be that the enzyme system in honey is analogous to that responsible for the Krebs tricarboxylic acid cycle in various muscle and brain tissues.

The presence of formic acid is not out of keeping with such an idea; Toeniessen & Brinkmann (1930) suggested that formic acid might be a product of the metabolism of pyruvate in the biological synthesis of succinic acid, but more recent work makes this doubtful. In any case the evidence for the presence of formic acid in honey is not absolutely conclusive.

The optimum pH range for honey invertase has been shown by Nelson & Cohn (1924) to be 5·5 to 6·3, i.e. well on the acid side of neutrality, so that the presence of an enzyme system of this kind ensures that the nectar will acquire the optimum acidity for the maximum inversion of sucrose. It is interesting to note that they found the higher pH to be beneficial in the early stages of the inversion, whereas the reaction rate was greater at the lower pH after part of the sugar had been hydrolysed. Whether this is the sole function of the acids in honey is, of course, not known. Both the royal jelly fed to the queen and the larval food of the workers are decidedly acid, having a pH range of 4 to 4·5, so that an acid-producing mechanism may well have other functions not connected with invertase action.

Acknowledgment

The author is indebted to Rowntree & Co. Ltd., York, for the use of laboratory facilities.

49 Muncastergate
York

Received 9 April, 1951

References

Barker, S. B. & Summerson, W. H. (1941). *J. biol. Chem.* **138**, 535.
Farnsteiner, K. (1908). *Z. Nahr. Genussm.* **15**, 598.
Friedemann, T. E., Cotonio, M. & Schaffer, P. A. (1927). *J. biol. Chem.* **73**, 335.
Gordon, J. J. & Quastel, J. H. (1939). *Biochem. J.* **33**, 1332.
Grossfeld, J. & Payfer, R. (1939). *Z. Untersuch. Lebensmitt.* **78**, 1.
Heiduschka, A. (1911). *Schweiz. med. Wschr.* **49**, 725; *Pharm. Zentralh.* **52**, 1051.
Lothrop, R. E. (1947). 'A.B.C. & X.Y.Z. of Bee Culture' (Medina, U.S.A.: Root).
Nelson, E. K. & Mottern, H. H. (1931). *Industr. Engng Chem.* **23**, 335.
Nelson, J. M. & Cohn, D. J. (1924). *J. biol. Chem.* **61**, 193.
Pryce-Jones, J. (1942–43). *Proc. Linn. Soc. Lond.* Part 2, 129.
Steigmann, A. (1943). *J. Soc. chem. Ind.* **62**, 176.
Toenissen, E. & Brinkmann, E. (1930). *Hoppe-Sley Z.* **187**, 137.

THE CHRYSANTHEMUMCARBOXYLIC ACIDS.

II.—Esterification of the Chrysanthemic Acids *

By S. H. HARPER and H. W. B. REED

Esterification of (±)-*cis*- and (±)-*trans*-chrysanthemic acids in methanolic sulphuric acid gives the expected methyl chrysanthemates together with methyl δ-methoxydihydrochrysanthemates. Normal esterification of the carboxyl group is accompanied, in part, by acid-catalysed addition of methanol to the ethylenic bond of the *iso*butenyl group. Methyl (±)-*cis*-δ-methoxydihydrochrysanthemate is also formed on methanolysis of (±)-*cis*-dihydrochrysanthemo-δ-lactone.

Ozonization of the methyl chrysanthemates, followed by hydrogenolysis of the ozonides, gives methyl (±)-*cis*- and (±)-*trans*-3-formyl-2 : 2-dimethyl*cyclo*propane-1-carboxylates in low yield. The (±)-*trans*-aldehydo-ester is also obtained, though also in low yield, by Rosenmund reduction of (±)-*trans*-3-carbomethoxy-2 : 2-dimethyl*cyclo*propane-1-carbonyl chloride and by Raney-nickel hydrogenolysis of ethyl (±)-*trans*-3-carbomethoxy-2 : 2-dimethyl*cyclo*propane-1-carbothiolate, both prepared from (±)-*trans*-caronic acid.

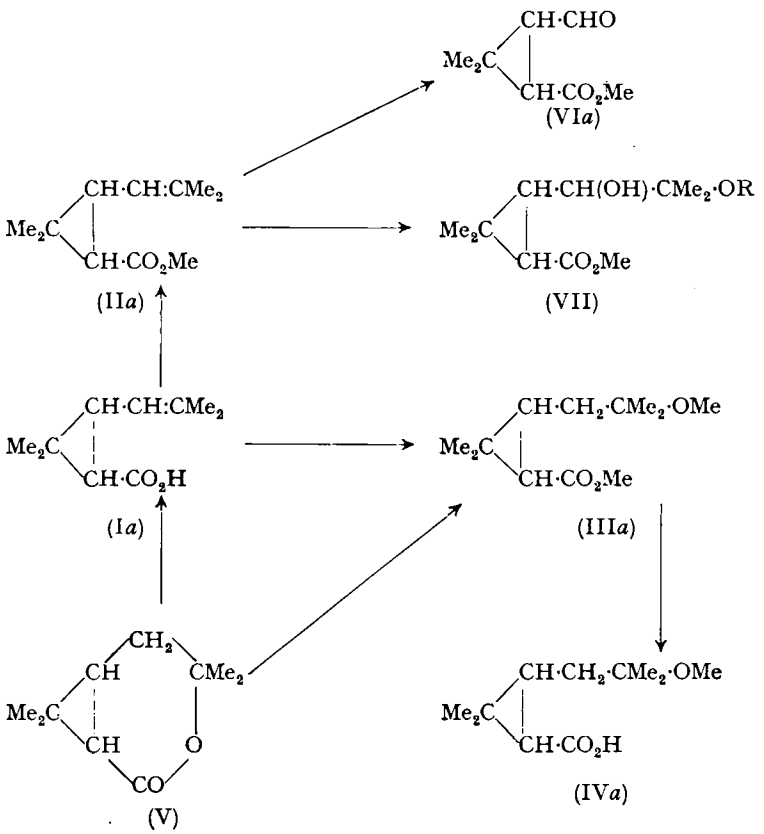
With the intention of using methyl (±)-*cis*- and (±)-*trans*-chrysanthemates as intermediates for the synthesis of stereoisomers of chrysanthemumdicarboxylic acid, it became necessary to

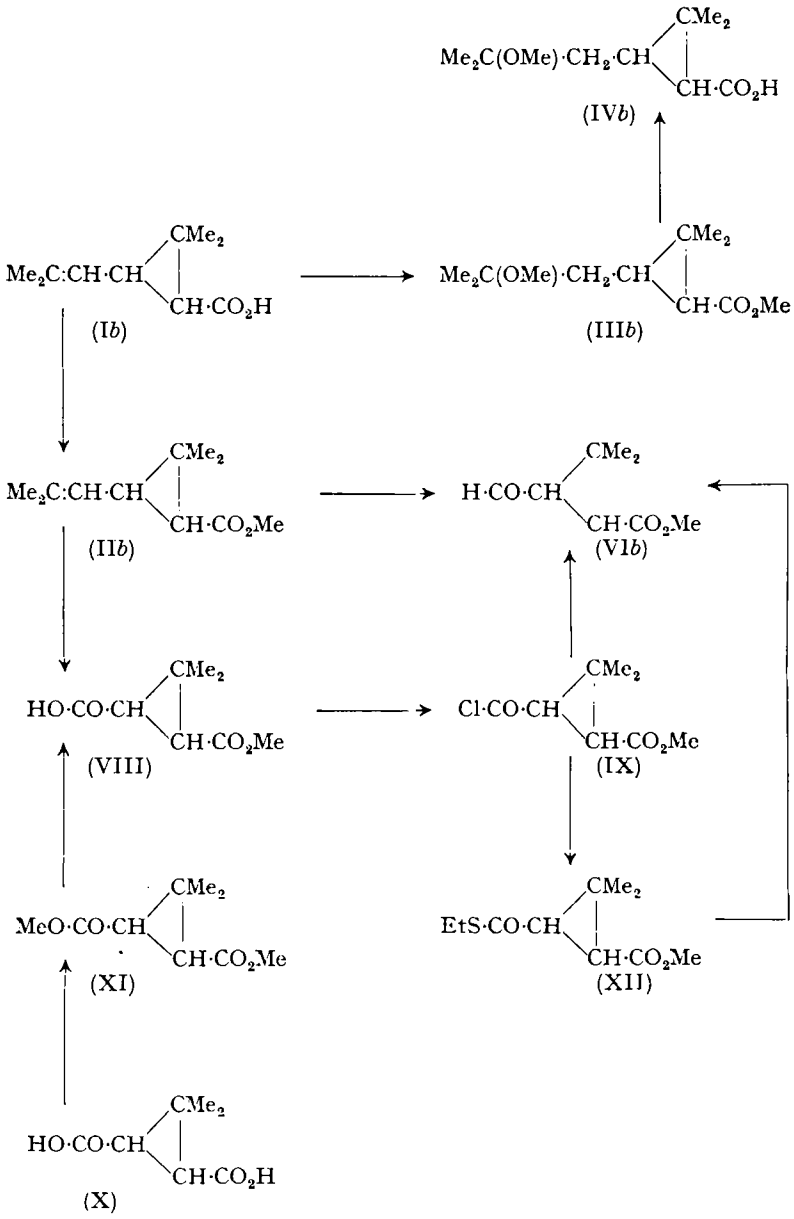
* Read before the Fine Chemicals Group on 16 February, 1951.

prepare these esters on a larger scale than hitherto—in fact, only the (±)-*trans*-ester had been described previously (Campbell & Harper, 1945)—and to study their oxidation.

Esterification of (±)-*cis*-chrysanthemic acid (I*a*) in approximately 2N-methanolic sulphuric acid gave a product which distilled over a 20° range and was evidently heterogeneous. Fractional distillation yielded the expected methyl ester, together with a higher-boiling ester which formed the major product. The identity of the lower-boiling ester as methyl (±)-*cis*-chrysanthemate (II*a*) was confirmed by analysis and by regeneration of (±)-*cis*-chrysanthemic acid on hydrolysis. Similar esterification of (±)-*trans*-chrysanthemic acid (I*b*) likewise yielded a heterogeneous product, separated by fractional distillation into the known methyl (±)-*trans*-chrysanthemate (II*b*), as the major product, and a higher-boiling ester. Although the refractive index of our preparation of methyl (±)-*trans*-chrysanthemate was not quite as high as that recorded by Campbell & Harper (1945) we believe our preparation to be the purer; its authenticity was confirmed by regeneration of (±)-*trans*-chrysanthemic acid on hydrolysis. As is common for *cis–trans*-isomers the *cis*-ester had the higher refractive index and density and hence showed a much smaller exaltation of molecular refraction than the *trans*-ester.

The higher-boiling esters were isomeric, their analyses agreeing with the empirical formula $C_{12}H_{22}O_3$, i.e. methyl chrysanthemate plus the elements of methanol. Hydrolysis gave isomeric crystalline acids, their analyses agreeing with the empirical formula $C_{11}H_{20}O_3$, i.e. chrysanthemic acid plus the elements of methanol. The acids were further characterized by the preparation of *p*-phenylphenacyl esters. These acids did not absorb bromine in carbon tetrachloride solution and were not reduced by hydrogen over Adams catalyst in glacial acetic acid. The saturated character of these unusual products of esterification precludes any structure that might arise from the fission of the *cyclo*propane ring and, taken in conjunction with their empirical formulae, it was evident that addition of methanol to the side-chain ethylenic bond of the chrysanthemic acids had occurred, as well as normal esterification of the carboxyl group. We would expect the stages of the former process to be akin to those of the hydration of the chrysanthemic acids discussed in Part III (Crombie, Harper & Thompson, 1951). Hence these esters should be methyl δ-methoxydihydrochrysanthemates (III*a* and III*b*) and the acids should be





δ-methoxydihydrochrysanthemic acids (IV*a* and IV*b*). Confirmation that the abnormal ester from (±)-*cis*-chrysanthemic acid is methyl (±)-*cis*-δ-methoxydihydrochrysanthemate (III*a*) has been obtained by Crombie *et al.* (1951), who have shown that crystalline (±)-*cis*-δ-methoxydihydrochrysanthemic acid (IV*a*) and its *p*-phenylphenacyl ester prepared by them from (±)-*cis*-dihydrochrysanthemo-δ-lactone (V) are identical with the methoxydihydrochrysanthemic acid and its *p*-phenylphenacyl ester obtained by us from the ester (III*a*). By analogy the abnormal ester from (±)-*trans*-chrysanthemic acid is methyl (±)-*trans*-δ-methoxydihydrochrysanthemate (III*b*).

Although the acid-catalysed hydration of unconjugated ethylenic bonds is a well established phenomenon a similar addition of alcohols has rarely been observed. Countless esterifications of olefinic acids have been recorded without comment in the literature. However, the addition of methanol to *iso*butene (Edlund & Evans, 1933) and to *iso*pentene (Reychler, 1907) to give *tert.*-ethers by heating at or below 95° C. with methanolic sulphuric acid has been recorded;

while Triebs (1937) has shown that 1-methyl-, 1-ethyl-, and 1-*iso*propyl-*cyclo*hexene similarly give the 1-alkyl-1-methoxy*cyclo*hexane on refluxing with 15% (w/v) methanolic sulphuric acid. The formation of *tert.*-ethers in these cases clearly bears out the argument we have used. Hence normal esterification of the carboxyl group in the chrysanthemic acids is accompanied, in part, by acid-catalysed addition of methanol to the *iso*butenyl group. However, this does not account for the much larger proportion of methoxy-ester formed from the (±)-*cis*-acid. We suggest that with this acid (I*a*) part is lactonized to (±)-*cis*-dihydrochrysanthemo-δ-lactone (V), which Crombie *et al.* (1951) have shown readily undergoes methanolysis to the methoxy-ester (III*a*).

With a view to preparing methyl (±)-*cis*- and (±)-*trans*-3-formyl-2 : 2-dimethyl*cyclo*propane-1-carboxylates (VI*a* and VI*b*, respectively) the oxidative fission of the side-chain of the methyl chrysanthemates was investigated. Ozonization appeared feasible provided that, on decomposition of the ozonides, oxidation to the methyl hydrogen caronates could be prevented (cf. Campbell & Harper, 1945). Of the methods for decomposing ozonides that of Fischer, Düll & Ertel (1932) using catalytic hydrogenolysis appeared most suitable.

The calculated quantity of ozonized oxygen was passed into a solution of the methyl chrysanthemate in ethyl acetate maintained at 0° C. The ozonized solution was then added to a suspension of pre-reduced palladium on calcium carbonate catalyst in ethyl acetate and hydrogenolysis was continued until absorption ceased. With methyl (±)-*cis*-chrysanthemate (II*a*) the uptake of hydrogen was only 10% of theoretical and was not raised above 15% by using up to 100% excess ozone. Nevertheless, on distillation small quantities of the desired *cis*-aldehydo-ester (VI*a*) were obtained as a volatile solid that crystallized in the side-arm of the distilling flask, but the yield did not exceed 7%. It was characterized as its semicarbazone and its 2 : 4-dinitrophenylhydrazone to facilitate future identification. Similar ozonization of methyl (±)-*trans*-chrysanthemate (II*b*) resulted in rather larger uptakes of hydrogen (35–40% theoretical), again not significantly increased by using excess of ozone, but only low yields of the *trans*-aldehydo-ester (VI*b*) were obtained on distillation, as a low-melting, highly-soluble, volatile solid. Because of this ephemeral behaviour it was, like the *cis*-isomer, characterized as its *p*-nitrophenylhydrazone, 2 : 4-dinitrophenylhydrazone, and dimedon derivative. The low yield of *trans*-aldehydo-ester was not due to a rearrangement of the ozonide into the carboxylic acid, of the type encountered by Fischer *et al.* (1932), for extraction of the hydrogenated solution with alkali gave less than 10% of methyl hydrogen (±)-*trans*-caronate (VIII). Further variation of the experimental conditions led to the discovery that ozonolysis of methyl (±)-*trans*-chrysanthemate at − 78° C. led to a subsequent hydrogen uptake of 60% of theoretical and a 30% yield of *trans*-aldehydo-ester. A similar ozonization of the *cis*-ester (by Mr. R. A. Thompson), however, did not result in an increased uptake or yield of *cis*-aldehydo-ester.

Although the yields of aldehydo-esters obtained by ozonization were so poor as to preclude further synthetical work, other methods of oxidative fission of the methyl chrysanthemates proved even less successful. Successive treatment of methyl (±)-*cis*-chrysanthemate with *tert.*-butyl hydroperoxide in *tert.*-butanol and lead tetra-acetate in acetic acid gave no aldehydic product. Performic acid, however, reacted exothermically with this ester to give a formoxy-hydroxy-ester (probably VII, R = CHO), from which the formyl group was removed by boiling water. However, the crude glycol-ester (probably VII, R = H) gave no aldehydic product with lead tetra-acetate.

In a further effort to make methyl (±)-*trans*-3-formyl-2 : 2-dimethyl*cyclo*propane-1-carboxylate (VI*b*) accessible attention was directed to methods not requiring (±)-*trans*-chrysanthemic acid as a starting point. For such a purpose (±)-*trans*-3-carbomethoxy-2 : 2-dimethyl*cyclo*propane-1-carbonyl chloride (IX) appeared suitable, for Rosenmund reduction should lead directly to the *trans*-aldehydo-ester, or indirectly by Raney-nickel hydrogenolysis of the derived ethyl (±)-*trans*-3-carbomethoxy-2 : 2-dimethyl*cyclo*propane-1-carbothiolate (XII). These methods require as an intermediate methyl hydrogen (±)-*trans*-caronate (VIII) which previously has been prepared only by degradation of (±)-*trans*-chrysanthemic acid (Campbell & Harper, 1945). Although half-esters of dibasic esters are generally prepared from the acid anhydride, this is not possible with (±)-*trans*-caronic acid (X). However, we find that hydrolysis of methyl (±)-*trans*-caronate (XI) at room temperature with half an equivalent of ethanolic potassium hydroxide and separation of the acidic product gives a good yield of pure methyl hydrogen (±)-*trans*-caronate, readily isolated by virtue of its sparing solubility and high melting point. This half-ester (VIII) was converted into its acid chloride (IX) in nearly quantitative yield. In the presence of the usual catalyst poisons Rosenmund reduction of this acid chloride was very slow and incomplete, no aldehydo-ester being formed when using thiourea and only a trace when using the ' quinoline poison.' In the absence of a catalyst

poison, reduction was quicker but still incomplete. Distillation gave a product evidently containing some *trans*-aldehydo-ester (VI*b*), although this did not crystallize out, for treatment with 2 : 4-dinitrophenylhydrazine reagent and repeated crystallization of the derivative gave a 2 : 4-dinitrophenylhydrazone identical with that prepared above by the ozonization route. This method was clearly less satisfactory than ozonization and attention was turned to Raney-nickel hydrogenolysis.

Treatment of the acid chloride (IX) with ethanethiol gave the thiol-ester (XII) in good yield. Sulphur was split out when this ester was refluxed with Raney nickel in aqueous ethanol, but the product distilled over a wide range. Solid *trans*-aldehydo-ester sublimed out of the lower-boiling fractions, one of which set semi-solid. The higher-boiling fraction, although liquid, also yielded the *trans*-aldehydo-ester 2 : 4-dinitrophenylhydrazone with Brady reagent. This suggested that it contained the hemiacetal of the *trans*-aldehydo-ester, a supposition that was supported by the combustion data. Although the yield was not high Raney-nickel hydrogenolysis of the thiol-ester (XII) provides a feasible route to the *trans*-aldehydo-ester (VI*b*) from (±)-*trans*-caronic acid as the starting point.

Experimental

Esterification of (±)-cis-*chrysanthemic acid.*—(±)-*cis*-Chrysanthemic acid (70 g.) (Harper, Reed & Thompson, 1951) was dissolved in methanol (350 ml.), concentrated sulphuric acid (17·5 ml.) added, and the mixture refluxed for 4 hours. Half the methanol was then distilled off, water was added to the residue and the ester taken up in ether. The extract was washed with water, then with sodium hydrogen carbonate solution, and again with water, dried over calcium chloride and then distilled to give the mixed esters (67 g.) : (i) b.p. 86–90° c./8 mm. (21·7 g.), (ii) b.p. 90–97° c./8 mm. (15·1 g.), and (iii) b.p. 98–105° c./8 mm. (30·5 g.). Repeated fractional distillation then gave *methyl* (±)-cis-*chrysanthemate*, b.p. 82–83° c./7 mm., n_D^{25} 1·4624, d_4^{25} 0·9417, $[R_L]_D$ 53·25 (Calc. for $C_{11}H_{18}O_2$: 51·99) (Found : C, 71·8 ; H, 9·8. $C_{11}H_{18}O_2$ requires C, 72·5 ; H, 9·95%), and *methyl* (±)-cis-*δ-methoxydihydrochrysanthemate*, b.p. 97–98° c./7 mm., n_D^{25} 1·4490, d_4^{25} 0·9653, $[R_L]_D$ 59·54 (Calc. for $C_{12}H_{22}O_3$: 58·71) (Found : C, 68·0, 67·8 ; H, 10·3, 10·1. $C_{12}H_{22}O_3$ requires C, 67·3 ; H, 10·3%).

Methyl (±)-*cis*-chrysanthemate (1·0 g.) was hydrolysed by refluxing in ethanol (10 ml.) with potassium hydroxide (0·4 g.) for 30 minutes. Acidification and extraction yielded (±)-*cis*-chrysanthemic acid (0·51 g.), which after crystallization from ethyl acetate had m.p. 113° c.

Methyl (±)-*cis*-*δ*-methoxydihydrochrysanthemate (6·0 g.) was hydrolysed by refluxing in ethanol (30 ml.) with potassium hydroxide (3·0 g.) for 1 hour. Half of the ethanol was then distilled off, and the residue was cooled and acidified with dilute nitric acid. An oil separated which was taken up in ether, dried over calcium chloride, and the ether was distilled off to give the acid as an oil which slowly solidified. (±)-*cis-δ-Methoxydihydrochrysanthemic acid* was very soluble in the usual solvents but crystallized from ethyl acetate–light petroleum (b.p. 60–80° c.) as cubes, m.p. 89° c. (Found : C, 66·2, 66·3 ; H, 10·0, 10·0 ; OMe, 13·5% ; equiv. wt. 200·4. $C_{11}H_{20}O_3$ requires C, 66·0 ; H, 10·0 ; OMe, 15·5% ; equiv. wt., 200·3). The p-*phenylphenacyl* ester crystallized from light petroleum (b.p. 40–60° c.) in plates, m.p. 75° c. (Found : C, 76·2 ; H, 7·5. $C_{25}H_{30}O_4$ requires C, 76·1 ; H, 7·7%). The *p*-nitrobenzyl ester was also prepared but could not be obtained solid.

Esterification of (±)-trans-*chrysanthemic acid.*—(±)-*trans*-Chrysanthemic acid (60 g.) (Harper *et al.*, 1951) was esterified in 5% (v/v) methanolic sulphuric acid (200 ml.), by the same procedure as for the (±)-*cis*-acid, to give the mixed esters (63 g.) : (i) b.p. 85–95° c./9 mm. (52·0 g.), (ii) b.p. 95–105° c./9 mm.(7·1 g.), and (iii) b.p. 105–115° c./9 mm. (4·0 g.). Repeated fractional distillation then gave methyl (±)-*trans*-chrysanthemate, b.p. 85° c./8 mm., n_D^{25} 1·4595, d_4^{25} 0·9270, $[R_L]_D$ 53·80 (Calc. for $C_{11}H_{18}O_2$: 51·99), and *methyl* (±)-trans-*δ-methoxydihydrochrysanthemate*, b.p. 111–112° c./12 mm., n_D^{25} 1·4455 (Found : C, 67·5, 67·5 ; H, 10·3, 10·3. $C_{12}H_{22}O_3$ requires C, 67·3 ; H, 10·3%). Campbell & Harper (1945) recorded n_D^{25} 1·4614, d_4^{25} 0·9274, $[R_L]_D$ 53·97 for methyl (±)-*trans*-chrysanthemate.

A similar esterification of (±)-*trans*-chrysanthemic acid (38 g.) in 2·5% (v/v) methanolic sulphuric acid (200 ml.) gave the mixed esters (38·7 g.) : (i) b.p. 95–100° c./12 mm. (31·8 g.), (ii) b.p. 100–105° c./12 mm. (3·1 g.), and (iii) b.p. 105–120° c./12 mm. (3·8 g.).

Methyl (±)-*trans*-chrysanthemate (1·0 g.) was hydrolysed by the same procedure as for the (±)-*cis*-ester, to (±)-*trans*-chrysanthemic acid (0·48 g.), which after crystallization from ethyl acetate had m.p. 54° c.

Methyl (±)-*trans*-*δ*-methoxydihydrochrysanthemate (5·0 g.) was hydrolysed, by the same procedure as for the (±)-*cis*-ester, to (±)-trans-*δ-methoxydihydrochrysanthemic acid*, which was

obtained solid only with difficulty and was even more soluble than the *cis*-isomer, but crystallized from ethyl acetate as needles, m.p. 44° c. (Found : C, 66·0 ; H, 9·5 ; OMe, 11·5% ; equiv. wt., 200·5. $C_{11}H_{20}O_3$ requires C, 66·0 ; H, 10·0 ; OMe, 15·5% ; equiv. wt., 200·3). The p-*phenylphenacyl* ester crystallized from ethanol–water in plates, m.p. 70° c. (Found : C, 75·7 ; H, 7·7. $C_{25}H_{30}O_4$ requires C, 76·1 ; H, 7·7%). The *p*-nitrobenzyl ester was also prepared but could not be obtained solid.

The infra-red absorption spectra of methyl (±)-*cis*- and (±)-*trans*-chrysanthemate in the region 6·5–14·0 μ. were very similar, except that the spectrum of the *cis*-isomer showed strong absorption at 12·7 μ., also present in the spectrum of methyl (±)-*cis*-δ-methoxydihydrochrysanthemate, which was absent from the spectrum of methyl (±)-*trans*-chrysanthemate.

Ozonization of methyl (±)-cis-*chrysanthemate.*—Of several experiments the following is typical : Methyl (±)-*cis*-chrysanthemate (4·55 g.) dissolved in dry ethyl acetate (100 ml.) was maintained at 0° c. and treated with ozonized oxygen, of which the ozone content had been checked before the experiment, until a 50% excess was passed in. Meanwhile a 5% palladium on calcium carbonate catalyst (0·5 g.) was reduced under ethyl acetate (50 ml.) and then the ozonized solution was added. Reduction was effected at room temperature during 12 hours, when 102 ml. hydrogen (19° c., 762 mm.) was absorbed. The solvent was distilled from the catalyst-freed solution, with the use of a column, and the residue was distilled at 10 mm. until the *cis*-aldehydo-ester (0·25 g.) collected in the side-arm. *Methyl* (±)-cis-3-*formyl*-2 : 2-*dimethyl*-cyclo*propane*-1-*carboxylate* was converted directly into its *semicarbazone*, which formed prisms sparingly soluble in ethyl acetate, m.p. 197° c. (Found : C, 50·3 ; H, 6·8. $C_9H_{15}O_3N_3$ requires C, 50·7 ; H, 6·9%), and into its 2 : 4-*dinitrophenylhydrazone*, which formed yellow laths from ethanol, m.p. 148° c. (Found : C, 50·1 ; H, 5·0 ; N, 17·0. $C_{14}H_{16}O_6N_4$ requires C, 50·0 ; H, 4·8 ; N, 16·7%).

Ozonization of methyl (±)-trans-*chrysanthemate.*—By the procedure described above methyl (±)-*trans*-chrysanthemate (5·0 g.) absorbed 387 ml. hydrogen (19° c., 760 mm.) after ozonization at − 78° and gave 1·3 g. *trans*-aldehydo-ester. *Methyl* (±)-trans-3-*formyl*-2 : 2-*dimethyl*cyclo*propane*-1-*carboxylate* was very soluble but on crystallization from ethyl acetate at −40° c. had m.p. 84–86° c. (Found : C, 62·0 ; H, 7·2. $C_8H_{12}O_3$ requires C, 61·5 ; H, 7·6%). The p-*nitrophenylhydrazone* crystallized as yellow needles from aqueous methanol, m.p. 158° c. (Found : C, 57·8 ; H, 5·8. $C_{14}H_{17}O_4N_3$ requires C, 57·7 ; H, 5·9%) ; the 2 : 4-*dinitrophenylhydrazone* crystallized as orange plates from ethanol, m.p. 151° c. (Found : C, 49·9 ; H, 4·7 ; N, 16·8. $C_{14}H_{16}O_6N_4$ requires C, 50·0 ; H, 4·8 ; N, 16·7%), and the *dimedon* derivative crystallized as irregular prisms from aqueous methanol, m.p. 152° c. (Found : C, 68·5 ; H, 8·1. $C_{24}H_{34}O_6$ requires C, 68·9 ; H, 8·2%).

Action of performic acid on methyl (±)-cis-*chrysanthemate.*—Methyl (±)-*cis*-chrysanthemate (4·53 g.) was added to a mixture of 28% hydrogen peroxide (3·12 g.) and 98% formic acid (15 ml.), when the temperature rose to 40° c. After 2 hours water was added, the product taken up in ether, washed with sodium hydrogen carbonate, dried over calcium chloride and distilled to give *methyl* (±)-cis-δ-*formoxy*-γ-*hydroxydihydrochrysanthemate* (3·5 g.), b.p. 79° c./0·2 mm. (Found : C, 59·4 ; H, 8·4. $C_{12}H_{20}O_5$ requires C, 59·0 ; H, 8·2%).

Methyl hydrogen (±)-trans-*caronate.*—A mixture of (±)-*trans*-caronic acid (37 g.), concentrated sulphuric acid (5 ml.), and methanol (250 ml.) was refluxed for 2 hours and then part of the methanol distilled off. The residue was diluted with water and the product taken up in ether. This solution was extracted with sodium hydrogen carbonate, dried over magnesium sulphate, and distilled to give methyl (±)-*trans*-caronate (37 g.), b.p. 103–105° c./13 mm. (in another preparation, b.p. 106–107° c./15 mm.). The b.p. (93° c./25 mm.) of methyl (−)-*trans*-caronate recorded by Staudinger & Ruzicka (1924) would appear to be in error. Acidification of the sodium hydrogen carbonate extract gave methyl hydrogen (±)-*trans*-caronate (1·5 g.), m.p. 103° c. (cf. Campbell & Harper, 1945).

Methyl (±)-*trans*-caronate (37 g.) was added to a cold solution of potassium hydroxide (11·2 g.) in methanol (90 ml.) and set aside at room temperature overnight. Part of the methanol was distilled off, the residue diluted with water, and unhydrolysed ester taken up in ether. Acidification of the aqueous layer to methyl orange with concentrated hydrochloric acid gave the half-ester as an oil which crystallized on seeding. The partial hydrolysis was repeated on the unhydrolysed ester, to give finally 25·6 g. methyl hydrogen (±)-*trans*-caronate, m.p. 103° c. after crystallization from light petroleum (b.p. 60–80° c.).

(±)-trans-3-*Carbomethoxy*-2 : 2-*dimethyl*cyclo*propane*-1-*carbonyl chloride.*—Methyl hydrogen (±)-*trans*-caronate (10·0 g.) was warmed with thionyl chloride (8 ml.) in light petroleum (50 ml., b.p. 60–80° c.) until gas evolution ceased. Distillation then gave the acid chloride (10·7 g., 97%), b.p. 91–93° c./12 mm.

Rosenmund reduction of the acid chloride.—By the procedure of *Org. Synth.* (**21**, 84) the acid chloride (8·3 g.) was reduced by a stream of hydrogen in boiling xylene (25 ml., distilled from sodium) containing 5% palladium on barium sulphate catalyst (1·0 g.). After 8 hours no further hydrochloric acid was evolved. The xylene was distilled from the catalyst-freed solution through a column and the residue distilled to give crude (±)-*trans*-aldehydo-ester (3·5 g.), b.p. 90–120° C./10 mm. The 2 : 4-dinitrophenylhydrazone, after repeated crystallization from ethanol, formed orange plates, m.p. 150° C., not depressed on admixture with the derivative described above (Found: C, 50·35; H, 4·85. Calc. for $C_{14}H_{16}O_8N_4$: C, 50·0; H, 4·8%). The use of the ' quinoline poison ' or of thiourea gave less satisfactory results.

Ethyl (±)-trans-3-*carbomethoxy*-2 : 2-*dimethyl*cyclo*propane*-1-*carbothiolate.*—The undistilled acid chloride from methyl hydrogen (±)-*trans*-caronate (10·0 g.), dissolved in benzene (25 ml.) and pyridine (5 ml.), was cooled in ice and treated with ethyl mercaptan (7·5 ml.). Next day water was added and the benzene layer washed with aqueous sulphuric acid and then with sodium hydrogen carbonate. Fractional distillation then gave *ethyl* (±)-trans-3-*carbomethoxy*-2 : 2-*dimethyl*cyclo*propane*-1-*carbothiolate* (8·4 g., 78%), b.p. 137–138° C./18 mm. (Found: C, 55·5; H, 7·4. $C_{10}H_{16}O_3S$ requires C, 55·5; H, 7·45%).

Raney-nickel hydrogenolysis of the thiol-ester.—The thiol-ester (8·4 g.) was refluxed in a water (25 ml.)–ethanol (50 ml.) mixture containing an ethanolic suspension of Raney nickel (25 ml., *ca.* 10 g.; this proved insufficient and about twice this quantity would have been better) during 5 hours. The alcohol was distilled from the filtered solution, through a column, the product was taken up in ether, dried over magnesium sulphate, and then distilled at 17 mm. to give the fractions: (i) b.p. 105–115° C. (0·70 g.), (ii) b.p. 115–120° C. (0·93 g.) (Found: C, 58·9; H, 7·5. Calc. for $C_8H_{10}O_3$; C, 61·5; H, 7%), (iii) b.p. 120–130° C. (1·05 g.) (Found: C, 58·3; H, 8·25. $C_{10}H_{18}O_4$ requires C, 58·8; H, 8·8%), (iv) b.p. 130–136° C. (3.13 g.). Traces of solid (±)-*trans*-aldehydo-ester sublimed out of fractions (ii) and (iii). Fractions (i)–(iii) gave a 2 : 4-dinitrophenylhydrazone, which after crystallization from methanol formed orange plates, m.p. 150° C. with prior softening. Fraction (iv) was unchanged thiol-ester, hence was retreated with Raney-nickel suspension (20 ml.) in a water (20 ml.)–ethanol (40 ml.) mixture as above. The product was distilled at 17 mm. to give the fractions: (v) b.p. 108–120° C. (0·43 g.) and (vi) b.p. 120–127° C. (0·87 g.). (±)-*trans*-Aldehydo-ester crystallized out from fraction (v).

Microanalyses are by Drs. Weiler & Strauss, Oxford. The infra-red absorption spectra were recorded with a Grubb Parsons spectrometer using the pure liquids in cells of 20–50-μ. thickness.

Acknowledgments

One of us (H. W. B. R.) gratefully acknowledges a maintenance grant from the Department of Scientific and Industrial Research and a grant from the Research Fund of the Chemical Society which has defrayed part of the expenses of this investigation.

King's College (University of London)
Strand, W.C.2

Received 20 April, 1951

References

Campbell, I. G. M. & Harper, S. H. (1945). *J. chem. Soc.* 283.

Crombie, L., Harper, S. H. & Thompson, R. A. (1951). *J. Sci. Food Agric.* **2**, 421.

Edlund, K. R. & Evans, T. W. (1933). B.P. 393,753; also U.S.P. 1,968,600 (1934).

Fischer, F. G., Düll, H. & Ertel, L. (1932). *Ber. dtsch. chem. Ges.* **65**, 1467.

Harper, S. H., Reed, H. W. B. & Thompson, R. A. (1951). *J. Sci. Food Agric.* **2**, 94.

Reychler, A. (1907). *Bull. Soc. chim. Belg.* **21**, 71.

Staudinger, H. & Ruzicka, L. (1924). *Helv. chim. Acta* **7**, 201.

Triebs, W. (1937). *Ber. dtsch. chem. Ges.* **70**, 589.