

168. *The Caryophyllenes. Part IV.*

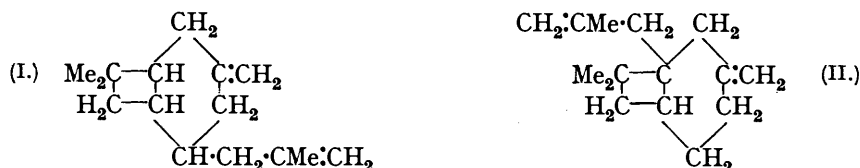
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IN Part I (J., 1934, 1806), where the isolation of caryophyllenic and norcaryophyllenic acids was first described, the assumption was made that these acids had the *cis*-configuration. This appeared to be justified (a) by the fact that norcaryophyllenic acid gave on digestion with acetyl chloride an oil only slowly soluble in sodium carbonate solution and (b) by analogy with pinic and norpinic acids. In view of synthetical experiments now in progress, it became necessary to confirm this configuration, more especially since it has been shown by Rydon (this vol., p. 593) and by Ruzicka, Zimmermann, and Huber (*Helv. Chim. Acta*, 1936, **19**, 343) that norcaryophyllenic acid, m. p. 126°, is the *trans*-acid, the *cis*-acid having m. p. 149—150°. Since we had been able to degrade caryophyllenic acid to norcaryophyllenic acid, m. p. 126° (J., 1935, 532), it appeared to us probable that the former acid also had the *trans*-configuration. This we have now been able to confirm. When *trans-d*-caryophyllenic acid, m. p. 80—81°, is heated with acetic anhydride at 220° under pressure, it yields the liquid *anhydride*, b. p. 157—158°/12 mm., of the *cis*-acid, from which the acid can be obtained by digestion with water. *cis-Caryophyllenic acid*, which is feebly levorotatory, has m. p. 77—78°, and thus differs little in melting point from the *trans*-acid, although a mixture of the two begins to soften at about 65°. They can, however, readily be distinguished by the preparation of the *dianilides*, that derived from the *trans*-acid being very sparingly soluble.

In our last communication (J., 1935, 1581) we drew attention to the important bearing which the keto-acid, C₁₁H₁₈O₃, first prepared by Semmler and Mayer (*Ber.*, 1911, **44**, 3662)

had on the structure of β - and γ -caryophyllenes. It was stated by these authors that this acid behaved abnormally with sodium hypobromite, being oxidised, not to homocaryophyllenic acid, $C_{10}H_{16}O_4$, but to caryophyllenic and *as*-dimethylsuccinic acids. We have now repeated this oxidation with a pure specimen of the keto-acid regenerated from the semicarbazone and in agreement with Ruzicka and Wind (*Helv. Chim. Acta*, 1931, **14**, 422) find the oxidation to proceed normally. Homocaryophyllenic acid, which is an oil, has been characterised by the preparation of the *dianilide*, m. p. 179—180°. This acid has become of increased interest, since Treibs (*Ber.*, 1936, **69**, 41) considers it to be formed also by the degradation of betulol.

We suggested (*loc. cit.*, p. 1582) that β - and γ -caryophyllenes differed in that the former contained an *isopropenyl* and the latter an *isopropylidene* group in the side chain. On this assumption it was anticipated that oxidation of γ -caryophyllene nitrosochloride would provide a convenient route to the above-mentioned keto-acid. Preliminary experiments, made in collaboration with Mr. W. G. Wainwright, B.Sc., have shown the main products of the ozonolysis to be neutral and they lead us to suggest that γ -caryophyllene may possibly be more correctly represented by either (I) or (II). If this should prove to be correct,



the keto-acid must originate from the "tautomeric" *isopropylidene* form of β -caryophyllene. It is hoped that experiments now in progress may enable us to elucidate this point.

EXPERIMENTAL.

cis-Caryophyllenic Acid.—*trans-d*-Caryophyllenic acid (10 g.) was heated with acetic anhydride (25 c.c.) at 220° for 6 hours; fractionation of the oil gave *caryophyllenic anhydride* (6 g.), b. p. 157—158°/12 mm. (Found: C, 64.6; H, 7.1. $C_9H_{12}O_3$ requires C, 64.3; H, 7.1%). After the anhydride had been boiled with water, slow evaporation of the solvent gave *cis*-caryophyllenic acid, m. p. 77—78°, in large glassy prisms; in chloroform (*c*, 3.645) $[\alpha]_{5461} - 7.4^\circ$ (Found: C, 57.9; H, 7.4. $C_9H_{14}O_4$ requires C, 58.1; H, 7.5%). The acid was more readily soluble in the ordinary organic solvents than the *trans*-acid and it crystallised from *cyclohexane* in long needles, m. p. 78°. In admixture with the *trans*-acid, softening occurred at 65°, but the mixture did not clear until 85—87°, well above the m. p.'s of the two constituents. Like the *trans*-acid, the *cis*-acid gave a sparingly soluble copper salt with copper acetate. The *dianilide* crystallised from dilute alcohol (50%) in long fine needles, m. p. 190° (Found: N, 8.2. $C_{21}H_{24}O_2N_2$ requires N, 8.3%). The *dianilide* of the *trans*-acid separated from *cyclohexanone* in plates, m. p. 282°, very sparingly soluble in alcohol and acetone (Found: N, 8.4%). The *di-p*-phenylphenacyl ester of the *trans*-acid crystallised from alcohol in balls of needles, m. p. 121—122°, with softening at 117° (Found: C, 77.8; H, 6.1. $C_{37}H_{34}O_6$ requires C, 77.4; H, 5.9%).

Homocaryophyllenic Acid.—The semicarbazone of the keto-acid (2.5 g.) was hydrolysed by heating on the water-bath with dilute sulphuric acid (10%) for 30 minutes. The keto-acid was extracted in ether, converted into the sodium salt, and treated ice-cold with an excess of sodium hypobromite for 1 hour; the bromoform was then removed by ether. Homocaryophyllenic acid was isolated, after acidification of the alkaline solution, as an oil (2 g.) (Found: *M*, 198. Calc.: *M*, 200). The *dianilide* was obtained solid by the slow evaporation of its solution in dilute acetone; it then crystallised from dilute alcohol (50%) in plates, m. p. 179—180° (Found: C, 75.0; H, 7.5; N, 8.0. $C_{22}H_{26}O_2N_2$ requires C, 75.4; H, 7.4; N, 8.0%). The diamide and the *di-p*-phenylphenacyl ester were prepared but could not be obtained crystalline.

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