772. *Experiments on the Synthesis of the Pyrethrins. Part XI.* Synthesis of* cis-*Pyrethrolone and Pyrethrin I: Introduction of the* cis-*Penta-2 : 4-dienyl System by Selective Hydrogenation.*†

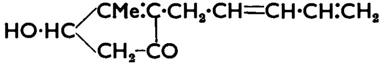
By L. Crombie, S. H. Harper, and F. C. Newman.

When 1 mol. of hydrogen is added to a monosubstituted vinylacetylene in the presence of a palladium catalyst, a *cis*-vinylic diene is produced. Absorption of hydrogen does not cease at this stage, even when poisoned catalysts are used, but continues until the vinyl grouping is saturated, and gives a *cis*-mono-olefin. With poisoned catalysts, gas absorption then becomes very slow. The hydrogenations are not completely selective.

Intermediates described in Part X are used in synthesis of (±)-*cis*-pyrethrolone, which is found to be identical with pyrethrolone B-2 of natural origin. The final stage in this synthesis involves controlled hydrogenation of a vinylacetylene system to produce the *cis*-diene side-chain. Improvements to our earlier synthesis of (±)-*trans*-pyrethrolone are described.

From synthetic (±)-*cis*-pyrethrolone the diastereoisomeric mixture of esters (+)-*cis*-pyrethronyl (+)-*trans*-chrysanthemate and (−)-*cis*-pyrethronyl (−)-*trans*-chrysanthemate is prepared: the former is natural pyrethrin I. Other insecticidal rethrins having pent-4-en-2-ynyl and hexa-*trans*-2 : *trans*-4-dienyl side-chains are reported.

In Part X * the preparation of potential intermediates for the synthesis of *cis*-pyrethrolone (I), containing the terminal grouping $\mathrm{{\cdot}CH_2{\cdot}C{\vdots}C{\cdot}CH{:}CH_2}$, was described. Attention is now turned to the selective hydrogenation of these intermediates as a means of introducing the *cis*-penta-2 : 4-dienyl system.

(I) 

$$\mathrm{HO{\cdot}HC}\begin{cases}\mathrm{CMe{:}C{\cdot}CH_2{\cdot}CH\overset{c}{=}CH{\cdot}CH{:}CH_2}\\ \mathrm{CH_2{-}CO}\end{cases}$$

Although catalytic semihydrogenation of an isolated acetylenic bond at a supported palladium catalyst is a well-established method of introducing a *cis*-ethylenic bond, generally of good stereochemical purity,[1] the method has been less used for compounds

---

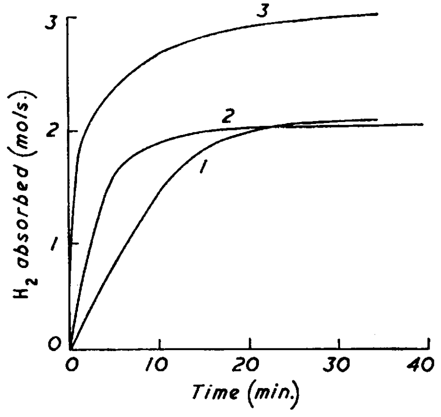
* Part X, *J.*, 1956, 126.

† Read in abstract at the XIVth Internat. Congr. Pure and Applied Chemistry, Zürich, July, 1955.

[1] Campbell and Campbell, *Chem. Rev.*, 1942, **31**, 77; Crombie, *Quart. Rev.*, 1952, **6**, 101.

containing the acetylenic bond conjugated with an ethylenic bond. Evidence has accumulated that in the hydrogenation of such enyne systems reduction continues beyond the uptake of 1 mol. of hydrogen and even if reduction is interrupted at this point the diene is contaminated with unchanged enyne and oversaturated material.[2] A further complication is associated with the substituted vinylacetylenes with which we are concerned. Lebedev, Kobliansky, and Yakubchik,[3] using platinum black, and Dupont,[4] using Raney nickel as catalyst, showed that monosubstituted olefins, $R\cdot CH{:}CH_2$, are reduced much more rapidly than more substituted olefins. If this reduction of a vinyl group were to occur (over a supported palladium catalyst) concurrently with semihydrogenation of the acetylenic linkage, then the difficulty in isolating a pure *cis*-diene from partial reduction of the $\cdot CH_2\cdot C{\vdots}C\cdot CH{:}CH_2$ system might be even greater than for the system $\cdot CH_2\cdot C{\vdots}C\cdot CH{:}CH\cdot CH_2\cdot$.

To examine the efficacy of supported palladium catalysts in the selective hydrogenation of the $\cdot CH_2\cdot C{\vdots}C\cdot CH{:}CH_2$ system, the reduction of oct-7-en-5-yn-2-one, its semicarbazone, and hept-6-en-4-ynoic acid [5] was studied. In all three cases, when the poisoned catalysts of Isler *et al.*[6] and of Lindlar [7] were used, 2 mols. of hydrogen were absorbed without appreciable change in rate of uptake. Absorption then practically ceased. Even with palladised barium sulphate, absorption of the third mol. of hydrogen occurred more slowly than that of the first 2 mols. (see Figure). By increasing the proportion of quinoline to Lindlar catalyst the rate of absorption was slowed but there was no break in the curve when 1 mol. of hydrogen had been absorbed.



Hydrogenation of oct-7-en-5-yn-2-one semicarbazone using (1) *Isler catalyst,* (2) *Lindlar catalyst, and* (3) *palladium–barium sulphate catalyst.*

As most of the ketones and acids that might result from the hydrogenation of oct-7-en-5-yn-2-one and hept-6-en-4-ynoic acid were available from our earlier work, it has been possible to identify the products formed on absorption of 1 and 2 mols. of hydrogen and hence deduce the course of reduction. We find, in agreement with Lebedev *et al.* and Dupont, that oct-7-en-2-one, a monosubstituted olefin, is reduced more rapidly than oct-*trans*-5-en-2-one, a disubstituted olefin, over both Lindlar catalyst and palladised barium sulphate (the two reactions are much slower in the presence of the former catalyst). Preparative hydrogenation of oct-7-en-5-yn-2-one over Lindlar catalyst, to an uptake of 2 mols. of hydrogen, gave a monoethylenic ketone, and comparison of its semicarbazone and 2 : 4-dinitrophenylhydrazone with authentic specimens showed that it was somewhat impure oct-*cis*-5-en-2-one.[8] The nature of the impurities was indicated by its infrared

---

[2] (*a*) Heilbron, Jones, and Sondheimer, *J.*, 1947, 1586; (*b*) Crombie, Harper, and Thompson, *J.*, 1951, 2906; (*c*) Crombie, *J.*, 1955, 1007; (*d*) Allan, Jones, and Whiting, *J.*, 1955, 1862; (*e*) Butenandt, Hecker, and Zachau, *Chem. Ber.*, 1955, **88**, 1185.

[3] Lebedev, Kobliansky, and Yakubchik, *J.*, 1925, **127**, 417.

[4] Dupont, *Bull. Soc. chim. France*, 1936, 1021, 1030.

[5] Crombie, Harper, Newman, Thompson, and Smith, *J.*, 1956, 126.

[6] Isler, Huber, Ronco, and Kofler, *Helv. Chim. Acta*, 1947, **30**, 1911.

[7] Lindlar, *ibid.*, 1952, **35**, 446.

[8] Harper and Smith, *J.*, 1955, 1512.

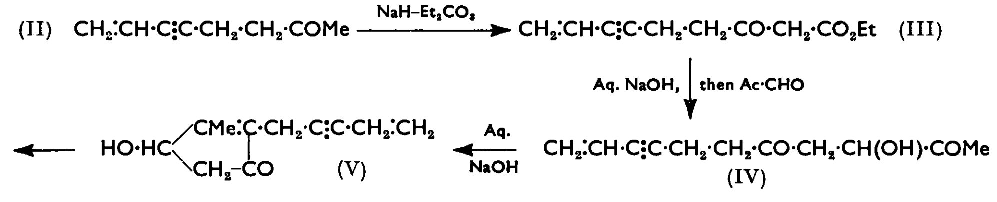
spectrum. Weak absorption at 910 and 995 cm.$^{-1}$ (unconjugated vinyl) suggested a little oct-7-en-2-one, and a weak band at 967 cm.$^{-1}$ (*trans*-$CHR\colon CHR'$) suggested either oct-*trans*-6-en-2-one or oct-*trans*-5-en-2-one. Similar hydrogenation of hept-6-en-4-ynoic acid over Lindlar catalyst, to an uptake of 2 mols., gave a heptenoic acid and examination of its *p*-bromophenacyl ester showed it to be slightly impure hept-*cis*-4-enoic acid.[9]

Absorption of 2 mols. of hydrogen, over supported palladium catalysts, by the $\cdot CH_2\cdot C\vdots C\cdot CH\colon CH_2$ system thus proceeds mainly by selective reduction of the acetylenic to a *cis*-ethylenic linkage and by reduction of the terminal vinyl group. It remained to find out whether these processes are consecutive or concurrent.

Reduction of oct-7-en-5-yn-2-one over Lindlar catalyst, with interruption of the reaction when 1 mol. of hydrogen had been absorbed, gave products whose intensity of ultraviolet absorption (max. at 227 mμ; ε 9700—12,400) showed that the *cis*-diene ketone was present, though the infrared spectrum indicated that the hydrogenation had not been fully selective. On a larger scale, fractional distillation of the crude product gave material having max. at 227 mμ (ε 14,300—14,700). That this was substantially pure octa-*cis*-5 : 7-dien-2-one was confirmed by comparison of the infrared spectrum with that of authentic ketone prepared by the elimination of toluene-*p*-sulphonic acid from 8-toluene-*p*-sulphonyloxyoct-*cis*-5-en-2-one.[5] Mixed melting points of the semicarbazones and 2 : 4-dinitrophenylhydrazones showed no depressions. Similar hydrogenation of hept-6-en-4-ynoic acid gave substantially pure hepta-*cis*-4 : 6-dienoic acid, having max. at 226 mμ (ε 14,500). In the main, therefore, reduction of the acetylenic bond in vinylacetylenes takes place before that of the terminal vinyl group, as has been claimed by Zonis [10] and by Zal'kind and Khudekova.[11]

The way was then clear for the synthesis of *cis*-pyrethrolone, and, bearing in mind the greater stability of the pent-4-en-2-ynyl system over the *cis*-penta-2 : 4-dienyl system, we decided to make the selective hydrogenation the final stage.

Oct-7-en-5-yn-2-one (II) was converted, successively, by procedures previously devised,[12, 13] into ethyl 2-oxo-oct-7-en-5-yne-1-carboxylate (III), its sodium salt, and 3-hydroxyundec-10-en-8-yne-2 : 5-dione (IV). The ultraviolet light absorption of these intermediates showed that the conjugated enyne system was unaffected by reagents used in the synthesis. Cyclisation then gave (±)-pent-4-en-2-ynylrethrolone (V), which readily formed a crystalline semicarbazone. That the product had the gross structure assigned to it was established by hydrogenation of the semicarbazone over palladised barium sulphate, with an uptake of 3 mols. of hydrogen, to the known tetrahydropyrethrolone semicarbazone.[14]



The ultraviolet light absorption of the hydroxy-ketone (max. at 226 mμ, ε 21,100) and its semicarbazone (max. at 227 and 267 mμ, ε 18,900 and 21,900) established the presence of a conjugated enyne chromophore. The latter was confirmed by the infrared spectrum of the hydroxy-ketone [conjugated disubstituted acetylene 2230 (m), conjugated vinyl 975 (s) and 925 (s), hydrogen-bonded hydroxyl 3410 (s), secondary hydroxyl 1052 (s), conjugated carbonyl stretching 1699 (s), conjugated ethylene 1652 (s) cm.$^{-1}$].

Catalytic hydrogenation of (±)-pent-4-en-2-ynylrethrolone over Lindlar catalyst to an uptake of 0·9 mol. of hydrogen gave the best specimen of (±)-*cis*-pyrethrolone (I), which

---

[9] Crombie and Harper, *J.*, 1952, 869.
[10] Zonis, *J. Gen. Chem.* (*U.S.S.R.*), 1939, **9**, 2191; *Chem. Abs.*, 1940, **34**, 4052.
[11] Zal'kind and Khudekova, *J. Gen. Chem.* (*U.S.S.R.*), 1940, **10**, 521; *Chem. Abs.*, 1940, **34**, 7847.
[12] Crombie, Edgar, Harper, Lowe, and Thompson, *J.*, 1950, 3552.
[13] Schechter, Green, and LaForge, *J. Amer. Chem. Soc.*, 1949, **71**, 3165; 1952, **74**, 4902.
[14] Crombie, Elliott, and Harper, *J.*, 1950, 971.

readily formed a crystalline semicarbazone. This product was identical with naturally derived pyrethrolone B-2[2b, 15] (infrared spectrum and mixed m. p. of the semicarbazones).

Ultraviolet-light absorptions of *cis*-pyrethrolone and precursors containing the *cis*-penta-2 : 4-dienyl system (Table) all have considerably lower intensities, owing to the diene chromophore, than their *trans*-counterparts : the wavelength of maximal absorption is similar in both stereoisomers. Small amounts of impurity in the *cis*-forms, resulting from the partial hydrogenation procedure, may be a contributory cause of the lower ε values but it is likely that the main cause is stereochemical. The system under consideration (VI; $R = CH_2$, $R' = H$) is best compared with that of methyl deca-*trans*-2 : *cis*-4- and -*trans*-2 : *trans*-4-dienoate (VI; $R = n\text{-}C_5H_{11}$, $R' = CO_2Me$),[2c] methyl *trans*-2 : *cis*-4- and -*trans*-2 : *trans*-4-sorbate (VI; $R = Me$, $R' = CO_2Me$),[2d] hexa- and deca-*trans*-2 : *cis*-4- and -*trans*-2 : *trans*-4-dienol (VI; $R = Me$ or $n\text{-}C_5H_{11}$, $R' = CH_2{\cdot}OH$),[2c, e] and nona-*trans*-5 : *cis*-7- and -*trans*-5 : *trans*-7-dien-2-one (VI; $R = Me$, $R' = CH_2{\cdot}CH_2{\cdot}COMe$).[16] In all these cases there is a fall in $\varepsilon_{max.}$ when the *cis*-linkage is introduced, despite the fact that steric hindrance to coplanarity, as deduced from models, is apparently small and there is no alteration in chromophore length. Nevertheless there is greater non-bonded interaction in the *cis*-forms and some consequences are discussed elsewhere.[2c] Piperylene itself is unusual in that both the *cis*- and the *trans*-form absorb, in solution, at the same wavelength and with equal intensity.[17] In the gas phase, however, *trans*- is reported to have a much higher $\varepsilon_{max.}$ than *cis*-piperylene.[18] Although *cis*-butadienylmethylcarbinol (hexa-*cis*-3 : 5-dien-2-ol) [17] and *cis*-1-phenylbutadiene [19] have lower $\varepsilon_{max.}$ values than their *trans*-counterparts, comparison with the system considered in this work is less valid as steric hindrance to coplanarity in the *cis*-forms is considerable : in *cis*-1-phenylbutadiene this is associated with a marked shift in the wavelength of maximal absorption (*cis*-, max. at 265—269 mμ, ε 18,400; *trans*-, max. at 280 mμ, ε 29,800).

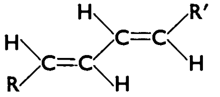
Ultraviolet-light absorption of compounds containing the cis- *and* trans-*penta*-2 : 4-*dienyl chromophore.*

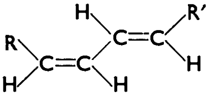
	cis			*trans*		
	$\lambda_{max.}$ (mμ)	ε	Δε *	$\lambda_{max.}$ (mμ)	ε	Δε *
$CH_2{:}CH{\cdot}CH{:}CH{\cdot}CH_2{\cdot}OH$	227	14,300	14,300	226	25,200	25,200
$CH_2{:}CH{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$	226	14,500	14,500	—	—	—
$CH_2{:}CH{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}CH_3$	226	16,100	16,100 [a]	226	22,400	22,400
				(226	23,000	23,000) [b]
$CH_2{:}CH{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}CH_2{\cdot}CO_2Et$	—	—	—	226	27,800	27,800 [b]
$CH_2{:}CH{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}CH_2{\cdot}CH(OH){\cdot}CO{\cdot}CH_3$	—	—	—	226	22,600	22,600
				(226	27,500	27,500) [b]
Pyrethrolone (I)	227	26,000	14,200 [c]	227	37,400	25,600 [c]
				(227	33,000	23,900) [b,d]
Semicarbazone of (I)	228	18,300	14,000 [e]	227	27,500	23,200 [e]
	265	20,700	—	265	22,600	—

* Increase of ε at 227 mμ (*ca.* $\lambda_{max.}$) due to the $CH_2{:}CH{\cdot}CH{:}CH{\cdot}CH_2$ chromophore.

[a] Part X. [b] Part VII. [c] Computed by deduction of ε_{227} 11,800 for tetrahydropyrethrolone (max. at 230 mμ). [d] Computed by deduction of ε_{227} 9100 for tetrahydropyrethrolone (max. at 227 mμ). [e] Computed by deduction of ε_{227} 4300 for tetrahydropyrethrolone semicarbazone (max. at 264 mμ, ε 16,000).

(VIa)





(VIb)

For comparison with (±)-*cis*-pyrethrolone, preparation of (±)-*trans*-pyrethrolone was repeated by our earlier route,[2b] though the conditions were varied in an attempt to raise the overall yield. When 2 : 3-dichlorotetrahydropyran was treated with ethanolic ammonia

---

[15] West, *J.*, 1946, 463.

[16] Crombie, Harper, and Smith, unpublished work.

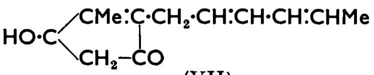
[17] Braude and Coles, *J.*, 1951, 2085.

[18] Jacobs and Platt, *J. Chem. Phys.*, 1948, **16**, 1142.

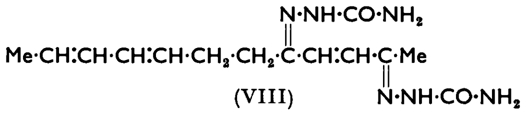
[19] Grummitt and Christoph, *J. Amer. Chem. Soc.*, 1949, **71**, 4157.

and then, without isolation of the 3-chloro-2-ethoxytetrahydropyran, treated with potassium hydroxide, the yield of 2-ethoxy-5 : 6-dihydro-2-pyran obtained earlier [2b] could not be reproduced, and a large proportion of 3-chloro-2-ethoxytetrahydropyran was recovered. Experiments showed that 3-chloro-2-ethoxytetrahydropyran eliminated hydrogen chloride much more rapidly with potassium hydroxide in hot diethylene glycol and this modification gave a consistent 40—45% yield of 2-ethoxy-5 : 6-dihydro-2-pyran. Since these experiments were completed Riobé has used ethylene glycol.[20] The use of 2 : 3-dibromotetrahydropyran was re-examined, and it was found that the decomposition which occurred on removal of the solvent (carbon tetrachloride) could be avoided by bromination in methylene chloride at −35° and removal of the solvent below 0° under reduced pressure. However, the yield of 2-ethoxy-5 : 6-dihydro-2-pyran was not improved. A crystalline semicarbazone was readily obtained from *trans*-octa-5 : 7-dien-2-one and this important intermediate was further characterised by ultraviolet and infrared absorption spectra. Improved yields were obtained at the ethoxycarbonylation stage by the use of the procedure of Schechter *et al.*[13] The final (±)-*trans*-pyrethrolone was obtained in enhanced purity, as judged by $\varepsilon_{\text{max.}}$ (37,400 against 33,000 found previously [2b]), and by the ready formation of a crystalline semicarbazone (a semicarbazone was not obtained from our earlier preparation). This semicarbazone, although having the same m. p. as (±)-*cis*-pyrethrolone semicarbazone, gave a small but distinct depression of m. p. on admixture.

We have similarly prepared a diene analogue of pyrethrolone, sorbylrethrolone (VII), by successive conversion of sorbylacetone (nona-*trans*-5 : *trans*-7-dien-2-one *) into ethyl 2-oxonona-*trans*-5 : *trans*-7-diene-1-carboxylate, its sodium salt, and 3-hydroxydodeca-*trans*-8 : *trans*-10-diene-2 : 5-dione. The hydroxy-dione readily formed an " anhydrodisemicarbazone " which must be the disemicarbazone (VIII) of the triene-dione, rather than the pyrazoline (IX), for the ultraviolet absorption spectrum is consistent with the presence of a N:C·C:C·C:N system (max. at 315 mμ; ε 36,000). Similar " anhydrodisemicarbazones " have been obtained from 3-hydroxy-alkane- and -alkene-2 : 5-diones by Henze and Muller [21] and by Schechter, Green, and LaForge,[13] who considered, but did not exclude, the pyrazoline formulation. Cyclisation of the hydroxy-dione gave (±)-sorbylrethrolone, which formed a crystalline semicarbazone.

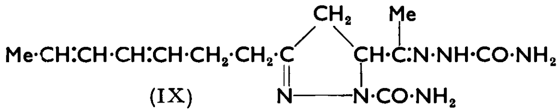


(VII)



$$\mathrm{Me{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}}\overset{\mathrm{N{\cdot}NH{\cdot}CO{\cdot}NH_2}}{\overset{\|}{\mathrm{C}}}\mathrm{{\cdot}CH{:}CH{\cdot}}\underset{\mathrm{N{\cdot}NH{\cdot}CO{\cdot}NH_2}}{\underset{\|}{\mathrm{C}}}\mathrm{{\cdot}Me}$$

(VIII)



(IX)

For insecticidal assay, (±)-*cis*-pyrethrolone was esterified with (+)-*trans*-chrysanthemic acid, through the acid chloride, to give a pyrethrin I [the mixed diastereoisomers (+)-*cis*-pyrethronyl (+)-*trans*-chrysanthemate and (—)-*cis*-pyrethronyl (+)-*trans*-chrysanthemate, the former of which is the naturally occurring ester]. (±)-Pent-4-en-2-ynylrethrolone was similarly esterified with (+)-*trans*-chrysanthemic acid, and (±)-sorbylrethrolone with (±)-*trans*-chrysanthemic acid. To avoid loss by thermal decomposition, none of these esters was purified by distillation, but all of them showed very high potency towards mustard beetle. Details of this and other insecticidal tests will be reported elsewhere.

EXPERIMENTAL

Ultraviolet-light absorptions were determined for EtOH solutions by Mrs. I. Boston with a Hilger Medium Quartz Spectrograph. Some of the infrared-light absorptions were determined

---

* The preparation of all the stereoisomeric nona-5 : 7-dien-2-ones and a study of their spectral properties will be the subject of a future communication.

[20] Riobé, *Bull. Soc. chim. France*, 1952, 305.

[21] Henze and Muller, *Z. physiol. Chem.*, 1930, **193**, 88.

with a Grubb-Parsons single-beam spectrometer and others with a Grubb-Parsons double-beam spectrometer.

Benzene solutions of 2 : 4-dinitrophenylhydrazones were chromatographed on alumina before crystallisation from ethanol. M. p.s are corrected.

Catalysts.—5% Palladised calcium carbonate was prepared by the procedure of Busch and Stöve,[22] 5% palladised barium sulphate as given by Houben,[23] and lead-poisoned palladised calcium carbonate deactivated by quinoline by the procedure of Lindlar.[7] The Isler catalyst [6] (palladised charcoal deactivated by quinoline) was a gift from Dr. F. Sondheimer, whom we thank.

Preparative Hydrogenation Procedure.—Catalytic hydrogenations were conducted at room temperature and atmospheric pressure, generally in ethyl acetate. On completion or on interruption at the appropriate uptake, Filter-Cel was added. After filtration, the filtrate was washed (if quinoline had been added), with portions of 15% hydrochloric acid, then water, and dried ($MgSO_4$), and the product isolated by distillation.

*Hydrogenation of Oct-7-en-2-one and Oct-*trans*-5-en-2-one.*—Oct-7-en-2-one from our earlier preparation [9] gave a *semicarbazone*, crystallising as plates, m. p. 112·0—112·5°, from aqueous ethanol (Found: C, 59·0; H, 9·60. $C_9H_{17}ON_3$ requires C, 59·0; H, 9·35%). Regenerated from the semicarbazone by aqueous oxalic acid, oct-7-en-2-one had b. p. 66°/12 mm., n_D^{20} 1·4306. The 2 : 4-dinitrophenylhydrazone had m. p. 65·0—65·5°. Catalytic hydrogenation of the semicarbazone gave octan-2-one semicarbazone, m. p. and mixed m. p. 124·5°. Catalytic hydrogenation of *oct-*trans*-5-en-2-one* [9] *semicarbazone*, m. p. 62·5—63·5° [from light petroleum (b. p. 60—80°)] (Found: C, 58·9; H, 9·25. $C_9H_{17}ON_3$ requires C, 59·0; H, 9·35%), similarly gave octan-2-one semicarbazone, m. p. and mixed m. p. 124°.

*Oct-*cis*-5-en-2-one.*—Oct-7-en-5-yn-2-one [8] (488 mg.), hydrogenated over lead-poisoned palladised calcium carbonate (Lindlar) (100 mg.) in the presence of quinoline (35 mg.) to an uptake of 2 mols. (40 min.), gave impure oct-*cis*-5-en-2-one (350 mg.), b. p. 67—69°/17 mm., n_D^{20} 1·4316. The semicarbazone (Found: C, 59·4; H, 9·4. Calc. for $C_9H_{17}ON_3$: C, 59·0; H, 9·35%) had m. p. 103·5—104·5°, raised on admixture with an authentic specimen [8] of m. p. 114°. The 2 : 4-dinitrophenylhydrazone (Found: C, 55·4; H, 6·05. Calc. for $C_{14}H_{18}O_4N_4$: C, 54·9; H, 5·9%) had m. p. 64°, raised on admixture with an authentic specimen [8] of m. p. 67·5°. In a similar experiment, but using quinoline (70 mg.), an uptake of 2 mols. of hydrogen was achieved in 4 hr.

*Octa-*cis*-5 : 7-dien-2-one.*—Oct-7-en-5-yn-2-one (2·38 g.) was hydrogenated over lead-poisoned palladised calcium carbonate (Lindlar) (total, 1·0 g.) in the presence of quinoline (total, 1·0 g.) to an uptake of 1 mol. of hydrogen. The smaller amount of catalyst and quinoline first added was quickly deactivated and more was added to complete the hydrogenation. Fractional distillation gave octa-*cis*-5 : 7-dien-2-one (0·91 g.), b. p. 62—67°/5 mm., n_D^{20} 1·467—1·473, max. at 228 mμ (ε 15,000) (Found: C, 77·2; H, 9·55. Calc. for $C_8H_{12}O$: C, 77·4; H, 9·75%). The *semicarbazone* (Found: C, 59·75; H, 8·5. $C_9H_{15}ON_3$ requires C, 59·65; H, 8·35%), crystallised thrice from aqueous ethanol, had m. p. 112·5—113·5°, raised to 112·5—114·0° on admixture with the derivative of m. p. 115·0—115·5° prepared by the elimination route.[5] The 2 : *4-dinitrophenylhydrazone* (Found: C, 55·15; H, 5·2. $C_{14}H_{16}O_4N_4$ requires C, 55·2; H, 5·3%) had m. p. 55·0—55·5° and when admixed with the derivative of m. p. 52·5—53·5°, prepared by the elimination route,[5] had m. p. 53—54·5°.

*Hept-*cis*-4-enoic Acid.*—Hept-6-en-4-ynoic acid (622 mg.),[5] hydrogenated over lead-poisoned palladised calcium carbonate (Lindlar) (500 mg.) in the presence of quinoline (1·1 g.) to an uptake of 2 mols. (10 min.), gave slightly impure hept-*cis*-4-enoic acid (500 mg.), b. p. 116·0—116·5°/12 mm., n_D^{20} 1·4426. The *p*-bromophenacyl ester, crystallised from aqueous ethanol, had m. p. 41—42° raised to 41—42·5° on admixture with the authentic ester [9] of m. p. 44°. Crombie and Harper [9] record b. p. 116°/12 mm., n_D^{20} 1·4400, for hept-*cis*-4-enoic acid.

*Hepta-*cis*-4 : 6-dienoic Acid.*—Hept-6-en-4-ynoic acid (621 mg.), hydrogenated over lead-poisoned palladised calcium carbonate (Lindlar) (300 mg.) in the presence of excess of quinoline (1·1 g.) to an uptake of 1 mol. of hydrogen (15 min.), gave *hepta-*cis*-4 : 6-dienoic acid* (240 mg.), b. p. 122—124°/12 mm., n_D^{20} 1·4749 (for light absorption see Table) (Found: C, 67·0; H, 8·1. $C_7H_{10}O_2$ requires C, 66·7; H, 8·0%). The *p-bromophenacyl ester* was formed readily and crystallised as plates (from aqueous ethanol), m. p. 80—81° (Found: C, 56·0; H, 4·6. $C_{15}H_{15}O_3Br$ requires C, 55·7; H, 4·7%).

[22] Busch and Stöve, *Ber.*, 1916, **49**, 1063.

[23] Houben, " Die Methoden der Organische Chemie," Thieme, Leipzig, Vol. II, p. 500.

Ethyl 2-*Oxo-oct*-7-*en*-5-*yne*-1-*carboxylate*.—By the procedure of Part V,[12] on a 0·05—0·20-molar scale, oct-7-en-5-yn-2-one was treated with sodium hydride in ethyl carbonate–ether, to give *ethyl* 2-*oxo-oct*-7-*en*-5-*yne*-1-*carboxylate* (44—46%), b. p. 77—85°/0·1 mm., 88—98°/0·3 mm., n_D^{20} 1·478—1·483, max. at 223 and 228 mμ (ε 14,000 and 11,600) (Found: C, 67·75; H, 7·25. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·25%). The consistent b. p. spread might be due to partial separation of keto- and enol forms or to some methylene-*C* substitution.

3-*Hydroxyundec*-10-*en*-8-*yne*-2 : 5-*dione*.—By a procedure similar to that of Part V,[12] ethyl 2-oxo-oct-7-en-5-yne-1-carboxylate (11·1 g.) was shaken under nitrogen with 3% aqueous sodium hydroxide (85 ml.) during 6 hr. at 20° and then set aside overnight at 0°. A little insoluble oil was removed by light petroleum and recovered by distillation (b. p. 80—90°/12 mm., n_D^{20} 1·476; 0·3 g.). It was identified as oct-7-en-5-yn-2-one, presumably formed by ketonic hydrolysis, by conversion into the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 67—68°.

68% w/v Aqueous pyruvaldehyde (7·3 ml.) was added to the clear alkaline solution and the pH adjusted to 8·5. The mixture was kept at 35°, separation of oil starting after 20 min. When this appeared complete (*ca.* 5 ml.) sodium chloride was added and the product isolated with ether. Drying (Na_2SO_4) and distillation gave 3-*hydroxyundec*-10-*en*-8-*yne*-2 : 5-*dione* (4·61 g., 42%), b. p. 115—117°/0·1 mm., n_D^{20} 1·5035, max. at 223 and 232 mμ (ε 13,600 and 8900) (Found: C, 67·7; H, 7·35. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·25%).

The aqueous layer was acidified with concentrated hydrochloric acid (an oil separated) and warmed to 50°, but little decarboxylation occurred. Extraction with ether, drying (Na_2SO_4), and distillation (b. p. 60—90°/0·4 mm.) gave a crystalline product (0·15 g.), which after crystallisation from light petroleum (b. p. 40—60°) was identified as hept-6-en-4-ynoic acid by m. p. and mixed m. p. 57—58·5°. In addition, some polymeric material was obtained but no hydroxy-dione was present in this extract (contrast Part V [12]).

(±)-*Pent*-4-*en*-2-*ynylrethrolone* [(±)-4-*Hydroxy*-3-*methyl*-2-(*pent*-4-*en*-2-*ynyl*)cyclo*pent*-2-*en*-1-*one*].—3-Hydroxyundec-10-en-8-yne-2 : 5-dione (8·6 g.) was added during 1 hr. to 2% sodium hydroxide solution (125 ml.) containing a trace of quinol and stirred at 10°. After a further hour's stirring at room temperature, sodium chloride was added and the product isolated with ether. Distillation gave (±)-*pent*-4-*en*-2-*ynylrethrolone* (3·27 g., 42%), b. p. 128—131°/0·1 mm., n_D^{20} 1·5520, light-absorption max. in Table (Found: C, 74·8; H, 6·95. $C_{11}H_{12}O_2$ requires C, 74·95; H, 6·85%). Stored at 0° in the presence of quinol and under nitrogen, the hydroxy-ketone did not deteriorate during several months.

The *semicarbazone* was formed readily with semicarbazide hydrochloride in pyridine and crystallised from ethanol as needles, light-absorption max. in Table (Found: C, 61·8; H, 6·6. $C_{12}H_{15}O_2N_3$ requires C, 61·8; H, 6·5%). When heated, the semicarbazone blackened and sintered without a definite m. p. or decomposition temperature. Catalytic hydrogenation of the semicarbazone over palladised barium sulphate, with an uptake of 3 mols. of hydrogen, gave tetrahydropyrethrolone semicarbazone, m. p. and mixed m. p. 174—175°.

(±)-cis-*Pyrethrolone* [(±)-4-*Hydroxy*-3-*methyl*-2-(*penta*-cis-2 : 4-*dienyl*)cyclo*pent*-2-*en*-1-*one*]. (±)-Pent-4-en-2-ynylrethrolone (500 mg.), hydrogenated over lead-poisoned palladised calcium carbonate (Lindlar) catalyst (100 mg.) in the presence of quinoline (250 mg.) to an uptake of 0·9 mol. of hydrogen, gave (±)-cis-*pyrethrolone* (200 mg.), b. p. 120—123°/0·06 mm., n_D^{20} 1·536, light absorption see Table (Found: C, 73·9; H, 7·95. $C_{11}H_{14}O_2$ requires C, 74·1; H, 7·9%).

In another reduction, over 200 mg. of catalyst with 200 mg. of quinoline, the uptake was very rapid and the product, max. at 227 mμ (ε 21,800) (Found: C, 73·6; H, 8·2%), contained some overhydrogenated material. The *semicarbazone* prepared from this by the semicarbazide hydrochloride–pyridine method and crystallised from ethanol had m. p. 198·5—200° (decomp.) (immersed at 195°; rise in temp. 5° per min.) (for light absorption see Table) (Found: C, 61·1; H, 7·4. $C_{12}H_{17}O_2N_3$ requires C, 61·2; H, 7·3%). Admixed with pyrethrolone B-2 semicarbazone [m. p. 205—206° (decomp.)], the m. p. was raised to 201—203° (decomp.) (immersed at 195°). On admixture with (±)-*trans*-pyrethrolone semicarbazone [m. p. 199—200° (decomp.)], the m. p. was lowered to 194—195° (decomp.) (immersed at 190°).

(±)-*Tetrahydropyrethrolone* [(±)-4-*Hydroxy*-3-*methyl*-2-*pentyl*cyclo*pent*-2-*en*-1-*one*].—By the procedure used above for (±)-pent-4-en-2-ynylrethrolone, ethyl 2-oxo-octane-1-carboxylate (44 g.) was converted into 3-hydroxyundecane-2 : 5-dione and, without distillation, this was cyclised to (±)-tetrahydropyrethrolone (12·6 g., 32% overall), b. p. 134—137°/0·4 mm., n_D^{20}

[24] Quennehen and Normant, *Compt. rend.*, 1949, **228**, 1301.

[25] Woods and Sanders, *J. Amer. Chem. Soc.*, 1946, **68**, 2483.

1·4901, max. at 230 mμ (ε 11,800) (Found: C, 72·1; H, 10·0. Calc. for $C_{11}H_{18}O_2$: C, 72·5; H, 10·0%). Prepared with semicarbazide hydrochloride in pyridine and crystallised from ethyl acetate, the semicarbazone formed prisms, m. p. 175·5—177°, max. at 264 mμ (ε 16,000; ε_{227} *ca.* 4300) (Found: C, 60·5; H, 8·85. Calc. for $C_{12}H_{21}O_2N_3$: C, 60·2; H, 8·85%). By use of commercial aqueous pyruvaldehyde a yield of 9% (overall) of (±)-tetrahydropyrethrolone having max. at 227 mμ (ε 9100) was obtained previously.[2b]

2-*Ethoxy*-5 : 6-*dihydro*-2-*pyran*.—Material from 2 : 3-dichlorotetrahydropyran,[2b] insoluble in aqueous phosphoric acid, was washed with sodium carbonate solution, dried, and fractionally distilled. The largest fraction, b. p. 73·0—73·5°/14 mm., n_D^{20} 1·4565 (Found: C, 50·3; H, 7·7; Cl, 24·9; OEt, 23·2. Calc. for $C_7H_{13}O_2Cl$: C, 51·0; H, 7·95; Cl, 21·6; OEt, 27·3%), was mainly 3-chloro-2-ethoxytetrahydropyran. Quennehen and Normant[24] record b. p. 73—74°/13 mm., for 3-chloro-2-ethoxytetrahydropyran prepared by the action of sodium ethoxide on 2 : 3-dichlorotetrahydropyran.

Potassium hydroxide (100 g.) was added to crude 3-chloro-2-ethoxytetrahydropyran (150 g.) in diethylene glycol (400 ml.), and the mixture stirred at 160—170° under reflux for 2 hr. The product was isolated by distillation under reduced pressure. Redistillation gave 2-ethoxy-5 : 6-dihydro-2-pyran[25] (46·5 g., 40%), b. p. 50—52°/13 mm., n_D^{20} 1·443—1·446.

Octa-trans-5 : 7-*dien*-2-*one*.—The ketone formed a *semicarbazone*, crystallising from aqueous ethanol as plates, m. p. 96·5—98° (Found: C, 59·9; H, 8·55. $C_9H_{15}ON_3$ requires C, 59·65; H, 8·35%).

(±)-trans-*Pyrethrolone* [(±)-4-*Hydroxy*-3-*methyl*-2-(*penta*-trans-2 : 4-*dienyl*)cyclo*pent*-2-*en*-1-*one*].—By the procedure used above for (±)-pent-4-en-2-ynylrethrolone, ethyl 2-oxo-octa-*trans*-5 : 7-diene-1-carboxylate (13·1 g.) was converted into 3-hydroxyundeca-*trans*-8 : 10-diene-2 : 5-dione (4·8 g., 37%), b. p. 112—113°/0·1 mm., n_D^{20} 1·5000. No hydroxy-dione was obtained on acidification of the extracted aqueous layer. Cyclisation then gave (±)-*trans*-pyrethrolone (52%), b. p. 132—134°/0·15 mm., n_D^{20} 1·5447. For light absorption see Table. A *semicarbazone* was formed readily in semicarbazide hydrochloride–pyridine and, crystallised from ethanol, had m. p. 199—200° (decomp.) (Found: C, 61·3; H, 7·3. $C_{12}H_{17}O_2N_3$ requires C, 61·25; H, 7·3%). Catalytic hydrogenation of the semicarbazone over palladised barium sulphate, with an uptake of 2 mols. of hydrogen, gave (±)-tetrahydropyrethrolone semicarbazone, m. p. and mixed m. p. 175—176°.

Ethyl 2-*Oxonona*-trans-5 : trans-7-*diene*-1-*carboxylate*.—By the procedure of Part V,[12] nona-*trans*-5 : *trans*-7-dien-2-one (22·1 g.) was ethoxycarbonylated, to *ethyl* 2-*oxonona*-trans-5 : trans-7-*diene*-1-*carboxylate* (14·3 g., 43%), b. p. 89—99°/0·2 mm., n_D^{20} 1·478—1·484, max. 228 mμ (ε 25,200) (Found: C, 68·9; H, 8·55. $C_{12}H_{18}O_3$ requires C, 68·6; H, 8·65%).

3-*Hydroxydodeca*-trans-8 : trans-10-*diene*-2 : 5-*dione*.—By procedure A of Part V,[12] ethyl 2-oxonona-*trans*-5 : *trans*-7-diene-1-carboxylate (6·0 g.) was hydrolysed and treated with 68% aqueous pyruvaldehyde, to give 3-*hydroxydodeca*-trans-8 : trans-10-*diene*-2 : 5-*dione* (3·23 g., 54%), b. p. 126—133°/0·4 mm., n_D^{20} 1·498—1·502, max. at 227 mμ (ε 26,600) (Found: C, 68·7; H, 8·65. $C_{12}H_{18}O_3$ requires C, 68·6; H, 8·65%).

By the procedure of Schechter *et al.*[13] the hydroxy-dione gave an immediate precipitate with semicarbazide hydrochloride in pyridine–ethanol. On crystallisation from ethanol the yellow sparingly soluble "*anhydrodisemicarbazone*" (*dodeca*-trans-3 : trans-8 : trans-10-*triene*-2 : 5-*dione disemicarbazone*) had m. p. 224—227° (decomp.), max. at 227 and 315 mμ (ε 24,000 and 36,000) (Found: C, 54·75; H, 7·0. $C_{14}H_{22}O_2N_6$ requires C, 54·85; H, 7·25. Calc. for the disemicarbazone, $C_{14}H_{24}O_3N_6$: C, 51·85; H, 7·45%).

(±)-*Sorbylrethrolone* [(±)-2-(*Hexa*-trans-2 : trans-4-*dienyl*)-4-*hydroxy*-3-*methyl*cyclo*pent*-2-*en*-1-*one*].—By the procedure of Part V,[12] 3-hydroxydodeca-*trans*-8 : *trans*-10-diene-2 : 5-dione (2·9 g.) was cyclised to (±)-*sorbylrethrolone* (0·80 g., 30%), b. p. 130—138°/0·2 mm., n_D^{20} 1·539, max. at 227 mμ (ε 30,000) (Found: C, 74·9; H, 8·5. $C_{12}H_{16}O_2$ requires C, 74·95; H, 8·4%). The reason for the comparatively low ε value is uncertain. The *semicarbazone* prepared with semicarbazide hydrochloride in pyridine–ethanol and crystallised from ethanol had m. p. 210—212° (decomp.) (Found: C, 62·45; H, 7·6. $C_{13}H_{19}O_2N_3$ requires C, 62·6; H, 7·65%). No maleic anhydride adduct could be obtained from sorbylrethrolone.

Chrysanthemic Esters.—By the procedure of Part V,[12] interaction of (±)-pent-4-en-2-ynylrethrolone (508 mg.) and (+)-*trans*-chrysanthemoyl chloride (573 mg.) in pyridine–benzene, and heating the product at 0·05 mm./60° for 1 hr., gave (±)-*pent*-4-*en*-2-*ynylrethronyl* (+)-trans-*chrysanthemate* (780 mg.), n_D^{20} 1·523, max. at 225 mμ (ε 29,000) (Found: C, 77·35; H, 8·35. $C_{21}H_{26}O_3$ requires C, 77·3; H, 8·05%).

In a similar way, interaction of (±)-*cis*-pyrethrolone (114 mg.) and (+)-*trans*-chrysanthemoyl chloride (133 mg.) gave (±)-*cis-pyrethronyl* (+)-trans-*chrysanthemate* (205 mg.), n_D^{20} 1·514, max. at 225 mμ (ε 28,900) (Found: C, 75·4; H, 8·7. $C_{21}H_{28}O_3$ requires C, 76·8; H, 8·6%).

Interaction of (±)-sorbylrethrolone (500 mg.) and (±)-*trans*-chrysanthemoyl chloride (535 mg.) gave (±)-*sorbylrethronyl* (±)-trans-*chrysanthemate*, n_D^{20} 1·517, max. at 226 mμ (ε 38,300) (Found: C, 77·1; H, 9·0. $C_{22}H_{30}O_3$ requires C, 77·15; H, 8·85%).

We are indebted to the Central Research Fund of the University for financial assistance, and to Roche Products Ltd. for samples of Lindlar catalyst. F. C. N. gratefully acknowledges a Maintenance Grant from the Department of Scientific and Industrial Research.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, SOUTH KENSINGTON,
LONDON, S.W.7 (L. C.).
KING'S COLLEGE (UNIVERSITY OF LONDON), STRAND, LONDON, W.C.2 (S. H. H. AND F. C. N.).
[Present address of S. H. H.: UNIVERSITY COLLEGE OF RHODESIA AND NYASALAND,
SALISBURY, S. RHODESIA.]
[*Received, May 22nd,* 1956.]