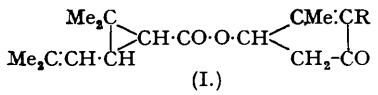
703. *Experiments on the Synthesis of the Pyrethrins. Part V. Synthesis of Side-chain Isomers and Analogues of Cinerone, Cinerolone, and Cinerin-I.*

By L. Crombie, A. J. B. Edgar, S. H. Harper, (Miss) M. W. Lowe, and D. Thompson.

Routes to 2-ketoalkene-1-carboxylic (γ-alkenylacetoacetic) esters are surveyed and the synthesis of natural cinerolone (*cis*-crotylrethrolone) (cf. Part IV) extended to more accessible side-chain isomers and the lower homologue, allylrethrolone. Several such esters are hydrolysed and the sodium salts condensed with pyruvaldehyde in aqueous solution to give 3-hydroxyalkene-2 : 5-diones, which are cyclised by alkali to (±)-alkenylrethrolones. These keto-alcohols are esterified with one or more of (±)-*trans*-, (+)-*trans*-, (−)-*trans*-, and (±)-*cis*-chrysanthemic acids to give a series of alkenylrethrins, isomeric with or analogous to cinerin-I, for comparisons of their insecticidal potencies with that of pyrethrum extract.

The sodio-derivatives of the 2-ketoalkene-1-carboxylic esters are condensed with bromoacetone and subsequently cyclised with alkali to give further alkenylrethrones (cf. Part II), isomeric with or analogous to cinerone and possessing jasmone-like odours.

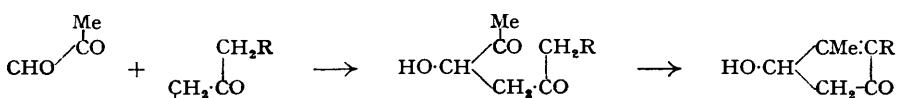
Until recently the total synthesis of esters of the type (I), of which cinerin-I (I*a*) and pyrethrin-I (I*b*) occur naturally as insecticidal constituents of pyrethrum flowers (*Chrysanthemum cinerariifolium*), has been limited to examples where R is alkyl (I*c* and *d*) (Crombie, Elliott, Harper, and Reed, *Nature*, 1948, **162**, 222; Crombie, Elliott, and Harper, Part III, *J.*, 1950, 971).



(I.)

(I*a*; R = $CH_2{\cdot}CH{:}CHMe$-*cis*) (I*e*; R = $CH_2{\cdot}CH{:}CH_2$)
(I*b*; R = $CH_2{\cdot}CH{:}CH{\cdot}CH{:}CH_2$) (I*f*; R = $CH_2{\cdot}CH{:}CHMe$-*trans*)
(I*c*; R = $CH_2{\cdot}CH_2{\cdot}CH_2Me$) (I*g*; R = $CH_2{\cdot}CH_2{\cdot}CH{:}CH_2$)
(I*d*; R = $CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Me$) (I*h*; R = $CH_2{\cdot}CMe{:}CH_2$)

These esters were obtained by reaction of the 2-alkyl-3-methyl*cyclo*pent-2-en-1-one (alkylrethrone) with *N*-bromosuccinimide, and subsequent treatment of the 4-bromo-ketone with silver (±)-*trans*- or (±)-*cis*-chrysanthemate. This method is not capable of direct extension to the preparation of alkenylrethrins (I; R = alkenyl) (see Part III) owing to simultaneous allylic substitution in the side-chain of the alkenylrethrone. Then Schechter, Green, and LaForge (*J. Amer. Chem. Soc.*, 1949, **71**, 1517) briefly reported that the condensation in aqueous solution of pyruvaldehyde with sodium 2-ketoalkene-1-carboxylates (γ-alkenylacetoacetates) (III; R = alkenyl) gave 3-hydroxyalkene-2 : 5-diones (IV; R = alkenyl), which were cyclised by aqueous sodium hydroxide to the alkenylrethrolones (II; R = alkenyl) (for an exposition of this nomenclature, see Harper, *Chem. and Ind.*, 1949, 636; *Pyrethrum Post*, 1950, **2**, No. 1, 20). Several of these keto-alcohols were esterified with naturally derived (+)-*trans*-



(III.) (IV.) (II.)

(II*a*—*h*, as for I)

chrysanthemic acid and with the mixed (±)-*cis*- and (±)-*trans*-acids obtained by the addition of ethyl diazoacetate to 2 : 5-dimethylhexa-2 : 4-diene (cf. Campbell and Harper, Part I, *J.*,

1945, 283). These esters were tested for " knock-down " effect and insecticidal activity against houseflies by Gersdorff (*J. Econ. Entomol.*, 1949, **42**, 532; *Soap*, 1949, **25**, No. 11, 129) with results, particularly for allylrethrin (I*e*), that make the supersession of natural pyrethrum by a synthetic analogue a distinct possibility (*Chem. Eng. News*, 1949, **27**, 930, 1942, 2074; 1950, **28**, 1138, 1234, 2170; *Agric. Chemicals*, 1949, **4**, No. 6, 57, No. 7, 63; Stoddard and Dove, *Soap*, 1949, **25**, No. 10, 118; Moore, *J. Econ. Entomol.*, 1950, **43**, 207).

As a logical development from our synthesis of cinerone, cinerolone, and cinerin-I (Crombie and Harper, *Nature*, 1949, **164**, 534; Part IV, *J.*, 1950, 1152), we have used this condensation to obtain more accessible alkenylrethrolones. We now describe the synthesis of alk-2-enyl and alk-3-enyl side-chain isomers and analogues of *cis*-cinerolone and their esterification with individual chrysanthemic acids to give a series of alkenylrethrins, in the main isomeric with cinerin-I, containing the minimum of diastereoisomers. We also describe the synthesis of several alkenylrethrones, additional to those already reported (Harper, Part II, *J.*, 1946, 892; Part IV, *loc. cit.*), of interest for their jasmone-like odours. After completion of much of this work, Schechter, Green, and LaForge (*J. Amer. Chem. Soc.*, 1949, **71**, 3165) published the experimental details of the preparation of several alkenylrethrolones, using procedures rather different from those we had developed, but have not, so far as we are aware, published any descriptions of their synthetic esters.

The sodium γ-alkenylacetoacetates (III), required for the synthesis of alkenylrethrolones, are conveniently prepared by the hydrolysis of the corresponding methyl or ethyl esters. These are also intermediates for the synthesis of alkenylrethrones, and in earlier (cf. Part II, *loc. cit.*; Crombie, Elliott, and Harper, Part III, *J.*, 1950, 971; Part IV, *loc. cit.*) and unpublished work the methyl esters were prepared by the following sequence of reactions (route *A*) :

$$\mathrm{ROH} \xrightarrow{\text{HCl or HBr}} \mathrm{RCl\ or\ RBr} \xrightarrow{\mathrm{CHNa(CO_2Et)_2\text{-}EtOH}} \mathrm{RCH(CO_2Et)_2} \xrightarrow{\text{aq. NaOH}}$$

$$\mathrm{RCH(CO_2H)_2} \xrightarrow{\text{heat}} \mathrm{RCH_2{\cdot}CO_2H} \xrightarrow{\mathrm{SOCl_2}} \mathrm{RCH_2{\cdot}COCl} \xrightarrow{\mathrm{CHNaAc{\cdot}CO_2Et\text{-}EtOH}}$$

$$\mathrm{RCH_2{\cdot}CO{\cdot}CHAc{\cdot}CO_2Et} \xrightarrow{\text{NaOMe–MeOH at 20°}} \mathrm{RCH_2{\cdot}CO{\cdot}CH_2{\cdot}CO_2Me}$$

(where R is the alkenyl or alkyl group ultimately becoming the side-chain).

When the homologous alcohol was the more readily available or the more suitable, the shorter sequence (route *B*) was used :

$$\mathrm{RCH_2{\cdot}OH} \xrightarrow{\mathrm{HBr\ or\ PBr_3\text{-}C_5H_5N}} \mathrm{RCH_2Br} \xrightarrow{\mathrm{Mg\text{-}Et_2O,\ then\ CO_2}} \mathrm{RCH_2{\cdot}CO_2H}, \text{ then as route } \textit{A}.$$

A variant on route *B* was to pass from the bromide to the cyanide and thence to the acid (route *C*). The use of $\mathrm{RCH_2{\cdot}OH}$ is doubly advantageous for by following route *A* the homologous alkenylrethrolone is accessible from the one starting material. However, an attractive alternative (route *D*) to any of the foregoing makes use of the direct carbethoxylation of alkenyl methyl ketones with ethyl carbonate, particularly when sodium hydride is available as the condensing agent in preference to the forced condensation procedure necessary with sodium methoxide (cf. Wallingford, Homeyer, and Jones, *J. Amer. Chem. Soc.*, 1941, **63**, 2252; Soloway and LaForge, *ibid.*, 1947, **69**, 2677) :

$$\mathrm{ROH} \xrightarrow{\text{HCl or HBr}} \mathrm{RCl\ or\ RBr} \xrightarrow{\mathrm{CHNaAc{\cdot}CO_2Et\text{-}EtOH}} \mathrm{RCHAc{\cdot}CO_2Et}$$

$$\xrightarrow{\text{aq. NaOH at 20°}} \mathrm{RCH_2{\cdot}COMe} \xrightarrow{\mathrm{NaH\text{-}Et_2CO_3\text{-}Et_2O}} \mathrm{RCH_2{\cdot}CO{\cdot}CH_2{\cdot}CO_2Et}$$

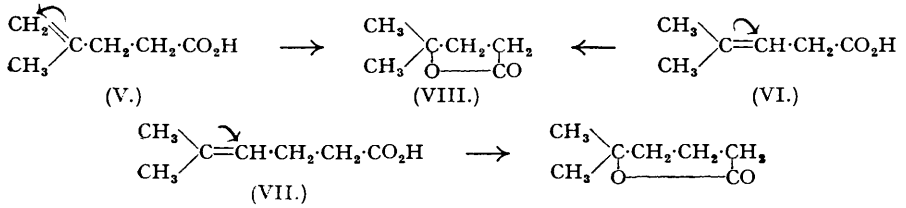
We have reduced commercial crotonaldehyde to *trans*-crotyl alcohol, by the use of lithium aluminium hydride (cf. Nystrom and Brown, *ibid.*, 1947, **69**, 1197), a simpler and more expeditious procedure than reduction with aluminium *iso*propoxide; this alcohol was converted by route *D* into ethyl γ-*trans*-crotylacetoacetate (cf. the use of route *A* in Part II; retention of the *trans*-configuration is discussed in Part IV, *loc. cit.*). This ester was hydrolysed and the sodium salt condensed with pyruvaldehyde in weakly alkaline aqueous solution to give *trans*-3-hydroxy-*n*-dec-8-ene-2 : 5-dione, which in more strongly alkaline medium underwent cyclisation to (±)-*trans*-cinerolone (II*f*). (±)-*trans*-Cinerolone is of interest as being the geometrical isomer of natural cinerolone and a comparison was tabulated in Part IV. It was characterised as the semicarbazone and the acetate semicarbazone, which, as expected, had higher melting points than the corresponding derivatives of either naturally derived (±)-cinerolone or synthetic (±)-*cis*-cinerolone, and gave marked melting-point depressions on admixture. When using our

melting-point procedure (Part IV, *loc. cit.*) we have not been able to reproduce the high melting point (222—223°) recorded for this semicarbazone by Schechter, Green, and LaForge (*loc. cit.*), which may be due to the unusually rapid heating (10° per minute) employed by these authors.

Ethyl γ-*n*-butylacetoacetate, prepared by the direct carbethoxylation of *n*-amyl methyl ketone, similarly yielded (±)-dihydrocinerolone (II*c*). The **3** : **5**-dinitrobenzoate was identical with the derivative of the keto-alcohol obtained from the action of *N*-bromosuccinimide on dihydrocinerone (Part III, *loc. cit.*). This identity provides corroboration of the course of the reactions deduced in Part III.

n-Pent-4-en-1-ol, from the ring scission of tetrahydrofurfuryl chloride, has been used as the starting material for the preparation of ethyl γ-*n*-but-3-enylacetoacetate by route *C*. We had previously prepared the corresponding methyl ester from *n*-but-3-en-1-ol by route *A* (Part II, *loc. cit.*). This exemplifies the dual value of alcohols containing a double bond in the **3** : **4** or more remote position, for we have also used *n*-pent-4-en-1-ol as the starting material for the preparation of methyl γ-*n*-pent-4-enylacetoacetate by route *A* and thence of 3-methyl-2-*n*-pent-4′-enyl*cyclo*pent-2-en-1-one (Part III, *loc. cit.*). Completion of the synthesis from ethyl γ-*n*-but-3-enylacetoacetate yielded (±)-2-*n*-but-3′-enyl-4-hydroxy-3-methyl*cyclo*pent-2-en-1-one (II*g*).

To prepare the 2-methylallyl isomer (II*h*) of cinerolone we first investigated route *A*, starting from the alkenylation of ethyl malonate with 2-methylallyl chloride. Decarboxylation of the crystalline 2-methylallylmalonic acid yielded a product which, even after purification by dissolution in aqueous sodium hydrogen carbonate and liberation under ether at room temperature, had far too high an equivalent weight. Furthermore, after titration a pleasant-smelling oil remained undissolved. Clearly lactonisation had readily occurred, reminiscent of that of the



(V.) (VIII.) (VI.)

(VII.)

isomeric pyroterebic acid (VI) (Linstead, *J.*, 1932, 115) and of 4-methylpent-3-ene-1-carboxylic acid (VII) (Linstead and Rydon, *J.*, 1933, 580). In our acid the polarisation of the terminal double bond should lead to preferential formation of the same γ-lactone (VIII) as is formed from pyroterebic acid. Following Linstead and Rydon's procedure, of liberating the acid from ice-cold solution under light petroleum, we were able to isolate pure 3-methylbut-3-ene-1-carboxylic acid (V) and characterise it by a crystalline *p*-bromophenacyl ester. Because of this complication we turned to the inherently more attractive route *D*, and again starting with 2-methylallyl chloride obtained ethyl γ-2-methylallylacetoacetate without difficulty. Completion of the synthesis yielded the required branched-chain isomer, (±)-4-hydroxy-3-methyl-2-2′-methylallyl*cyclo*pent-2-en-1-one (II*h*).

Condensation with bromoacetone of the sodio-derivative of the intermediary ethyl γ-2-methylallylacetoacetate, prepared by use of either sodium hydride in ether or sodium ethoxide in ethanol, and cyclisation of the product with aqueous sodium hydroxide (cf. Part II, *loc. cit.*) gave the branched-chain isomer of cinerone, 3-methyl-2-2′-methylallyl*cyclo*pent-2-en-1-one. Although this ketone gave the expected deep-red **2** : **4**-dinitrophenylhydrazone of sharp melting point, the semicarbazone melted over a wide range and even after crystallisation from three different solvents still appeared heterogeneous. No satisfactory explanation for this has been found. The ultra-violet absorption spectrum of the semicarbazone (a single absorption band at 2650 A., due to the C:C·C:N·N chromophore, and none at 2950—3050 A.) showed that this was not due to partial isomerisation of the side-chain double bond into the *iso*propylidene position, which might have occurred in the presence of the alkali during cyclisation, although we have never observed this with *n*-alk-2′-enylrethrones. A model shows overlap of the 2′-methyl group with the 3-methyl and with the carbonyl group, but isomerism due to restricted rotation would not provide an explanation.

In preparing, by route *D*, the lower homologue of cinerolone, allylrethrolone (II*e*), we have particularly investigated variations of the experimental procedures for the condensation of sodium γ-allylacetoacetate with pyruvaldehyde, and the subsequent cyclisation, in an attempt to

improve upon the otherwise mediocre yields at these stages. In neither step, and this also applies to the other condensations and cyclisations described in this paper, have we been able to obtain the yields since recorded by Schechter, Green, and LaForge (*loc. cit.*), even when repeating their procedures. In our experience of the condensation of sodium γ-allylacetoacetate with pyruvaldehyde in aqueous solution at pH 8·0—8·5, acidification and warming followed by extraction gives a better yield of 3-hydroxy-*n*-non-8-ene-2 : 5-dione than does direct extraction of the alkaline reaction mixture. This may be due to incomplete decarboxylation of the intermediary sodium 3-hydroxy-2 : 5-diketo-*n*-non-8-ene-4-carboxylate at pH 8·0—8·5. This would agree with the findings of Henze (*Z. physiol. Chem.*, 1930, **189**, 121; Henze and Müller, *ibid.*, 1930, **193**, 88; 1933, **214**, 281), on whose work our procedure, for the condensation of sodium acetoacetate with pyruvaldehyde at pH 8·0—8·5, is based. Henze acidified and warmed the reaction mixture to complete decarboxylation. However, this contrasts with Schechter, Green, and LaForge's finding (*loc. cit.*) that " decarboxylation proceeds spontaneously under the conditions of the reaction, the final product being the hydroxy-diketone, which can be extracted directly from the alkaline reaction mixture," and also with Schöpf's observation of spontaneous decarboxylation when condensing aldehydes (*e.g.*, *o*-aminobenzaldehyde) with acetoacetic acids in the pH range 3—11, although at pH 13 the carboxyl group was retained (Schöpf and Lehmann, *Annalen*, 1932, **497**, 11; Schöpf and Thierfelder, *ibid.*, 1935, **518**, 127; cf. Schöpf, *J. Amer. Chem. Soc.*, 1950, **72**, 2816).

Condensation of the sodio-derivative of the intermediary ethyl γ-allylacetoacetate with bromoacetone, and cyclisation of the product with alkali gave 2-allyl-3-methyl*cyclo*pent-2-en-1-one, which was characterised as the semicarbazone (m. p. 220—222°) and deep-red 2 : 4-dinitrophenylhydrazone. This analogue of jasmone is mentioned without preparative details in G.P. 658,920 (Heine A.G.), though presumably it had been made by Staudinger and Ruzicka's less satisfactory route (*Helv. Chim. Acta*, 1924, **7**, 245; cf. Treff and Werner, *Ber.*, 1935, **68**, 640).

A correlation emerges, for these *n*-alkenylrethrones, between the melting point of the ketone

Formula.	Alkenyl(or Alkyl)rethrin.	$\lambda_{max.}$, A., in EtOH.	$\varepsilon_{max.}$	$[\alpha]_D^{21}$ in $CHCl_3$.
I*f*	(±)-*trans*-Cineronyl (±)-*trans*-chrysanthemate	2285	20,100	—
I*f*	(±)-*trans*-Cineronyl (±)-*cis*-chrysanthemate	2280	16,550	—
I*g*	(±)-*n*-But-3′-enylrethronyl (+)-*trans*-chrysanthemate	2280	16,300	—
I*h*	(±)-2′-Methylallylrethronyl (±)-*trans*-chrysanthemate	2280	15,300	—
I*h*	,, ,, ,, (second prepn.)	2265	18,900	—
I*h*	(±)-2′-Methylallylrethronyl (+)-*trans*-chrysanthemate	2275	15,800	−4·66°
I*h*	(±)-2′-Methylallylrethronyl (±)-*cis*-chrysanthemate	2270	15,400	—
I*h*	,, ,, ,, (second prepn.)	2275	14,800	—
I*c*	(±)-*n*-Butylrethronyl (±)-*trans*-chrysanthemate	2270	18,900	—
I*c*	,, ,, ,, (Part III)	2280	19,950	—
I*c*	(±)-*n*-Butylrethronyl (±)-*cis*-chrysanthemate	2280	18,200	—
I*c*	,, ,, ,, (Part III)	2290	18,600	—
I*d*	(±)-*n*-Amylrethronyl (±)-*trans*-chrysanthemate (Part III)	2275	21,950	—
I*d*	(±)-*n*-Amylrethronyl (±)-*cis*-chrysanthemate (Part III)	2285	19,000	—
I*e*	(±)-Allylrethronyl (±)-*trans*-chrysanthemate	2270	17,200	—
I*e*	,, ,, ,, (second prepn.)	2280	15,500	—
I*e*	(±)-Allylrethronyl (+)-*trans*-chrysanthemate	2265	15,500	−4·63
I*e*	(±)-Allylrethronyl (−)-*trans*-chrysanthemate	2280	21,200	+2·47
I*e*	(±)-Allylrethronyl (±)-*cis*-chrysanthemate	2270	18,400	—
I*e*	,, ,, ,, (second prepn.)	2275	16,000	—

semicarbazone and the position of the side-chain double bond. The *n*-alk-2-enylrethrones give semicarbazones of m. p. >200°, whereas the *n*-alk-3-(4, etc.)enyl isomers have m. p. <190°. Natural *cis*-jasmone (*cis*-*n*-pent-2-enylrethrone) semicarbazone, m. p. 204—206°, *trans*-jasmone semicarbazone, m. p. 202—204° (Crombie and Harper, *Perfumery and Essential Oil Record*, 1950, **41**, 197), and the few other synthetic *n*-alkenylrethrones described in the literature [*n*-pent-4-enyl, m. p. 164—165°; *n*-hex-3-enyl, m. p. 158—159°; *n*-non-8-enyl, m. p. 150° (Heine A.G., *loc. cit.*)] all conform. An exception is dihydropyrethrone (semicarbazone, m. p. 202°) to which has been tentatively ascribed, we believe erroneously, the *n*-pent-3-enyl structure (La Forge and Haller, *J. Org. Chem.*, 1938, **2**, 546; West, *J.*, 1945, 421).

Each of the foregoing keto-alcohols has been esterified by interaction, in the presence of pyridine, with the acid chloride of one or more of (±)-*trans*-, (+)-*trans*-, (−)-*trans*-, and (±)-*cis*-chrysanthemic acid (Part I, *loc. cit.*), to give a series of structural and steric isomers and analogues of cinerin-I (see the Table). These esters were purified by distillation in a high vacuum, although

only obvious impurities were rejected in the foreruns and residues, for each product consists of one or or more pairs of diastereoisomers. Consistently with this we observed some spread of boiling point and of refractive index. It is general experience that combustion-analyses for carbon and hydrogen do not provide a sure guide to the purity either of naturally-derived or of resynthesised pyrethrins and cinerins, and we have encountered this difficulty with the synthetic alkenylrethrins (cf. the similar difficulty with alkenylrethrones, Part II, *loc. cit.*). In an endeavour to assess the purity of our products we have determined their ultra-violet light absorption (see the Table). Their absorption maximum at 2275 ± 10 A. accords closely with that recorded by Gillam and West (*J.*, 1942, 671) for naturally-derived pyrethrin-I (2270 A.). It is noteworthy that the introduction of the acyloxy-radical into the methylene group in the γ-position of the triply substituted αβ-unsaturated ketonic chromophore shifts the absorption maximum to a shorter wavelength by 50—100 A. As the structural variations are remote from the chromophoric centre any marked change of $\lambda_{max.}$ or of $\varepsilon_{max.}$ is not to be expected and none of significance is discernible. The assay of pyrethrum extracts by measurement of this ultra-violet absorption maximum was considered by Gillam and West (*J. Soc. Chem. Ind.*, 1944, **63**, 23) but rejected as offering no advantage over chemical methods of assay. Nevertheless it has recently been applied by Beckley (*Pyrethrum Post*, 1950, **2**, No. 1, 23) to the rapid assay of Kenya pyrethrum, with the use of an empirical factor. The validity of this application has been discussed by one of us (Harper, *Proc. 2nd Internat. Congr. Crop Protection*, London, 1949, in the press), and the results presented here support this discussion.

The alkenylrethrins derived from (+)-*trans*-chrysanthemic acid are lævorotatory, as are the natural pyrethrins and resynthesised cinerins, esterification of a (+)- or a (±)-alcohol with a (+)-acid leading to a (−)-ester. No comparable data exist for naturally derived cinerin-I, although LaForge and Barthel (*J. Org. Chem.*, 1947, **12**, 199) record $[\alpha]_D^{27}$ −14·26° (whether in solution or as the neat ester is not clear for neither solvent nor density is given) for (±)-*cis*-cineronyl (+)-*trans*-chrysanthemate, resynthesised from the naturally derived components.

These synthetic alkenylrethrins are being tested as insecticides against the house-fly (*Musca domestica*) by Dr. E. A. Parkin and Mr. A. A. Green of the Insecticides Section, Pest Infestation Laboratory, and against other species of insects, including plant-feeding species, by Dr. C. Potter and Mr. M. Elliott of the Insecticides Department, Rothamsted Experimental Station. The results and a discussion of their bearing on the relationship of structure to toxicity will be published elsewhere.

Experimental.

Microanalyses and determinations of optical rotation are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorr. The ultra-violet light absorption data were determined in purified ethanol by us with a Hilger Uvispek Photoelectric Spectrophotometer H700. Refractive indices were determined at room temperature, generally 20° ± 4°, and within this range adjusted to 20° by the use of $\Delta_{n_D} = -0{\cdot}0004$ per degree. At temperatures outside this range refractive indices are recorded as observed.

Route A *Experiments.*

3-*Methylbut*-3-*ene*-1 : 1-*dicarboxylic Acid.*—2-Methylallyl chloride (170 g.) was added dropwise during eight hours to the stirred hot solution of ethyl sodiomalonate, prepared by dissolving sodium (43 g.) in ethanol (1 l.; dried by the sodium–ethyl phthalate method) and then adding ethyl malonate (300 g.). After refluxing overnight, as much alcohol as possible was removed by distillation, the residue diluted with water, and the crude ester (402 g., 92%) isolated by extraction. On distillation the bulk had b. p. 104—118°/14 mm., n_D^{20} 1·4344.

The crude ethyl 2-methylallylmalonate (200 g.) was cautiously added in portions to a hot solution of sodium hydroxide (95 g.) in water (250 ml.) and hydrolysis completed by refluxing the solution for 4 hours. The hydrolysate was cooled, acidified (Congo red), and thoroughly extracted with ether. Evaporation of this extract gave the crude oily acid (133 g.), which slowly deposited crystals when kept in a vacuum desiccator. Addition of a little benzene and filtration gave 3-*methylbut*-3-*ene*-1 : 1-*dicarboxylic acid* (2-methylallylmalonic acid) (76 g.). A portion crystallised from benzene formed needles, m. p. 101°, almost invisible in suspension (Found : C, 53·3; H, 6·4. $C_7H_{10}O_4$ requires C, 53·1; H, 6·3%). The acid was characterised as its p-*nitrobenzyl* ester, m. p. 85°, which separated as primrose-yellow needles from ethanol (Found : C, 58·9; H, 4·9. $C_{21}H_{20}O_8N_2$ requires C, 58·8; H, 4·7%).

3-*Methylbut*-3-*ene*-1-*carboxylic Acid.*—Recrystallised 3-methylbut-3-ene-1 : 1-dicarboxylic acid (20 g.) was heated at 140° until evolution of carbon dioxide ceased. Distillation then gave, after rejection of a lower-boiling forerun (0·4 g.), crude 3-methylbut-3-ene-1-carboxylic acid which was collected in two fractions : (i) b. p. 116·5—119°/34 mm. (10·0 g.), n_D^{20} 1·4368 (Found : Equiv., 231); and (ii) b. p. 119—120°/34 mm. (2·4 g.), n_D^{20} 1·4380 (Found : Equiv., 157). Equivalents were determined at 25° by direct tiration with 0·05N-baryta ($C_6H_{10}O_2$ requires 114·1), and it was observed that an oil (lactone) remained undissolved. A portion of fraction (ii) (73% acid) was treated with saturated sodium hydrogen carbonate solution and extracted with ether, and the aqueous solution acidified (Congo red) under ether. On distillation fractions were obtained similar to the above (Found : Equiv., 237 and 180, respectively). It was concluded that this acid readily undergoes lactonisation.

To obtain lactone-free acid, recrystallised 3-methylbut-3-ene-1 : 1-dicarboxylic acid (10 g.) was heated at 140° for 2 hours and then treated with saturated sodium hydrogen carbonate solution. After four extractions with ether the aqueous solution was cooled in ice, covered with light petroleum, and just acidified (Congo red) with shaking. The separated light petroleum layer was dried and evaporated, and the residue distilled, giving *3-methylbut-3-ene-1-carboxylic acid* (2·72 g., 38%), b. p. 93—94°/9 mm., n_D^{20} 1·4386 (Found : Equiv., 114·1). The p-*bromophenacyl* ester formed needles, m. p. 83° (Found : C, 54·2; H, 4·8. $C_{14}H_{15}O_3Br$ requires C, 54·1; H, 4·85%).

Route C *Experiments.*

*Methyl 2-Keto-*n*-hept-6-ene-1-carboxylate.*—Tetrahydrofurfuryl alcohol (5 moles) was converted into tetrahydrofurfuryl chloride (75%), b. p. 57—58°/30 mm., and thence by ring scission with sodium into *n*-pent-4-en-1-ol (84%), b. p. 134—137°, n_D^{20} 1·4555, by following the procedure detailed in *Org. Synth.*, 1945, **25**, 84. The *n*-pent-4-en-1-ol (1·5 moles) was then converted, with phosphorus tribromide at −25° to −30°, into *n*-pent-4-enyl bromide (69%), b. p. 128—130°, n_D^{20} 1·4640, which with potassium cyanide in ethylene glycol at 90° gave *n*-pent-4-enyl cyanide (83%), b. p. 75—80°/35 mm., n_D^{20} 1·4289. The cyanide was hydrolysed with boiling aqueous potassium hydroxide to *n*-hex-5-enoic acid (78%), b. p. 100—104°/15 mm., n_D^{20} 1·4355, following LaForge, Green, and Gersdorff's procedure (*J. Amer. Chem. Soc.*, 1948, **70**, 3707). *n*-Hex-5-enoyl chloride, b. p. 60—64°/30 mm., n_D^{20} 1·4533, prepared in 99% yield from the acid by using thionyl chloride, was condensed with ethyl sodioacetoacetate in ether and then without distillation the ethyl α-*n*-hex-5-enylacetoacetate was treated with cold methanolic sodium methoxide to give methyl γ-*n*-but-3-enylacetoacetate (38% for the two stages), b. p. 135—144°/40 mm., n_D^{20} 1·4472, following the procedure used in Part II (*J.*, 1946, 892).

Route D *Experiments.*

Dried and redistilled crotonaldehyde (123 g., 1·75 mol.) (b. p. 101—102°) in ether (300 ml.) was reduced with ethereal lithium aluminium hydride (19 g., 0·5 mol.; in 600 ml.), following Nystrom and Brown's procedure (*J. Amer. Chem. Soc.*, 1947, **69**, 1197). Distillation of the product yielded *trans*-crotyl alcohol (97 g., 77%), b. p. 119—121°, n_D^{20} 1·4265. Nystrom and Brown record a 70% yield.

The alcohol (75 g.) was converted into *trans*-crotyl bromide (103 g., 73%), b. p. 100—104°, n_D^{20} 1·4768, by the method given in *Org. Synth.*, Coll. Vol. I, 2nd Edn., p. 25.

Alkenyl Methyl Ketones.—The procedure detailed in *Org. Synth.*, Coll. Vol. I, 2nd Edn., pp. 248 and 351 was followed, the undistilled crude intermediary ethyl α-alkenylacetoacetate being hydrolysed at room temperature and the alkenyl methyl ketone isolated by steam-distillation.

On a 2-mol. scale allyl chloride yielded *n*-hex-5-en-2-one (46%; based on the ethyl acetoacetate; 10% excess of halide was used), b. p. 126—129°, n_D^{20} 1·4197, and on a 4-mol. scale the product (50%) had b. p. 123—129°, n_D^{20} 1·4180. Schechter, Green, and LaForge (*J. Amer. Chem. Soc.*, 1949, **71**, 3165) have since recorded a 48% yield of ketone, b. p. 127—132°, n_D^{27} 1·4170, by hydrolysis with 11% potassium hydroxide at 0—5°.

On a 2-mol. scale 2-methylallyl chloride yielded 5-methylhex-5-en-2-one (54%), b. p. 148—150·5°, n_D^{20} 1·4305. Kimel and Cope (*ibid.*, 1943, **65**, 1992) recorded a 51% yield of ketone, b. p. 148—149°, n_D^{25} 1·4279, by hydrolysis with boiling 10% potassium hydroxide, whereas Schechter, Green, and LaForge (*loc. cit.*) have since recorded a 62% yield of ketone, b. p. 145—150°, n_D^{27} 1·4278, by hydrolysis with 15% potassium hydroxide at 0—5°.

On a 0·75-mol. scale *trans*-crotyl bromide yielded *trans-n*-hept-5-en-2-one (54%, based on the halide; 59%, based on the ethyl acetoacetate), b. p. 148—152°, n_D^{20} 1·4285. Schechter, Green, and LaForge (*loc. cit.*) have since recorded an 81% overall yield by the use of 2 mols. of ethyl acetoacetate.

Ethyl γ-Alkenyl(and Alkyl)acetoacetates.—Soloway and LaForge's procedure (*ibid.*, 1947, **69**, 2677) was followed for the carbethoxylation of the alkenyl(and alkyl)methyl ketones (1 mol.) with ethyl carbonate (2 mols.) by the use of sodium hydride (2 mols.) as the condensing agent. Contrary to Green and LaForge (*ibid.*, 1948, **70**, 2287) and to Swamer and Hauser (*ibid.*, 1950, **72**, 1352), we have not observed any marked influence of further grinding of commerical sodium hydride on the yield in this reaction. Like Schechter, Green, and LaForge (*loc. cit.*) we have observed a change of refractive index of these β-keto-esters with time. Evidently on distillation in a Pyrex-glass apparatus some separation of the enolic form occurs, followed by slow reversion to the equilibrium mixture at room temperature in a Pyrex flask or more rapidly (*ca.* 5 minutes) in contact with the soft-glass prisms of a refractometer. The refractive indexes recorded are the equilibrium values. The still residues generally solidified on cooling, and we tentatively identify these products of further condensation as homologues of 3-acetyl-2-hydroxy-2-methyl-4-pyrone (see, *n*-hexyl methyl ketone).

On a 0·75-mol. scale *n*-hex-5-en-2-one yielded ethyl 2-keto-*n*-hex-5-ene-1-carboxylate (84%), b. p. 60—65°/0·2 mm., n_D^{20} 1·4425. In an earlier experiment on a 1-mol. scale a 72% yield was obtained of a product, b. p. 78—86°/1·5 mm., n_D^{20} 1·4425. Schechter, Green, and LaForge (*loc. cit.*) have since recorded a 77% yield of product, b. p. 107—111°/14 mm., n_D^{28} 1·4393.

On a 1-mol. scale 5-methylhex-5-en-2-one yielded ethyl 2-keto-5-methylhex-5-ene-1-carboxylate (74%), b. p. 68—72°/0·2 mm., n_D^{20} 1·4479. Another run gave 67% yield, b. p. 75—77°/*ca.* 0·2 mm., n_D^{20} 1·4485. Schechter, Green, and LaForge (*loc. cit.*) have since recorded a 70% yield of product, b. p. 119—125°/16 mm., n_D^{27} 1·4468.

On a 0·5-mol. scale *trans-n*-hept-5-en-2-one yielded ethyl 2-keto-*trans-n*-hept-5-ene-1-carboxylate (65%), b. p. 76—85°/0·4 mm., n_D^{20} 1·4474. LaForge, Green, and Gersdorff (*loc. cit.*) recorded an 85% yield of product, b. p. 110—120°/10 mm., n_D^{25} 1·4460.

On a 1-mol. scale *n*-heptan-2-one gave ethyl 2-keto-*n*-heptane-1-carboxylate (68%), b. p. 81—86°/0·5 mm., n_D^{20} 1·4318. Soloway and LaForge (*loc. cit.*) recorded a 79% yield of product, b. p. 108—112°/11 mm., n_D^{25} 1·4326; whereas Wallingford, Homeyer, and Jones (*ibid.*, 1941, **63**, 2252) recorded b. p. 75—78°/2 mm. (misprint for 0·2 mm. ?), n_D^{20} 1·4337.

In an early experiment on a 1-mol. scale *n*-octan-2-one gave ethyl 2-keto-*n*-octane-1-carboxylate, b. p. 97—99°/1·6 mm., n_D^{20} 1·4366, in only 27% yield, which was characterised by conversion into 3-*n*-hexyl-1-phenylpyrazol-5-one, m. p. 84—85°. [Wallingford, Homeyer, and Jones (*loc. cit.*) record b. p. 99—104°/2 mm., n_D^{21} 1·4373, m. p. 84—85°.] On cooling, the still-residue solidified (72 g.). A portion on crystallisation from methanol formed plates, m. p. 60—61° (Found : C, 70·1; H, 9·15. $C_{18}H_{28}O_4$ requires C, 70·1; H, 9·15%). We tentatively identify this substance as 3-n-*heptanoyl*-6-n-*hexyl*-2-*hydroxy*-4-*pyrone*.

Recently, on a 0·25-mole scale, we have obtained a 47% yield of ethyl 2-keto-octane-1-carboxylate, b. p. 90—93°/0·25 mm., n_D^{20} 1·4356, but this is still much below the yield obtained with *n*-heptan-2-one and the alken-2-ones.

We have also used the forced-condensation procedure with sodium ethoxide (1 mole) and ethyl carbonate (4—8 moles) (cf. Wallingford, Homeyer, and Jones, *loc. cit.*), and for the carbethoxylation of *n*-hex-5-en-2-one on a 0·5-mole scale we have found the following satisfactory :

Sodium (12·5 g.) was powdered under xylene, rinsed with dry ether, then transferred to a 3-necked flask and covered with dry ether (350 ml.). Ethanol (32 g.; 25% excess) was added and the suspension refluxed for 6 hours with stirring, after which the solvent was distilled off. The flask containing the residual sodium ethoxide was evacuated at 30 mm., and then attached to a heated 50 × 1·5 cm. helices-packed column with a vacuum partial-take-off, and ethyl carbonate (350 ml.) added. During 3 hours *n*-hex-5-en-2-one (49 g.) was added dropwise with stirring whilst ethyl carbonate (50 ml. portions) was also added at one-hourly intervals. Meanwhile a slow distillation was carried out at 50 mm. (bath temp. 65°, reflux ratio 5 : 1) and at the conclusion of the additions a further 100 ml. of distillate was collected. The still-residue was then cooled and acidified with aqueous acetic acid, and the oil separated. The aqueous layer was saturated with salt and extracted with ether (3 × 60 ml.), and the extracts bulked with the oil. After drying (Na_2SO_4), and removal of the solvent, fractional distillation gave ethyl 2-keto-*n*-hex-5-ene-1-carboxylate (49 g., 57%), b. p. 59—60°/0·1 mm., n_D^{20} 1·4425. By a similar procedure, but using sodium methoxide, Schechter, Green, and LaForge (*loc. cit.*) have obtained a 71% yield.

3-*Hydroxyalkene*(*and alkane*)-2 : 5-*diones*.

In general (procedure *A*), an aqueous solution of the sodium (or potassium) 2-ketoalkene (or alkane) carboxylate was prepared by shaking the ethyl (or methyl) ester (1 mol.) with 3—10% sodium or potassium hydroxide (1·1—1·25 mols.) for 72 hours at room temperature. Potassium hydroxide gave less deeply coloured solutions. Any undissolved oil, presumably re-formed alkenyl (or alkyl) methyl ketone, was removed at this stage. Without isolation of the carboxylic acid, neutralised aqueous pyruvaldehyde (1·1—1·25 mols.) was added and the mixture adjusted to pH 8·0 (narrow-range indicator paper) by the cautious addition of acid or alkali. This solution was set aside at 20—35°, whereupon an oil soon started to separate. When the separation of oil was judged complete (6—7 hours at 35°, up to 48 hours at 20°) it was run off and the aqueous layer acidified with hydrochloric acid. More oil separated on warming the solution to 50° and bubbling air or nitrogen through it. This oil was removed by ether extraction, and the process repeated until no more oil separated The aqueous layer was then saturated with salt and again extracted with ether. The oil and ether extracts were bulked and dried (Na_2SO_4), the solvent removed (column), and the product fractionally distilled at *ca.* 0·1 mm. through a 250 × 5 mm. unpacked vapour-jacketed column.

Unless otherwise stated, commercial aqueous " 30% " pyruvaldehyde was used. Assays by precipitation of the 2 : 4-dinitrophenylosazone with aqueous 2 : 4-dinitrophenylhydrazine hydrochloride and also by titration with barium hydroxide in the presence of hydrogen peroxide showed it to contain 35—36% pyruvaldehyde and by direct titration with barium hydroxide to be approx. normal with respect to organic acid. The appropriate volume of solution was neutralised with 10% sodium hydroxide before use.

3-*Hydroxy*-n-*non*-8-*ene*-2 : 5-*dione*.—Following procedure *A* ethyl 2-ketohex-5-ene-1-carboxylate (85·0 g.) was hydrolysed with 10% potassium hydroxide (350 ml.), and the resulting solution of sodium salt condensed with aqueous pyruvaldehyde (100 ml.) at 35° during 6 hours (total volume *ca.* 500 ml.; *i.e.*, *ca.* 1·0M.). After isolation as described, distillation at 0·15 mm. gave the fractions : (i) b. p. <89°, n_D^{20} 1·4321 (3·0 g.); (ii) b. p. 89—91°, n_D^{20} 1·4640 (4·2 g.); (iii) b. p. 91—93°, n_D^{20} 1·4688 (17·8 g.); (iv) b. p. 93—95°, n_D^{20} 1·4697 (9·5 g.); (v) b. p. 95—100°, n_D^{20} 1·4717 (3·1 g.). Fractions (ii)—(iv) represent a 37% yield of 3-hydroxy-*n*-non-8-ene-2 : 5-dione. In another experiment by this procedure the acetoacetate (28·3 g.) was hydrolysed with 3% sodium hydroxide (240 ml.) and then condensed with aqueous pyruvaldehyde (38 ml.) at 35° during 6 hours (total volume *ca.* 300 ml.; *i.e.*, *ca.* 0·5M.). On distillation at 0·5 mm., the product yielded the fractions : (i) b. p. <100°, n_D^{20} 1·4637 (0·48 g.); (ii) b. p. 100—101°, n_D^{20} 1·4675 (8·78 g.); (iii) b. p. 101—105°, n_D^{20} 1·4693 (1·45 g.); (iv) b. p. 105—107°, n_D^{20} 1·4702 (1·50 g.). Fractions (ii) and (iii) represent a 36% yield of hydroxy-diketone.

In other experiments, the intermediary carboxylic acid was isolated by cooling the hydrolysed solution to 0°, acidifying it to pH 3 with hydrochloric acid, and immediately extracting the solution with cold ether, followed by removal of the solvent under reduced pressure. Such acid (*ca.* 88 g., from 106 g. of ester) was added to ice-cold water (88 ml.) and neutralised with 10% sodium hydroxide (phenolphthalein) at 0°. To this solution was added neutralised aqueous pyruvaldehyde (170 ml., 25% excess) and the mixed solution (total volume *ca.* 400 ml., *i.e.*, *ca.* 1·5M.), adjusted to pH 8·0, set aside at room temperature. An oil started to separate after 30 minutes, and when separation was complete (48 hours)

this was collected and the aqueous layer extracted with ether (5 × 75 ml.), without acidification. The combined extracts and oil were dried (Na_2SO_4), the solvent removed (column), and the product fractionally distilled at *ca.* 0·1 mm. to give, after a small forerun, the fractions: (i) b. p. 57—80°, n_D^{20} 1·4608 (3·8 g.); (ii) b. p. 80—85°, n_D^{20} 1·4673 (5·1 g.); (iii) b. p. 85—87°, n_D^{20} 1·4694 (18·2 g.); (iv) b. p. 87—90°, n_D^{20} 1·4714 (7·4 g.); (v) b. p. 90—100°, n_D^{20} 1·4828 (4·2 g.). Redistillation of (i) and (v) gave a further 1·3 g., b. p. 83—86°, n_D^{20} 1·4666 (vi). For the next stage fractions (ii)—(iv) and (vi) were bulked, representing a 30% yield. By this method (procedure *B*) yields of 30—32% have been replicated but not improved upon. By using substantially this procedure Schechter, Green, and LaForge (*loc. cit.*) obtained a 58% yield of hydroxy-diketone, b. p. 85—90°/0·07 mm., n_D^{25} 1·4657.

3-*Hydroxy*-8-*methylnon*-8-*ene*-2 : 5-*dione*.—Following procedure *A* ethyl 2-keto-5-methylhex-5-ene-1-carboxylate (30·7 g.) was hydrolysed with 3% sodium hydroxide (240 ml.) and the resulting solution condensed with aqueous pyruvaldehyde (38 ml.) at 35° for 7 hours. Isolation as previously described and distillation at 0·4 mm. yielded, after a small forerun, the fractions: (i) b. p. 80—102°, n_D^{20} 1·4577 (0·6 g.); (ii) b. p. 102—112°, n_D^{20} 1·4675 (8·6 g.); (iii) b. p. 112—118°, n_D^{20} 1·4705 (3·2 g.); (iv) b. p. 118—122°, n_D^{20} 1·4732 (1·8 g.). Fractions (ii) and (iii) represent a 38% yield of 3-hydroxy-8-methylnon-8-ene-2 : 5-dione.

In another condensation by a variation of procedure *A*, the ester (92 g.) was hydrolysed with 10% potassium hydroxide (350 ml.; 25% excess) at 0—5° during 72 hours, with only occasional shaking, and the resulting solution mixed with aqueous pyruvaldehyde (120 ml.), adjusted to pH 8·0, and kept for 48 hours at room temperature. Again, isolation and distillation by the above procedure yielded the hydroxy-diketone (34·8 g.), b. p. 108—120°/*ca.* 0·1 mm., n_D^{20} 1·4698, in 38% yield. Schechter, Green, and LaForge (*loc. cit.*), by using a rather different procedure, obtained a 58% yield of hydroxy-diketone, b. p. 98—102°/0·3 mm., n_D^{25} 1·4687.

3-*Hydroxy*-trans-n-*dec*-8-*ene*-2 : 5-*dione*.—Following procedure *A* ethyl 2-keto-*trans*-*n*-hept-5-ene-1-carboxylate (18·6 g.) was hydrolysed with 3% sodium hydroxide (137 ml.), a little undissolved oil (0·85 g.) removed, and the solution then mixed with neutralised aqueous pyruvaldehyde (20·6 ml.). The whole was brought to pH 8·0—8·5 by saturation with carbon dioxide, and then set aside at 35° for 6 hours. Isolation as described above followed by fractional distillation yielded, after a small forerun, 3-hydroxy-*trans*-*n*-dec-8-ene-2 : 5-dione (8·75 g., 47%), b. p. 105—110°/*ca.* 0·1 mm., n_D^{20} 1·4681, together with 0·7 g. of less pure material, b. p. 110—115°/*ca.* 0·1 mm., n_D^{20} 1·4732. Schechter, Green, and LaForge (*loc. cit.*), who used a rather different procedure, report a 75% yield of product, b. p. 97—100°/0·1 mm., n_D^{25} 1·4679.

3-*Hydroxy*-n-*dec*-9-*ene*-2 : 5-*dione*.—By using procedure *B*, methyl 2-ketohept-6-ene-1-carboxylate (30 g.) was hydrolysed with 10% sodium hydroxide (150 ml.) for 48 hours. After liberation and isolation of the acid, dissolution in 10% sodium hydroxide gave the sodium salt which was condensed with neutralised aqueous pyruvaldehyde (40 ml.) for 8 hours at 35°, followed by 16 hours at room temperature. Isolation as previously described and fractional distillation at *ca.* 0·1 mm. gave, after a forerun (1·2 g.), the fractions: (i) b. p 84—94°, n_D^{29} 1·4630 (0·12 g.); (ii) b. p. 94—98°, n_D^{29} 1·4652 (2·90 g.); (iii) b. p. 98—100°, n_D^{29} 1·4687 (6·03 g.); (iv) b. p. 100—110°, n_D^{29} 1·4740 (0·32 g.). Fractions (ii) and (iii) represent a 28% yield of 3-hydroxy-*n*-dec-9-ene-2 : 5-dione. Schechter, Green, and LaForge (*loc. cit.*), by using a slightly different procedure, obtained a 77% yield of product, b. p. 94—97°/0·2 mm., n_D^2 1·4675.

3-*Hydroxy*-n-*decane*-2 : 5-*dione*.—Following procedure *A*, ethyl 2-ketoheptane-1-carboxylate (18·6 g.) was hydrolysed with 3% sodium hydroxide (165 ml.), undissolved oil (1·4 g.) removed, and the solution then mixed with neutralised aqueous pyruvaldehyde (19·25 ml.). The whole was brought to pH 8·0—8·5 by saturation with carbon dioxide, and set aside at 35° for 6 hours. After isolation as described above, fractional distillation yielded a forerun (0·2 g.) and then 3-hydroxy-*n*-decane-2 : 5-dione (8·24 g., 44%), b. p. 103—104°/*ca.* 0·1 mm., n_D^{20} 1·4522. In a condensation at room temperature for 3 days, the yield by this procedure was likewise 44%. Schechter, Green, and LaForge (*loc. cit.*), by the use of a somewhat similar procedure, obtained a 52% yield; their purified product had b. p. 93—95°/0·05 mm., n_D^{25} 1·4508.

In another experiment ethyl 2-ketoheptane-1-carboxylate (9·23 g.) was hydrolysed with 10% potassium hydroxide (35 ml.), a little oil then removed, and the solution cooled to −5° and acidified to pH 3. The solid β-keto-acid (6·85 g., 87%) was collected, washed with ice-water, and dried in a vacuum desiccator in the refrigerator. Then following procedure *B*, this acid in ice-water (20 ml.) was neutralised with 10% sodium hydroxide and condensed with freshly prepared pyruvaldehyde (4·50 g. in 5 ml. of water; made by the selenium dioxide oxidation of acetone; b. p. 68—80°/26 mm.; cf. Riley, Morley, and Friend, *J.*, 1932, 1875) for 24 hours at room temperature (total volume *ca.* 60 ml.; *i.e.*, *ca.* 0·7M.). After isolation as previously described, fractional distillation at *ca.* 0·1 mm. gave the hydroxy-diketone (3·58 g., 39% on the ester), b. p. 100—103°, n_D^{20} 1·4516.

*2-Alkenyl(and alkyl)-4-hydroxy-3-methyl*cyclo*pent-2-en*-1-*ones* [*Alkenyl(and alkyl)rethrolones*].

Cyclisation of the 3-hydroxyalkene(or alkane)-2 : 5-dione was effected by shaking it with 1—10% sodium hydroxide at room temperature (unless otherwise stated), under nitrogen, for 1—24 hours. The reddish-brown mixture was acidified with hydrochloric acid (1 : 3), saturated with sodium chloride, and thoroughly extracted with ether. After drying (Na_2SO_4) and removal of the solvent through a short packed column the product was fractionally distilled at *ca.* 0·1 mm. through a 250 × 5 mm. unpacked vapour-jacketed column. In these distillations it was found necessary to use a jacket fluid of rather higher b. p. than that of the material being fractionated; hence for all of the distillations described toluene was used. The product invariably boiled over a range, and more than one fractional distillation was generally necessary to isolate alkenyl(or alkyl)rethrolone suitable for esterification.

2-*Allyl*-4-*hydroxy*-3-*methyl*cyclo*pent*-2-*en*-1-one [*Allylrethrolone*].—3-Hydroxy-*n*-non-8-ene-2 : 5-dione (32 g.) was cyclised with 10% sodium hydroxide (220 ml.) for 1·5 hours, and the product isolated as described above. Distillation at *ca.* 0·1 mm. gave the fractions : (i) b. p. 54—99°, n_D^{20} 1·4803 (4·80 g.); (ii) b. p. 100—104°, n_D^{20} 1·5032 (3·50 g.); (iii) b. p. 104—107°, n_D^{20} 1·5091 (3·45 g.); (iv) b. p. 107—109°, n_D^{20} 1·5132 (4·35 g.); (v) b. p. 110—115°, n_D^{20} 1·5182 (2·10 g.). Fractions (ii)—(iv) represent a 39% yield of allylrethrolone. These fractions were bulked and redistilled at 0·07 mm. to give the fractions : (i) b. p. 78—85°, n_D^{20} 1·4872 (1·6 g.); (ii) b. p. 85—90°, n_D^{20} 1·5037 (0·98 g.); (iii) b. p. 90—92°, n_D^{20} 1·5112 (1·53 g.); (iv) b. p. 92—93°, n_D^{20} 1·5121 (1·55 g.); (v) b. p. 93—94°, n_D^{20} 1·5127 (2·11 g.); (vi) b. p. 94—95°, n_D^{20} 1·5132 (1·06 g.); (vii) b. p. 95—96°, n_D^{20} 1·5141 (0·35 g.). Fractions (iii)—(vi) were bulked for esterification, representing only a 22% yield. Other cyclisations with 2% sodium hydroxide for 24 hours did not give appreciably higher yields of once-distilled material. Our products invariably showed a spread of b. p. and refractive index, the latter being noticeably lower than that recorded by Schechter, Green, and LaForge (*loc. cit.*), who obtained a 59% yield of material, b. p. 100—103°/0·15 mm., n_D^{25} 1·5141.

4-*Hydroxy*-3-*methyl*-2-2′-*methylallyl*cyclo*pent*-2-*en*-1-*one* [2-*Methylallylrethrolone*].—3-Hydroxy-8-methylnon-8-ene-2 : 5-dione (34·8 g.) was cyclised with 2% sodium hydroxide (700 ml.) for 3 hours, and the product isolated as described above. Distillation gave a main fraction (10·79 g.), b. p. 123—140°/*ca.* 0·1 mm., which on redistillation at 0·07 mm. gave, after a small forerun, the fractions : (i) b. p. 110—114°, n_D^{20} 1·5048 (2·55 g.); (ii) b. p. 114—115°, n_D^{20} 1·5070 (3·66 g.); (iii) b. p. 115°, n_D^{20} 1·5099 (1·92 g.). Fractions (i)—(iii) represent a 29% yield of 2-methylallylrethrolone. Cyclisation of the hydroxy-diketone (5·52 g.) in 1% sodium hydroxide (120 ml.) for 24 hours and distillation gave a main cut (2·79 g.), b. p. 107—128°/0·08 mm., which on redistillation at 0·07 mm. gave, after a forerun (50 mg.), the fractions : (i) b. p. 114—116°, n_D^{20} 1·5022 (1·30 g.); (ii) b. p. 116—118°, n_D^{20} 1·5084 (0·62 g.). Fractions (i) and (ii) represent a 39% yield of alkenylrethrolone. A similar cyclisation of the hydroxydiketone (5·52 g.), but in 3% barium hydroxide (88 ml.) for 24 hours, and distillation at 0·1 mm. gave, after a forerun (0·37 g.), the fractions : (i) b. p. 100—111°, n_D^{20} 1·4828 (0·27 g.); (ii) b. p. 111—113°, n_D^{20} 1·5025 (0·09 g.); (iii) b. p. 113—115°, n_D^{20} 1·5112 (1·91 g.); (iv) b. p. 115—120°, n_D^{20} 1·5102 (0·20 g.). Fraction (iii) represents a 38% yield of alkenylrethrolone. Schechter, Green, and LaForge (*loc. cit.*) obtained a 66% yield of product, b. p. 115—120°/0·3 mm., n_D^{25} 1·5113.

2-trans-*Crotyl*-4-*hydroxy*-3-*methyl*cyclo*pent*-2-*en*-1-*one* [(±)-trans-*Cinerolone*].—3-Hydroxy-*trans*-*n*-dec-8-ene-2 : 5-dione (8·28 g.) was cyclised in 1% sodium hydroxide (180 ml.) for 5 hours and the product isolated as described above. Distillation gave a main fraction (2·75 g., 38% if assumed pure), b. p. 109—130°/*ca.* 0·1 mm., as a yellow oil from which shining needles separated during the distillation. The oil was decanted and redistilled at 0·06 mm. to give the fractions : (i) b. p. 80—116° (semi-solid), n_D^{20} 1·5048 (0·37 g.); (ii) b. p. 116—118° (trace of solid), n_D^{20} 1·5144 (1·30 g.) (Found : C, 72·2; H, 8·8. Calc. for $C_{10}H_{14}O_2$: C, 72·3; H, 8·5%); (iii) b. p. 118°, n_D^{20} 1·5128 (0·10 g.). Fraction (ii) represents a 18% yield of (±)-*trans*-cinerolone. The b. p. of this product was erroneously tabulated in Part IV (*J.*, 1950, 1152) as being at 0·6 mm. Schechter, Green, and LaForge (*loc. cit.*) record a 62% yield of product, b. p. 110—114°/0·15 mm., n_D^{25} 1·5143.

Following the procedure used in Part IV (*loc. cit.*) (±)-*trans*-cinerolone (80 mg.) was converted into the semicarbazone (32 mg.), which on recrystallisation from aqueous ethanol formed prisms, m. p. 208—209° (Found : C, 59·2; H, 7·7; N, 18·8. Calc. for $C_{11}H_{17}O_2N_3$: C, 59·2; H, 7·6; N, 18·3%). Light-absorption data and terminal-methyl content for this semicarbazone were tabulated in Part IV. Following the procedure used in Part IV (*loc. cit.*) (±)-*trans*-cinerolone (100 mg.) was converted into (±)-*trans*-cineronyl acetate semicarbazone, which on crystallisation from ethyl acetate had m. p. 157—159°.

2-n-*But*-3′-*enyl*-4-*hydroxy*-3-*methyl*cyclo*pent*-2-*en*-1-*one*.—3-Hydroxy-*n*-dec-9-ene-2 : 5-dione (8·93 g.) was cyclised in 10% sodium hydroxide for 1 hour at 29°. On isolation and distillation at *ca.* 0·1 mm., as described above, the product yielded, after a forerun (0·89 g.), the fractions : (i) b. p. 95—100°, n_D^{26} 1·4985 (0·37 g.); (ii) b. p. 100—105°, n_D^{26} 1·5012 (0·29 g.); (iii) b. p. 105—107°, n_D^{26} 1·5050 (1·41 g.); (iv) b. p. 107—108°, n_D^{26} 1·5052 (0·46 g.); (v) b. p. 108—115°, n_D^{26} 1·5071 (0·41 g.). Fractions (ii)—(iv) represent a 20% yield of alkenylrethrolone, which on redistillation at 0·03 mm. had b. p. 90—96°, n_D^{26} 1·5040—1·5054 (1·83 g.). Schechter, Green, and LaForge (*loc. cit.*) obtained a 47% yield of this product, b. p. 109—113°/0·2 mm., n_D^{25} 1·5089.

2-n-*Butyl*-4-*hydroxy*-3-*methyl*cyclo*pent*-2-*en*-1-*one* [(±)-*Dihydrocinerolone*].—3-Hydroxy-*n*-decane-2 : 5-dione (8·08 g.) was cyclised in 3% sodium hydroxide (59 ml.) for 21 hours at room temperature, and the product isolated as described above. Distillation at *ca.* 0·1 mm. gave, after a forerun (0·30 g.), the fractions : (i) b. p. 112—122°, n_D^{20} 1·4845 (2·43 g.); (ii) b. p. 122—132°, n_D^{20} 1·4940 (0·80 g.). Redistillation of (i) eliminated more forerun (0·29 g.) and then gave (iii) b. p. 113°, n_D^{20} 1·4925 (1·37 g.). Fractions (ii) and (iii) represent a 30% yield of (±)-dihydrocinerolone. Cyclisation of the hydroxy-diketone (2·37 g.) in 10% sodium hydroxide (26 ml.) for 1 hour gave a lighter coloured product but as before this did not give clear-cut fractions on distillation. After a forerun (0·09 g.), the following fractions were collected on distillation at *ca.* 0·1 mm. : (i) b. p. 110—120°, n_D^{20} 1·4576 (0·10 g.); (ii) b. p. 120—127°, n_D^{20} 1·4881 (0·72 g.); (iii) b. p. 130—142°, n_D^{20} 1·4946 (0·14 g.). Fractions (ii) and (iii) (from which a trace of solid separated) represent a 40% yield of (±)-dihydrocinerolone. Schechter, Green, and LaForge (*loc. cit.*) obtained a 63% yield of product, b. p. 110—113°/0·07 mm., n_D^{25} 1·4920. The 3 : 5-dinitrobenzoate (250 mg.), prepared from (±)-dihydrocinerolone (200 mg.), crystallised from light petroleum (b. p. 60—80°) as feathery needles, m. p. 109·5—111·5°. The 2 : 4-*dinitrophenylhydrazone*, prepared in alcoholic hydrochloric acid, formed from ethanol deep-red needles, m. p. 163·0—163·5° after softening at 159° (Found : C, 54·5; H, 5·7. $C_{16}H_{20}O_5N_4$ requires C, 55·1; H, 5·8%). Schechter, Green, and LaForge (*loc. cit.*) record m. p. 140·5—141·5° for this 2 : 4-dinitrophenylhydrazone, without giving an analysis. In general we find 2 : 4-dinitrophenylhydrazine unsatisfactory for characterising alkenyl(or

alkyl)rethrolones, for the products crystallise poorly, melt indefinitely, and are often only orange in colour instead of the expected deep-red indicative of the $\alpha\beta$-unsaturated carbonyl group.

Alkenyl(and alkyl)rethronyl Chrysanthemates [Alkenyl(and alkyl)rethrins].

The (±)-*trans*- and (±)-*cis*-chrysanthemic acids used were prepared by Mr. H. W. B. Reed by following the procedure detailed in Part I (*J.*, 1945, 283; cf. Part IV, *loc. cit.*); the (+)-*trans*-acid, isolated from pyrethrum extract, was kindly provided by Dr. W. Mitchell of Messrs. Stafford Allen and Sons, Ltd., and the (−)-*trans*-acid used was that prepared in Part I (*loc. cit.*).

The appropriate acid chloride was freshly prepared for each esterification by reaction of the acid with redistilled thionyl chloride in light petroleum (b. p. 40—60°) at room temperature, followed by distillation. Typical preparations (from 1·0—2·5 g. of acid) were: (±)-*trans*-chrysanthemoyl chloride (67%), b. p. 50—51°/0·15 mm., n_D^{20} 1·4856, also b. p. 96·0—96·5°/12 mm.; (+)-*trans*-chrysanthemoyl chloride (78—83%), b. p. 47—48°/0·1 mm., n_D^{20} 1·4852, also b. p. 96·5—99·5°/12 mm.; (−)-*trans*-chrysanthemoyl chloride (79%), b. p. 50—51°/0·15 mm., n_D^{20} 1·4867; (±)-cis-*chrysanthemoyl chloride* (72—79%), b. p. 50—51°/0·15 mm., n_D^{20} 1·4896, also b. p. 96·5—98°/12 mm., and b. p. 104—106°/18 mm., n_D^{20} 1·4907 (Found: C, 64·0; H, 8·2; Cl, 18·7. $C_{10}H_{15}OCl$ requires C, 64·5; H, 8·1; Cl, 19·0%). The *cis*-acid chloride was very susceptible to hydrolysis by traces of moisture, and was much less stable than the *trans*-isomer.

Esterification was effected by addition of the chrysanthemoyl chloride (1·0 mol.) to the alkenyl(or alkyl)rethrolone (1·1—1·25 mols.) in benzene containing pyridine (2 mols.) and setting aside the solution at room temperature overnight. With or without removal by filtration of the pyridine hydrochloride, the benzene solution was washed with saturated aqueous sodium hydrogen carbonate and then with water, and dried (Na_2SO_4), and the benzene and traces of pyridine removed at the water-pump at 100°. The viscous yellow product was distilled at *ca.* 10^{-3} mm. from a small pear-shaped single-necked flask, without a capillary leak, and the distillate collected from the ground tip of the short side-arm by a bent glass rod which could be rotated to direct the distillate into consecutive receivers. If necessary a forerun was removed and the product collected in two or three fractions, which showed some spread of b. p., due partly to the use of a mercury-in-glass thermometer and the small amount of vapour, but presumably mainly, together with a spread of refractive index, to the product consisting of one or more diastereoisomeric pairs of esters. For representative specimens for analysis and for insecticidal assay the main fractions were bulked and redistilled. Again, if necessary, a forerun was eliminated and the product collected in several fractions, but these were mixed and portions sealed under nitrogen and stored in the dark until required. Contrary to our experience when distilling the alkylrethrins prepared by the *N*-bromosuccinimide route (Part III, *J.*, 1950, 971), in no case during the present work have we observed the forerun to contain free chrysanthemic acid. Furthermore the alkenylrethrins were stable to distillation and could be redistilled without appreciable loss. In a few specimen straces of unidentified solid in the form of fine needles appeared at the liquid surface on storage.

(±)-*Allylrethronyl* (±)-trans-*Chrysanthemate.*—The reaction product from (±)-allylrethrolone (1·53 g.), (±)-*trans*-chrysanthemoyl chloride (1·60 g.), and pyridine (1·30 g.) in benzene (27 ml.) yielded on a second distillation at 2×10^{-3} mm. the fractions: (i) b. p. 70—127°, n_D^{20} 1·4897 (0·29 g.); (ii) b. p. 127—128°, n_D^{20} 1·5051 (0·29 g.); (iii) b. p. 128—129°, n_D^{20} 1·5056 (0·55 g.); (iv) b. p. 129—130°, n_D^{20} 1·5056 (0·36 g.). Fractions (ii)—(iv) were bulked (1·20 g., 47%) as the required *ester* (Found: C, 74·7; H, 8·85. $C_{19}H_{26}O_3$ requires C, 75·45; H, 8·7%).

In another preparation, the product from (±)-allylrethrolone (460 mg.), acid chloride (560 mg.), and pyridine (400 mg.) in benzene (8 ml.) gave on a second distillation at 7×10^{-3} mm. the fractions: (i) b. p. 134—135°, n_D^{20} 1·4991 (50 mg.) (Found: C, 75·25; H, 9·1%); (ii) b. p. 135·0—135·5°, n_D^{20} 1·5018 (110 mg.) (Found: C, 75·1; H, 9·1%); (iii) b. p. 135·5—136·0°, n_D^{20} 1·5031 (130 mg.) (Found: C, 75·4; H, 9·5%); (iv) b. p. 136—138°, n_D^{20} 1·5042 (40 mg.) (Found: C, 75·2; H, 8·75%). Fractions (ii)—(iv) were bulked (280 mg., 31%).

(±)-*Allylrethronyl* (+)-trans-*Chrysanthemate.*—The product from (±)-allylrethrolone (1·50 g.), (+)-*trans*-chrysanthemoyl chloride (1·55 g.), and pyridine (1·30 g.) in benzene (27 ml.) gave on a second distillation at 1×10^{-3} mm. the fractions: (i) b. p. 70—100°, n_D^{20} 1·4928 (0·12 g.); (ii) b. p. 100—101°, n_D^{20} 1·5038 (0·52 g.); (iii) b. p. 101·0—101·5°, n_D^{20} 1·5046 (0·28 g.); (iv) b. p. 101·5—102·0°, n_D^{20} 1·5054 (0·20 g.). Fractions (ii)—(iv) were bulked (1·00 g., 40%) as the required *ester* (Found: C, 74·4; H, 8·75%), α_D^{21} −0·28° (*l*, 0·5, *c*, 13·9 in chloroform).

(±)-*Allylrethronyl* (−)-trans-*Chrysanthemate.*—The product from (±)-allylrethrolone (1·42 g.), (−)-*trans*-chrysanthemoyl chloride (1·50 g.), and pyridine (1·20 g.) in benzene (24 ml.) gave on a second distillation at 1×10^{-3} mm. the fractions: (i) b. p. 90—100°, n_D^{20} 1·4926 (0·23 g.); (ii) b. p. 100—101°, n_D^{20} 1·5054 (0·34 g.); (iii) b. p. 101·0—101·5°, n_D^{20} 1·5054 (0·41 g.); (iv) b. p. 101·5—102·0°, n_D^{20} 1·5056 (0·38 g.). Fractions (ii)—(iv) were bulked (1·13 g., 47%) as the required *ester* (Found: C, 74·5; H, 8·8%), α_D^{21} + 0·11° (*l*, 0·5, *c*, 8·9 in chloroform).

(±)-*Allylrethronyl* (±)-cis-*Chrysanthemate.*—The product from (±)-allylrethrolone (1·48 g.), (±)-*cis*-chrysanthemoyl chloride (1·55 g.), and pyridine (1·30 g.) in benzene (27 ml.) gave on a second distillation at 2×10^{-3} mm. the fractions: (i) b. p. 80—108°, n_D^{20} 1·4925 (0·15 g.); (ii) b. p. 108—109°, n_D^{20} 1·5060 (0·37 g.); (iii) b. p. 109·0—109·5°, n_D^{20} 1·5062 (0·33 g.); (iv) b. p. 109·5—110·0°, n_D^{20} 1·5062 (0·35 g.). Fractions (ii)—(iv) were bulked (1·05 g., 42%) as the required *ester* (Found: C, 74·0; H, 8·8%).

In another preparation, the product from (±)-allylrethrolone (230 mg.), acid chloride (280 mg.), and pyridine (200 mg.) in benzene (4 ml.) gave on distillation at 8×10^{-3} mm. the fractions: (i) b. p. 127—129°, n_D^{20} 1·5004 (35 mg.); (ii) b. p. 129—130°, n_D^{20} 1·5031 (90 mg.) (Found: C, 74·9; H, 9·0%); (iii) b. p. 130—131°, n_D^{20} 1·5047 (160 mg.) (Found: C, 76·2; H, 9·55%); (iv) b. p. 131—136°, n_D^{20} 1·5069 (30 mg.). Fractions (ii) and (iii) were bulked (250 mg., 55%).

(±)-2-*Methylallylrethronyl* (±)-trans-*Chrysanthemate*.—The product from (±)-2-methylallylrethrolone (1·00 g.), (±)-*trans*-chrysanthemoyl chloride (1·07 g.), and pyridine (0·90 ml.) in benzene (10 ml.) gave, on a second distillation at 4 × 10^{-3} mm. and elimination of a small forerun, the fractions: (i) b. p. 122—132°, n_D^{20} 1·5014 (603 mg.); (ii) b. p. 132° falling to 120°, n_D^{20} 1·5045 (373 mg.); (iii) b. p. 120° falling, n_D^{20} 1·5047 (128 mg.). Fractions (i)—(iii) were bulked (1·10 g., 58%) as the required *ester* (Found: C, 75·7; H, 9·2. $C_{20}H_{28}O_3$ requires C, 75·95; H, 8·9%).

In another experiment, the product from the reaction of (±)-2-methylallylrethrolone (560 mg.), acid chloride (580 mg.), and pyridine (400 mg.) in benzene (8 ml.) gave on distillation at 5—9 × 10^{-3} mm. the fractions: (i) b. p. 114—124°, n_D^{20} 1·4985 (40 mg.); (ii) b. p. 124—130°, n_D^{20} 1·5012 (90 mg.); (iii) b. p. 130—135°, n_D^{20} 1·5014 (370 mg.) (Found: C, 76·0; H, 9·8%); (iv) b. p. 135—138°, n_D^{20} 1·5037 (20 mg.). Fractions (ii) and (iii) were bulked (460 mg., 47%).

(±)-2-*Methylallylrethronyl* (+)-trans-*Chrysanthemate*.—The product from (±)-2-methylallylrethrolone (1·20 g.), (+)-*trans*-chrysanthemoyl chloride (1·33 g.), and pyridine (1·2 ml.) in benzene (12 ml.) gave, on a second distillation at 2 × 10^{-3} mm. and elimination of a small forerun, the fractions: (i) b. p. 126—138°, n_D^{20} 1·5018 (0·81 g.); (ii) b. p. 134—138°, n_D^{20} 1·5042 (0·60 g.); (iii) b. p. 138° falling, n_D^{20} 1·5049 (0·16 g.). Fractions (i)—(iii) were bulked (1·57 g., 68%) as the required *ester* (Found: C, 76·4; H, 9·1%), α_D^{21} −0·27° (*l*, 0·5, *c*, 11·6 in chloroform).

(±)-2-*Methylallylrethronyl* (±)-cis-*Chrysanthemate*.—The product from (±)-2-methylallylrethrolone (1·00 g.), (±)-*cis*-chrysanthemoyl chloride (1·04 g.), and pyridine (0·90 ml.) in benzene (10 ml.) gave, on a second distillation at 3 × 10^{-4} mm. and elimination of a small forerun, the fractions: (i) b. p. 100—132°, n_D^{20} 1·5042 (0·912 g.); (ii) b. p. 132°, n_D^{20} 1·5070 (0·157 g.); (iii) b. p. 132° falling, n_D^{20} 1·5067 (0·183 g.). Fractions (i)—(iii) were bulked (1·25 g., 65%) as the required *ester* (Found: C, 75·7; H, 9·1%).

In another experiment, the product from (±)-2-methylallylrethrolone (250 mg.), the chrysanthemoyl chloride, and pyridine (200 mg.) in benzene (4 ml.) gave on distillation at 3 × 10^{-3} mm. the fractions: (i) b. p. 124—131°, n_D^{20} 1·5007 (70 mg.); (ii) b. p. 131—132·5°, n_D^{20} 1·5026 (50 mg.); (iii) b. p. 132·5—134°, n_D^{20} 1·5039 (130 mg.) (Found: C, 75·4; H, 9·2%); (iv) b. p. 134—136°, n_D^{20} 1·5039 (20 mg.). Fractions (ii)—(iv) were bulked (200 mg., 41%).

(±)-trans-*Cineronyl* (±)-trans-*Chrysanthemate*.—The reaction product from (±)-*trans*-cinerolone (280 mg.), (±)-*trans*-chrysanthemoyl chloride (290 mg., the same preparation as was used in Part IV, *loc. cit.*), and pyridine (0·2 ml.) gave, on distillation, a forerun (120 mg.), n_D^{20} 1·5061, and then the required *ester* collected in two fractions, b. p. 136—137°/5 × 10^{-3} mm.: (i) n_D^{20} 1·5071 (240 mg.) (Found: C, 76·2; H, 9·4. $C_{20}H_{28}O_3$ requires C, 75·95; H, 8·9%); (ii) n_D^{20} 1·5073 (100 mg.) (Found: C, 75·8; H, 8·75%). Fractions (i) and (ii) represent a 70% yield of ester.

(±)-trans-*Cineronyl* (±)-cis-*Chrysanthemate*.—The product from (±)-*trans*-cinerolone (260 mg.), (±)-*cis*-chrysanthemoyl chloride (290 mg.), and pyridine (0·15 ml.) in benzene (5 ml.) gave, on distillation, a forerun (26 mg.), n_D^{20} 1·5023, and then the required *ester* was collected in two fractions, b. p. 133—136°/7 × 10^{-3} mm.: (i) n_D^{20} 1·5054 (126 mg.) (Found: C, 76·2; H, 9·3%); (ii) n_D^{20} 1·5068 (118 mg.) (Found: C, 76·4; H, 9·2%). Fractions (i) and (ii) were bulked (244 mg., 49%).

(±)-n-*But*-3-*enylrethronyl* (+)-trans-*Chrysanthemate*.—The reaction product from (±)-*n*-but-3-enylrethrolone (1·55 g.), (+)-*trans*-chrysanthemoyl chloride (1·62 g.), and pyridine (1·30 g.) in benzene (27 ml.) gave on a second distillation at 1 × 10^{-3} mm. the fractions: (i) b. p. 74—100°, n_D^{20} 1·4928 (0·37 g.); (ii) b. p. 100·0—100·5°, n_D^{20} 1·5018 (0·58 g.); (iii) b. p. 100·5—101·0°, n_D^{20} 1·5019 (0·43 g.); (iv) b. p. 101·0—101·5°, n_D^{20} 1·5021 (0·10 g.). Fractions (ii)—(iv) were bulked (1·10 g., 40%) as the required *ester* (Found: C, 75·7; H, 9·3. $C_{20}H_{28}O_3$ requires C, 75·95; H, 8·9%).

(±)-n-*Butylrethronyl*(*Dihydrocineronyl*) (±)-trans-*Chrysanthemate*.—The product from (±)-dihydrocinerolone (252 mg.), (±)-*trans*-chrysanthemoyl chloride (290 mg.), and pyridine (200 mg.) in benzene (4 ml.) gave on distillation at 5 × 10^{-3} mm. the fractions: (i) b. p. <134·5°, n_D^{20} 1·4873 (20 mg.); (ii) b. p. 134·5—136·0°, n_D^{20} 1·4948 (140 mg.) (Found: C, 76·1; H, 10·1. Calc. for $C_{20}H_{30}O_3$: C, 75·5; H, 9·5%); (iii) b. p. 136—140°, n_D^{20} 1·4957 (100 mg.). Fractions (ii) and (iii) were bulked (240 mg., 48%) as the required ester.

(±)-n-*Butylrethronyl*(*Dihydrocineronyl*) (±)-cis-*Chrysanthemate*.—The product from (±)-dihydrocinerolone (252 mg.), (±)-*cis*-chrysanthemoyl chloride (290 mg.), and pyridine (200 mg.) in benzene (4 ml.) gave on distillation at 9 × 10^{-3} mm. the fractions: (i) b. p. 120—128°, n_D^{20} 1·4881 (20 mg.); (ii) b. p. 128—132°, n_D^{20} 1·4928 (60 mg.); (iii) b. p. 132—136°, n_D^{20} 1·4674 (Found: C, 75·5; H, 9·6%); (iv) b. p. 136—139°, n_D^{20} 1·4980 (80 mg.). Fractions (ii)—(iv) were bulked (290 mg., 58%) as the required ester.

Alkenyl(and alkyl)rethrones.

2-*Allyl*-3-*methyl*cyclo*pent*-2-*en*-1-*one* (*Allylrethrone*).—Ethyl 2-ketohex-5-ene-1-carboxylate (10·0 g.) was added to powdered sodium (1·63 g.) suspended in ether, and next day the solution was treated with bromoacetone (12·0 g.) (cf. Part II, *loc. cit.*). The undistilled product was stirred with 3% sodium hydroxide (200 ml.) at 70° for 2 hours, and on isolation the crude ketone (3·9 g.) had b. p. 63—70°/0·3 mm. Reaction in pyridine (2·5 ml.)–ethanol (10 ml.) with a solution of semicarbazide hydrochloride (2·7 g.) in water (2·7 ml.) yielded the semicarbazone (1·50 g.), which crystallised as plates, m. p. 220—222° (decomp.), from ethanol (Found: C, 61·5; H, 7·5; N, 21·6. Calc. for $C_{10}H_{15}ON_3$: C, 62·15; H, 7·75; N, 21·7%), $\lambda_{max.}$ 2650 A., $\varepsilon_{max.}$ 23,200. Hydrolysis of the semicarbazone (1·0 g.) with oxalic acid (1·7 g.) in water (10 ml.) yielded 2-allyl-3-methyl*cyclo*pent-2-en-1-one (0·19 g.), b. p. 125—126°/25 mm., n_D^{20} 1·4996 (Found: C, 78·6; H, 8·9. Calc. for $C_9H_{12}O$: C, 79·4; H, 8·9%) in rather low yield (27%). The ketone was further characterised as the 2 : 4-*dinitrophenylhydrazone*, which crystallised from ethanol in deep-red flattened needles, m. p. 173—174° (Found: C, 56·5; H, 5·0; N, 17·6. $C_{15}H_{16}O_4N_4$ requires C, 56·9; H, 5·0; N, 17·7%). G.P. 658,920 records b. p. 79—80°/0·7 mm. for this ketone and a semicarbazone, m. p. 217—219°.

3-*Methyl*-2-2′-*methylallyl*cyclo*pent*-2-*en*-1-*one* [2-*Methylallylrethrone*].—Ethyl 2-keto-5-methylhex-5-ene-1-carboxylate (18·4 g.) was added to a stirred suspension of sodium hydride (2·4 g.) in dry ether (50 ml.) during 30 minutes, which was then stirred (30 minutes), and bromoacetone (20 g.) added during another 30 minutes. The mixture was subsequently refluxed for 2 hours. Next day water was added, the ether layer separated and dried, and the ether removed under reduced pressure. The residual diketo-ester was stirred with 3% sodium hydroxide (400 ml.) at 70° for 3 hours, and the crude ketone isolated by acidification and ether extraction. The extract was dried and distilled to give 3-*methyl*-2-2′-*methylallyl*-cyclo*pent*-2-*en*-1-*one* (5·8 g.), b. p. 70—72°/0·4 mm. This was converted by the pyridine–ethanol–semicarbazide hydrochloride procedure into the *semicarbazone*, which on recrystallisation from ethanol, in which it was sparingly soluble, separated as plates, m. p. 194—210° (decomp.). Further successive crystallisations from glacial acetic acid and from ethylene glycol monoethyl ether failed either to sharpen or to raise the m. p. materially [195—215° (decomp.)].

In another preparation, the acetoacetic ester (9·2 g.) was added to a cooled solution of sodium (1·5 g.) in ethanol (30 ml.), followed by bromoacetone (10 g.), with stirring, over 30 minutes. The mixture was then heated under reflux for 2 hours. The diketo-ester was isolated, cyclised with 200 ml. of alkali, and the ketone (2·7 g.) distilled as above. A portion (1·66 g.) was converted into the semicarbazone (1·71 g.) which, after two crystallisations from ethylene glycol monoethyl ether, had m. p. 202—216° (decomp.) (Found: C, 63·7; H, 8·2. $C_{11}H_{17}ON_3$ requires C, 63·7; H, 8·25%), $\lambda_{max.}$ 2650 A., $\varepsilon_{max.}$ 23,750; and another portion (100 mg.) into the 2 : 4-*dinitrophenylhydrazone* (140 mg.) which formed deep-red plates, m. p. 154·5—156°, from ethanol (Found: C, 58·65; H, 5·45. $C_{16}H_{18}O_4N_4$ requires C, 58·2; H, 5·5%). An attempt to regenerate the ketone by hydrolysis of the semicarbazone (660 mg.) with hot aqueous oxalic acid gave an unexpectedly low yield of ketone (*ca.* 50 mg.), which had a jasmone-like smell.

2-n-*Amyl*-3-*methyl*cyclo*pent*-2-*en*-1-*one* (*Tetrahydropyrethrone*).—Ethyl 2-keto-octane-1-carboxylate (30·0 g.) was added during 2 hours to a suspension of powdered sodium (3·9 g.) in ether (150 ml.) and the mixture set aside overnight. Next day bromoacetone (21 g.) was added portionwise, and the reaction completed by refluxing the solution for 2 hours. Water and acid were added, the ether layer separated, and the aqueous layer again extracted with ether. The combined extracts were dried and evaporated. The crude diketo-ester (45 g.) was stirred with 3% sodium hydroxide (500 ml.) for 6 hours at 70°, then cooled, acidified, and well extracted with ether. Distillation of the product yielded a forerun (2·4 g.), probably octan-2-one, and then crude tetrahydropyrethrone (10·3 g.), b. p. 140—147°/22 mm. Treatment of the higher-boiling residue with alkali gave a further 2·0 g. of ketone (total 12·3 g., 51%). Conversion by the pyridine–ethanol–semicarbazide hydrochloride procedure into the semicarbazone (10·4 g.) (plates from methanol; m. p. 176·5—177·0°), hydrolysis of this with oxalic acid (20 g.) in water (100 ml.), and isolation of the product with light petroleum (b. p. 40—60°) gave the pure ketone (7·0 g.) (used in earlier work, see Part III, *loc. cit.*). The 2 : 4-dinitrophenylhydrazone formed dark-red needles, m. p. 122°, from ethanol (West, *J.*, 1945, 412, records m. p 121—122° for this derivative of the naturally derived ketone).

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