) and phosphoric oxide (3·0 g.) were distilled together at 12 mm. The crude distillate had b. p. 78—83°/12 mm., n_D^{20} 1·4289. The distillates from two such experiments were fractionated, to give *ethyl 2 : 5-dimethylhex-3-enoate* (5·2 g., 58%), b. p. 74—81°/11 mm., n_D^{20} 1·4272—1·4282. The main fraction had b. p. 76—78°/11 mm. (Found: C, 70·9; H, 10·5. $C_{10}H_{18}O_2$ requires C, 70·55; H, 10·65%). There was no high-intensity maximum in the region 215—300 mμ.

Dehydrogenation of Ethyl 2 : 5-Dimethylhex-3-enoate.—The ester (5 g.) was heated under reflux with carbon tetrachloride (35 ml.), *N*-bromosuccinimide (5·4 g.), and a trace of benzoyl peroxide. Reaction began after 15 min. and the product was then heated for 45 min. more and finally cooled to 0°. The succinimide was filtered off and dry pyridine (3·63 g.) added to the filtrate. The mixture was heated under reflux (1 hr.), cooled, washed with 2N-hydrochloric acid and then water, and dried ($MgSO_4$). Removal of the solvent and distillation at 8 mm. gave fractions: (i) b. p. to 88°, n_D^{20} 1·4586 (0·27 g.); (ii) b. p. 88—94°, n_D^{20} 1·4555 (0·62 g.); (iii) b. p. 94—100°, n_D^{20} 1·4602 (0·76 g.); (iv) b. p. 100—108° n_D^{20} 1·4700 (1·06 g.). Fraction (ii)

[18] Raichstein, *J. Russ. Phys. Chem. Soc.*, 1907, **39**, 587.

had max. 225 mμ (ε 11,500) and 269 mμ (ε 2600), and (iv) had max. 227 mμ (ε 9150) and 275—276 mμ (ε 4000).

Fraction (iv) (0·9 g.) was heated under reflux with phosphorus oxychloride (0·4 g.) in benzene (5 ml.) for 30 min. After washing with water, drying, and distillation, an ester (0·65 g.) was obtained having b. p. 99—103°/6 mm., n_D^{20} 1·4886. On hydrolysis this gave 2 : 5-dimethylsorbic acid (0·3 g.), m. p. 132—135°, raised on crystallisation to 137° (m. p. and mixed m. p.). Fraction (ii) (0·5 g.) on similar treatment gave 2 : 5-dimethylsorbic acid (0·07 g.), m. p. 137°. Fraction (iii) (0·6 g.) when hydrolysed without prior treatment with phosphorus oxychloride gave 2 : 5-dimethylsorbic acid (0·1 g.), m. p. 124—128°, raised by two recrystallisations to 137°.

1-Bromo-3-methylbut-2-ene.—3-Hydroxy-3-methylbut-1-ene was prepared by Campbell and Eby's method [19] in 34% yield and had b. p. 96·5—100·5°, n_D^{20} 1·4150. A mixture of the alcohol (12·5 g.) and dry pyridine (2·0 g.) was added slowly to a stirred solution of phosphorus tribromide (15 g.) in light petroleum (70 ml.; b. p. 40—60°), at 0°. After 30 min., ice-water was added and the petroleum layer separated and washed with sodium hydrogen carbonate solution and then water. Drying, evaporation, and distillation gave the bromide (8·25 g., 38%), b. p. 64—68°/70 mm., n_D^{20} 1·4958. By using the hydrobromic acid procedure of Mulliken *et al.* [20] the bromide was isolated in 28% yield, with b. p. 72—76°/80 mm., n_D^{20} 1·4934.

Diethyl 5-Methylhex-4-ene-2 : 2-dicarboxylate.—1-Bromo-3-methylbut-2-ene (21·1 g.) was added dropwise to ethyl sodiomethylmalonate prepared from sodium (3·3 g.) and ethyl methylmalonate (24·7 g.) in ethanol (80 ml.), and the product was heated under reflux for 2 hr. The ethanol was distilled and water (65 ml.) added to the residue. Separation of the organic layer, drying, evaporation, and distillation gave diethyl 5-methylhex-4-ene-2 : 2-dicarboxylate (19·5 g., 57%), b. p. 132—135°/16 mm., n_D^{20} 1·4410 (Found: C, 63·9; H, 8·8. Calc. for $C_{13}H_{22}O_4$: C, 64·4; H, 9·15%). Staudinger *et al.*[21] give b. p. 120—128°/12 mm.

2 : 5-Dimethylhex-4-enoic Acid.—The above ester (19·0 g.) was heated under reflux for 2 hr. with potassium hydroxide (13·2 g.) in ethanol (100 ml.). The ethanol was evaporated and water (60 ml.) added. After extraction with ether (4 × 15 ml.) the aqueous solution was acidified to Congo-red, and the product collected with ether. Evaporation gave the crude substituted malonic acid (14·5 g.), m. p. 86—89°. The latter (3·5 g.) was heated at 150° for 90 min. and extracted with 10% sodium hydrogen carbonate solution (50 ml.). The alkaline extract was thoroughly extracted with ether and then covered with a layer of ether and acidified at 0°, with vigorous shaking, by a solution of concentrated hydrochloric acid (6·3 ml.) in water (7 ml.). The ethereal layer was separated, washed, dried, and distilled, to give 2 : 5-*dimethylhex-4-enoic acid* (0·9 g., 34%), b. p. 100—103°/0·7 mm., n_D^{20} 1·4490 (Found: C, 66·9; H, 9·7%; equiv., 143·6. $C_8H_{14}O_2$ requires C, 67·55; H, 9·9%; equiv., 142).

The product from direct decarboxylation was contaminated with lactone: in one experiment the purification was omitted. On distillation two fractions were taken: (i) b. p. 125—127°/17 mm., n_D^{20} 1·4483 (18%), and (ii) b. p. 127—130°/17 mm., n_D^{20} 1·4496 (48%). The equivalent of (ii) was 205 (equivs. were determined with cold ethanolic alkali).

2 : 5-Dimethylhex-4-enoic acid was converted into its methyl ester with diazomethane and this had b. p. 78—80°/16 mm., n_D^{20} 1·4334. Bromination with *N*-bromosuccinimide, followed by dehydrobromination with pyridine or triethylamine, gave unpromising mixtures.

Stereoisomeric (±)-Diethyl Chrysanthemumdicarboxylates.—Ethyl 2 : 5-dimethylsorbate (11·0 g.), light petroleum (25 ml., b. p. 100—120°), and copper bronze (0·5 g.) [22] were heated to 100°. Ethyl diazoacetate (15 g.) was added slowly: there was vigorous evolution of nitrogen and the temperature in the flask rose to 115°. The product was heated under reflux for 2 hr., the copper bronze filtered off, and the filtrate distilled. After a fore-run, b. p. 42—98°/0·07 mm., n_D^{20} 1·4671—1·4678 (6·3 g.), *diethyl chrysanthemumdicarboxylate* (6·78 g., 41%), b. p. 98—106°/0·07 mm., n_D^{20} 1·4706, was obtained. There was a large residue. The redistilled analytical specimen had n_D^{20} 1·4726 (Found: C, 65·8; H, 8·8. $C_{14}H_{22}O_4$ requires C, 66·1; H, 8·7%).

In another experiment, ethyl 2 : 5-dimethylsorbate (12·0 g.) and ethyl diazoacetate (8·5 g.) were allowed to react under the above conditions. This gave a fore-run (9·7 g.), b. p. 54—104°/0·4 mm., n_D^{20} 1·4885—1·4947, and diethyl chrysanthemumdicarboxylate (3·82 g.),

[19] Campbell and Eby, *J. Amer. Chem. Soc.*, 1941, **63**, 216, 2683.
[20] Mulliken, Wakeman, and Gerry, *ibid.*, 1935, **57**, 1605.
[21] Staudinger, Muntwyler, Ruzicka, and Seilt, *Helv. Chim. Acta*, 1924, **7**, 390.
[22] Loose, *J. prakt. Chem.*, 1909, **79**, 505.

b. p. 104—118°/0·4 mm., n_D^{20} 1·4748. When the fore-run (9·7 g.) was again treated with ethyl diazoacetate (6·6 g.), a further 2·88 g. of dicarboxylate (b. p. 109—120°/0·45 mm., n_D^{20} 1·4710), making a total yield of 33%, was obtained.

The fore-runs remaining from such experiments were united: they showed absorption at 276 mμ and on redistillation had n_D^{20} 1·4694—1·4775. The united fractions (23 g.) yielded 2 : 5-dimethylsorbic acid (7·6 g.), m. p. 137°, on hydrolysis.

Stereoisomeric Ethyl Methyl (±)-*Chrysanthemumdicarboxylates.*—Methyl 2 : 5-dimethylsorbate (13 g.) when treated with ethyl diazoacetate (19 g.) as above gave material, b. p. 54—98° (mainly 54°)/0·25 mm., n_D^{20} 1·5000, and then the stereoisomeric dicarboxylates (7·0 g., 35%), b. p. 98—105°/0·2 mm., n_D^{20} 1·4763. This fraction was hydrolysed to the mixed acids (5·12 g., 89%), m. p. 165—185° (see below for separation).

Hydrolysis of Diethyl (±)-*Chrysanthemumdicarboxylate.*—The ester (6·7 g.; n_D^{20} 1·4706) was heated under reflux with potassium hydroxide (6 g.) in ethanol (70 ml.) for 1 hr. and the ethanol then evaporated. Water (60 ml.) was added to the residue, and the solution extracted with ether (3 × 15 ml.). Ether remaining in the aqueous phase was removed *in vacuo* and the solution acidified. The oily solid which separated solidified overnight and was then filtered off (4·51 g.). Fractional crystallisation from 5% acetic acid gave pure (±)-trans-*chrysanthemumdicarboxylic acid* (0·73 g.), m. p. 206·5—208° (Found: C, 60·4; H, 7·3%; equiv., 99·6. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%; equiv., 99·1). Light absorption: max. 235—236 mμ (ε 14,900).

Ozonolysis of (±)-trans-*Chrysanthemumdicarboxylic Acid.*—Ozonised oxygen was passed through a suspension of the acid (0·29 g.) in chloroform (20 ml.) at 0° until all the solid dissolved and absorption of ozone was complete. The solvent was removed *in vacuo* at 20° and the ozonide warmed with water (15 ml.) for 15 min. The water was distilled and the distillate treated with 2 : 4-dinitrophenylhydrazine in dilute hydrochloric acid: a yellow derivative was formed and, twice crystallised from glacial acetic acid, gave pyruvic acid 2 : 4-dinitrophenylhydrazone (0·09 g.), m. p. and mixed m. p. 220—221°. The residue from the distillation slowly solidified and was twice crystallised from nitromethane, to give (±)-*trans*-caronic acid (0·11 g.), m. p. and mixed m. p. 218—220°.

Authentic (±)-*trans*-caronic acid was prepared by ozonising (±)-*trans*-chrysanthemic acid, and, crystallised from nitromethane, had m. p. 219—220°. Similarly, (±)-*cis*-chrysanthemic acid gave *meso-cis*-caronic acid, m. p. 179—180° (from nitromethane).

Dimethyl (±)- *and* (+)-trans-*Chrysanthemumdicarboxylate.*—The synthetic (±)-acid (0·4 g.) with diazomethane in ether gave the (±)-trans-*ester* (0·33 g., 66%), m. p. 77—78·5°, raised on crystallisation from light petroleum (b. p. 60—80°) to m. p. 80—80·5°. It formed colourless prisms (Found: C, 63·4; H, 7·9. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·0%). Light absorption: max. 236 mμ (ε 16,800).

Naturally derived chrysanthemumdicarboxylic acid, m. p. 167—170°, was similarly esterified and the ester distilled (b. p. 83—84°/0·07 mm., n_D^{20} 1·4818; 79%). Light absorption: max. 236 mμ (ε 16,200). Staudinger and Ruzicka [1] give b. p. 87—88°/0·25 mm.

The two esters, when compared as 15% solutions in carbon tetrachloride, had identical infrared spectra.

(±)-cis-*Chrysanthemumdicarboxylic Acid.*—Mixed chrysanthemumdicarboxylic acids (9·18 g., 85%), m. p. 150—185°, were obtained by hydrolysing the reaction product, diethyl chrysanthemumdicarboxylate (13·8 g., n_D^{20} 1·4704—1·4728), as described above. The acids with diazomethane gave a semisolid mixture of dimethyl esters (10·0 g., 95%). When crystallised from light petroleum (b. p. 60—80°) dimethyl (±)-*trans*-chrysanthemumdicarboxylate (4·1 g.) separated, having m. p. 77—80°. This was filtered off and the filtrate evaporated and distilled. Five fractions were taken, the main one having b. p. 93—94°/0·2 mm., n_D^{20} 1·4825 (2·59 g.). There was a further 1·15 g. of product. b. p. 89—96°/0·2 mm., n_D^{20} 1·4858—1·4831. Subsequent operations were carried out on the main fraction which was nearly pure dimethyl (±)-*cis*-chrysanthemumdicarboxylate, max. 235 mμ (ε 12,800).

The ester (0·5 g.) was hydrolysed in the usual way to (±)-cis-*chrysanthemumdicarboxylic acid* (0·3 g.), m. p. 198—207°, raised by two crystallisations from nitromethane to 208—210° (Found: C, 60·6; H, 6·8%; equiv., 100·3. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%; equiv., 99·1). Light absorption: max. 235 mμ (ε 14,200). When this product was mixed with the (±)-*trans*-acid described above, the m. p. was 175—186°.

A similar separation was also carried out on the mixed acids (5·12 g.) obtained from the

ethyl methyl chrysanthemumdicarboxylate product. These gave the dimethyl ester mixture (5·52 g., 94%) which yielded methyl (±)-*trans*-chrysanthemumdicarboxylate (2·6 g.), m. p. and mixed m. p. 80°, and the methyl (±)-*cis*-ester (1·43 g.), b. p. 102—104°/0·35 mm., n_D^{20} 1·4835. The infrared spectrum of the latter was identical with that of the specimen described above.

Ozonolysis of Dimethyl (±)-cis-*Chrysanthemumdicarboxylate*.—Excess of ozone was passed through a solution of the methyl ester (1·0 g.) in methylene chloride (25 ml.) at 0°. The solvent was removed *in vacuo* at 20° and a solution of glacial acetic acid (2 ml.) in water (15 ml.) added to the residue, followed by 30% hydrogen peroxide (2 ml.). The solution was heated under reflux (1 hr.), cooled, and extracted with ether (4 × 5 ml.). The ethereal solution was dried and the solvent evaporated, leaving a solid residue which when crystallised from nitromethane yielded *meso-cis*-caronic acid (0·20 g.), m. p. 166—172°, raised by two further crystallisations to m. p. 178—179° (and mixed m. p.).

Under identical conditions methyl (±)-*trans*-chrysanthemate yielded (±)-*trans*-caronic acid, m. p. and mixed m. p. 218—220°, and not the half methyl ester.

Addition of Ethyl Diazoacetate to Ethyl 2 : 5-*Dimethylhexa*-3 : 5-*dienoate*.—Fractions (i), (ii), and (iii) from the Reformatski reaction described on p. 2749 were united: they contained approx. 90% of ethyl 2 : 5-dimethylhexa-3 : 5-dienoate. The material (5·2 g.) was dissolved in light petroleum (15 ml.; b. p. 100—120°), and copper bronze (0·1 g.) added. Ethyl diazoacetate (3·0 g.) was added dropwise to the mixture at 110° and the reaction carried out and the product worked up in the usual way. Fractionation gave an ester (4·48 g.), b. p. 104—110°/0·4 mm., n_D^{20} 1·4609—1·4613. The analytical specimen had b. p. 106—108°/0·4 mm., n_D^{20} 1·4612 (Found: C, 66·1; H, 8·6. Calc. for $C_{14}H_{22}O_4$: C, 66·1; H, 8·7%). Microhydrogenation, $1·2H_2$. Light absorption: no max. > 210 mμ: at 210 and 230 mμ, ε was 17,800 and 2,500 respectively: there was an inflexion at 219 mμ (ε 5800). Allan, Jones, and Whiting [23] give max. 204·5 mμ (ε 16,500) for methyl *trans*-crotonate. The ester showed infrared absorption at 1724 (α-unsaturated ester), 1640 (C=C), and 977 (*trans*-CH=CH·CO_2R?) cm.$^{-1}$. There was a strong band at 1176 cm.$^{-1}$.

A similar experiment with fractions (iv) and (v) (p. 2749) (5·0 g.) gave the same ester (3·16 g.), b. p. 94—99°/0·2 mm., n_D^{20} 1·4634—1·4639 (Found: C, 65·6; H, 8·8%). When heated under reflux (3·0 g.) with phosphorus oxychloride (1·7 g.) in benzene (14 ml.) for 20 min., the ester (2·0 g.) was recovered unchanged (b. p. 102—107°/0·25 mm., n_D^{20} 1·4629—1·4639).

The Conjugated Diene Acid, m. p. 187°.—The ester (4·2 g.) obtained from the first experiment described immediately above gave crude acid (2·71 g.), m. p. 160—172°, on alkaline hydrolysis. Five crystallisations from nitromethane gave pure *acid* (0·90 g.), m. p. 187°. Ester (2·0 g.) from the second experiment above gave crude acid (1·19 g.), m. p. 144—158°, raised by six crystallisations to 187° (0·28 g.): it was identical with the first specimen (Found: C, 60·7; H, 7·0. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%). Light absorption: max. 272—275 mμ (ε 31,400). Another specimen had max. 274 mμ (ε 24,500). On hydrogenation in methanol with palladium–barium sulphate, 1·99 mols. of hydrogen were absorbed. The infrared spectrum showed bands at 1694 (α-unsaturated acid), 1626 and 1600 (conjugated diene) cm.$^{-1}$.

A suspension of the acid (0·45 g.) in methylene chloride (15 ml.) was ozonised at 0° and the ozonide decomposed with water (15 ml.). The product was distilled but the distillate gave no identifiable 2 : 4-dinitrophenylhydrazone. The residue after distillation gave lævulic acid 2 : 4-dinitrophenylhydrazone, m. p. 212—213° (0·05 g.), mixed m. p. with an authentic specimen (m. p. 213°), 210—212°.

(±)-trans-*Pyrethric Acid*.—Synthetic dimethyl (±)-*trans*-chrysanthemumdicarboxylate (2·9 g.), m. p. 80°, was dissolved in absolute methanol (35 ml.), 0·494N-methanolic potassium hydroxide (25·9 ml.) was added, and the solution set aside for 22 hr. It was then heated under reflux (75 min.) and the methanol evaporated *in vacuo*. Water (30 ml.) was added and the unchanged dimethyl chrysanthemumdicarboxylate (0·65 g., m. p. 77—80°) filtered off and washed with water. The filtrate was extracted with ether and acidified to Congo-red. The precipitated oil was collected with ether (5 × 10 ml.), and the ethereal solution washed with a little water and dried ($MgSO_4$). Evaporation and distillation of the residue (1·72 g.) gave (±)-trans-*pyrethric acid* (1·08 g.), b. p. 129—143°/0·06 mm., as a viscous liquid (Found: C, 62·1; H, 7·4%; equiv., 212. $C_{11}H_{16}O_4$ requires C, 62·25; H, 7·6%; equiv., 212). Light absorption: max. 235 mμ (ε 15,900). After more than a year, specimens of this, and of the (±)-*cis*-stereoisomer, had crystallised.

[23] Allan, Jones, and Whiting, *J.*, 1955, 1865.

(+)-trans-*Pyrethric Acid.*—Dimethyl ester of naturally derived chrysanthemumdicarboxylic acid (4·64 g.), b. p. 105°/0·5 mm., was half-hydrolysed as above and the crude product distilled to give (+)-trans-*pyrethric acid* (2·77 g.), b. p. 130—145°/0·06 mm. (Found: C, 62·1; H, 7·6%; equiv., 210), absorption max. 236 mμ (ε 15,300), $[\alpha]_D^{16}$ +103·4° (*c* 1·18% in CCl_4). Staudinger and Ruzicka [1] give b. p. 129—130°/0·33 mm., $[\alpha]_D^{18}$ +103·9° (*c* 9·3% in CCl_4), for natural pyrethric acid.

Excess of ozone was passed through (+)-*trans*-pyrethric acid (0·6 g.) in methylene chloride (20 ml.) at 0°. The solvent was evaporated at 20° and water (25 ml.) added: the mixture was heated to 50° for 5 min. and poured into a solution of 2 : 4-dinitrophenylhydrazine in dilute hydrochloric acid. The precipitate (0·35 g.) was filtered off and dried. On treatment with benzene an insoluble yellow derivative remained undissolved, which when crystallised from light petroleum (b. p. 80—100°)–dioxan gave methyl pyruvate 2 : 4-dinitrophenylhydrazone (0·08 g.), m. p. 189—190°. After chromatography of the benzene solution on alumina, followed by elution with ether, the top orange band remaining on the column was isolated and extracted with sodium hydrogen carbonate solution. Acidification of the extract precipitated an acidic 2 : 4-dinitrophenylhydrazone (0·11 g.), m. p. 193—196°. When crystallised from dilute acetic acid small yellow needles, m. p. 198—199°, were obtained: the compound was not further identified but it may be the derivative of *trans*-3-formyl-2 : 2-dimethyl*cyclo*propane-1-carboxylic acid.

(±)-cis-*Pyrethric Acid.*—Dimethyl (±)-*cis*-chrysanthemumdicarboxylate (2·04 g.) was half-hydrolysed with 0·494N-methanolic potassium hydroxide (18·26 ml.) as above. The crude acid (0·76 g.) was distilled to give (±)-cis-*pyrethric acid* (0·44 g.), b. p. 130—147°/0·1 mm. (Found: C, 62·2; H, 7·5%; equiv., 206), absorption max. 233 mμ (ε 11,900).

(±)-trans-*Di- and Mono-ethyl Chrysanthemumdicarboxylate.*—Dimethyl (±)-*trans*-chrysanthemumdicarboxylate (3·0 g.) was half-hydrolysed with 0·488N-ethanolic potassium hydroxide (26·0 ml.) and worked up as previously described. The neutral product (0·77 g.) had m. p. 32·5—33·5° and analysed correctly for the *diethyl ester* (Found: C, 66·3; H, 8·5. $C_{14}H_{22}O_4$ requires C, 66·1; H, 8·7%). The acidic product, on distillation, gave *ethyl hydrogen* (±)-trans-*chrysanthemumdicarboxylate*, b. p. 135—143°/0·04 mm., m. p. 78° (Found: C, 63·7; H, 8·0%; equiv., 220, 222. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·0%; equiv., 226). Light absorption: max. 236 mμ (ε 16,100).

(±)-*Allylrethronyl* (±)-trans-*Pyrethrate.*—A solution of (±)-*trans*-pyrethric acid (0·69 g.) in light petroleum (7 ml.; b. p. 40—60°) containing thionyl chloride (0·43 g.) was set aside for 3 days. The light petroleum was evaporated and dry benzene (8 ml.) added. This solution was added to (±)-allylrethrolone (0·50 g.) and dry pyridine (0·51 g.) in dry benzene (5 ml.). Pyridine hydrochloride was at once precipitated and after 4 hr. the product was washed with saturated sodium hydrogen carbonate solution, dilute hydrochloric acid, and finally with water. The benzene solution was dried, evaporated, and distilled. After elimination of a small fore-run, (±)-allylrethronyl (±)-*trans*-pyrethrate was collected (0·32 g.; b. p. 170—184°/0·04 mm.). The substance could not be completely purified by distillation on the scale used (Found: C, 67·8; H, 7·4. Calc. for $C_{20}H_{26}O_5$: C, 69·35; H, 7·6%). Light absorption: max. 235 mμ (ε 26,200).

(±)-*Allylrethronyl* (±)-cis-*Pyrethrate.*—This was prepared by the above method from (±)-*cis*-pyrethric acid (0·195 g.) and allylrethrolone (0·13 g.). The ester (0·181 g.) was not distilled but heated at 100°/0·02 mm. for 30 min. and then at 70° for 90 min. (Found: C, 67·8; H, 7·3%). Light absorption: max. 232—233 mμ (ε 22,800).

(±)-*Allylrethronyl* (+)-trans-*Pyrethrate.*—By the same procedure, (+)-*trans*-pyrethric acid (1·0 g.) was converted into (±)-*allylrethronyl* (+)-trans-*pyrethrate* (0·50 g.), b. p. 170—180°/0·02 mm. (Found: C, 69·3; H, 7·5%). Light absorption: max. 232—234 mμ (ε 27,300).

Biological Testing.—The rethrins prepared above were tested for insecticidal activity against houseflies with results summarised below. The potency is expressed relatively to a standard natural pyrethrum extract and is on a weight basis.

	Relative potency
(±)-Allylrethronyl (+)-*trans*-chrysanthemate	3·16
(±)- ,, (±)-*trans*- ,, ...	1·53
(±)- ,, (±)-*cis*- ,, ...	1·12
(±)- ,, (+)-*trans*-pyrethrate	0·77
(±)- ,, (±)-*trans*- ,, ...	0·45
(±)- ,, (±)-*cis*- ,, ...	0·41

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