[Contribution from the Department of Chemistry, Imperial College]

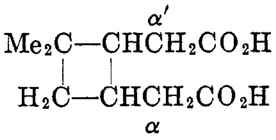
THE CONSTITUTION OF (+)-*trans*-CARYOPHYLLENIC ACID

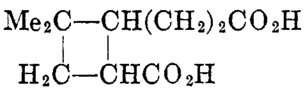
D. H. R. BARTON[1]

Received March 25, 1949

Oxidation of caryophyllene and various of its derivatives gives a mixture of (+)-*trans*-norcaryophyllenic acid and its homolog (+)-*trans*-caryophyllenic acid (1, 2, 3; compare 4, 5). The formula (I) for (+)-*trans*-norcaryophyllenic acid was deduced from degradational evidence by Ruzicka and Zimmermann (2) and by Ramage and Simonsen (6) and has been confirmed by Rydon's synthesis (7) of the (±)-*trans*- and (±)-*cis*-norcaryophyllenic acids and their resolution into optically active forms. Two formulas, (IIa) and (IIb), are possible for (+)-*trans*-caryophyllenic acid and it is generally considered that published evidence does not enable a distinction to be drawn between the two. It would appear, however, that this is not the case. Ruzicka, Bardhan, and Wind (8) showed that (+)-*trans*-caryophyllenic acid gave a tetramethylglycol (IIIa) or (IIIb) with the Grignard reagent, which on oxidation by chromic acid afforded $\alpha{:}\alpha{:}\alpha'{:}\alpha'$:-tetramethylglutaric acid (IV). The latter is not an expected oxidation product and its formation can best be explained by rearrangement of (IIIa) in the manner indicated. Since analogous rearrangements of (IIIb) *cannot* be devised to explain the reaction, the formula (IIa) is most probably correct for (+)-*trans*-caryophyllenic acid.

When caryophyllene is treated with maleic anhydride it gives an "adduct" which is undoubtedly formed by allylic substitution (2, 9). Vigorous oxidation of this "adduct" furnishes a mixture of homologous acids, among which have been identified (+)-*trans*-norcaryophyllenic acid (I), (+)-*trans*-caryophyllenic acid, (IIa) and (+)-*trans*-homocaryophyllenic acid (3). The latter acid must be represented by either (Va) or (Vb). Although a partial synthesis of (+)-*trans*-homocaryophyllenic acid was attempted by Ramage and Simonsen (10), their results were complicated by the possibility of racemization and no final conclusion as to its structure was reached. Now it is unlikely that oxidative attack on an acid of structure (Va) would proceed exclusively at the α rather than the α' position. This is true no matter whether the attack be radical or ionic in character. It would be anticipated, therefore, that oxidation of an acid of structure (Va) would give both (IIa) and (IIb), whereas degradation of the side chain of (Vb) could only give (+)-*trans*-caryophyllenic acid (IIa).


(Va)

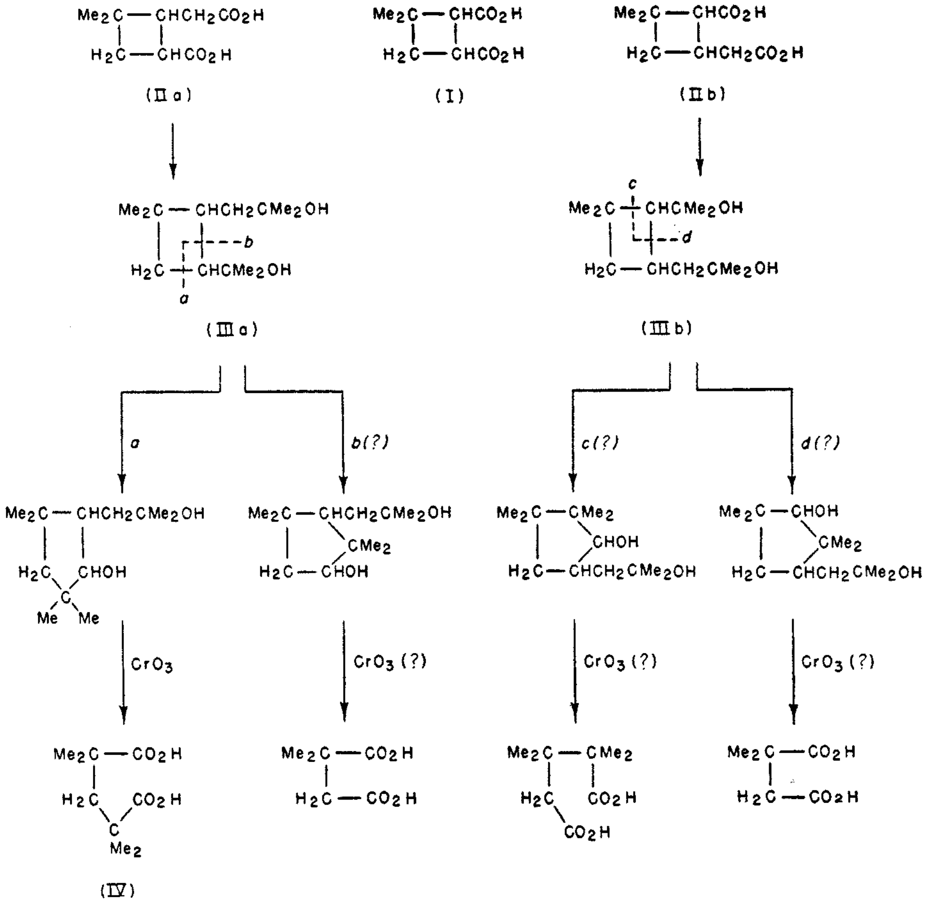

(Vb)

---

[1] Present address: Chemistry Department, Harvard University, Cambridge 38, Mass.

Since no indication has been found of the existence of (IIb) among the oxidation products of caryophyllene it seems probable that (+)-*trans*-homocaryophyllenic acid must be represented by (Vb) rather than (Va).

I am much indebted to Sir John Simonsen, F.R.S., for a valuable discussion on this and related ropics.



SUMMARY

Evidence bearing on the constitution of (+)-*trans*-caryophyllenic acid is critically discussed.

London S.W. 7, England

REFERENCES

(1) Evans, Ramage, and Simonsen, *J. Chem. Soc.*, 1806 (1934).
(2) Ruzicka and Zimmermann, *Helv. Chim. Acta*, **18**, 219 (1935).
(3) Ruzicka, Plattner, and Werner, *Helv. Chim. Acta*, **26**, 966 (1943).

(4) Semmler and Mayer, *Ber.*, **44,** 3657 (1911).
(5) Ruzicka, Bardhan, and Wind, *Helv. Chim. Acta*, **14,** 423 (1931).
(6) Ramage and Simonsen, *J. Chem. Soc.*, 532 (1935); 741 (1936).
(7) Rydon, *J. Chem. Soc.*, 593 (1936); 1340 (1937).
(8) Ruzicka, Bardhan, and Wind, *Helv. Chim. Acta*, **14,** 433 (1931).
(9) Ruzicka, Plattner, and Balla, *Helv. Chim. Acta*, **24,** 1219 (1941).
(10) Ramage and Simonsen, *J. Chem. Soc.*, 73 (1937).