A Two-stage Synthesis of (+)-*cis*-Homocaronic Acid from (+)-Car-3-ene

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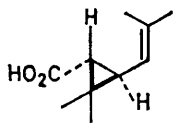
Summary Ozonolysis of (+)-4α-acetoxymethylcar-2-ene and of (+)-4α-acetylcar-2-ene and reaction of the products with alkaline hydrogen peroxide yields (+)-*cis*-homocaronic acid and (+)-*cis*-2,2-dimethyl-3-(3-oxobutyl)-cyclopropane-1-carboxylic acid.

THE biologically active (+)-*trans*-chrysanthemic acid, whose absolute configuration is as in (**1**)[1,2] is obtainable[3] from its (−)-*cis*-isomer (**2**), which, in turn, is formed[3] from (+)-*cis*-homocaronic acid (**3**; R = H).[2] (+)-Car-2-ene (**4**; R = H) would be an attractive starting point for the synthesis of (**3**; R = H) if it were more readily available. Its isomer, (+)-car-3-ene (**5**) is far more abundant in nature and the two isomers can be equilibrated,[4,5] but their separation is tedious. However, two derivatives of (+)-car-2-ene, namely (+)-4α-acetoxymethylcar-2-ene (**4**; R = α-CH_2-OAc)[6,7] and (+)-4α-acetylcar-2-ene (**4**; R = α-Ac),[7] both readily obtainable in high yields from (+)-car-3-ene (**5**), seemed to be useful starting materials for the synthesis of (**3**; R = H).

Each compound, (**4**; R = α-CH_2OAc) and (**4**; R = α-Ac), was ozonised at −60° in methanol. Hydrogen peroxide (30%) was added, the mixture was refluxed for 1·5 h, cooled to 0°, NaOH (33%) was slowly added, the final concentration of peroxide and alkali being *ca.* 7%, and the mixture was stirred overnight. The product was treated with diazomethane giving a mixture containing dimethyl (+)-*cis*-homocaronate (**3**; R = Me) and the (+)-*cis*-cyclopropane-carboxylate (**6**; $R^1 = R^2 = H$; R^3 = Me). The yields (by g.l.c.) of diester and keto-ester in the mixture from (**4**; R = CH_2OAc) were 75 and 19% respectively,; from (**4**; R = Ac) yields were less predictable, the best being 32·6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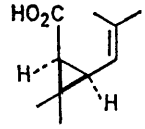
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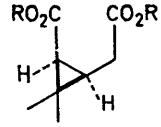
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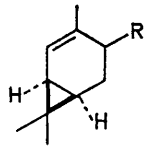
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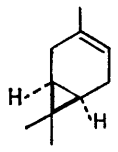
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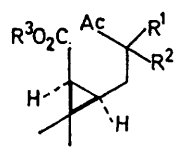
(6)

and 56·2%, in different experiments. The mixture was resolved by chromatography on silica in light petroleum–ether. The diester (**3**; R = Me),† eluted first, had b.p. 68° at 0·4 mmHg, $[\alpha]_D^{20}$ +42·8°, n_D^{20} 1·4473,[3] *m/e* 200 (M^+). In the presence of tris(dipivaloylmethanato)europium(III), the cyclopropyl proton n.m.r. multiplet [τ (60 MHz) 8·53; 2H] was resolved revealing a doublet (J 8·5 Hz) for the singly coupled cyclopropyl proton, in agreement with a *cis*-substituted cyclopropane.[8] The keto-ester (**6**; $R^1 = R^2 = H$; R^3 = Me),† further purified by preparative g.l.c., had $[\alpha]_D^{20}$ +28·1°, n_D^{20} 1·4542, *m/e* 198 (M^+), and was identical with a specimen prepared from (+)-car-2-ene (**4**; R = H).

The mechanism of formation of (+)-*cis*-homocaronic acid (**3**; R = H) has still to be clarified. The keto-acid (**6**; $R^1 = R^2 = R^3 = H$) is not an intermediate since it is unchanged on heating with alkaline peroxide. We suggest that a peroxy-compound (**6**; $R^1 = CH_2OAc$ or Ac; $R^2 = O_2H$; $R^3 = H$) is formed which in alkali loses the side chain, CH_2OAc or Ac, and the resulting α-peroxy-ketone is degraded[9] to the acid (**3**; R = H).

Satisfactory analyses for the two esters were obtained.

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† Characterized by i.r. and n.m.r. spectroscopy.

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