174 Chemistry of Natural Products

Arbusov and Naumov^{*} have recently established by means of the **Electron Diffraction studies** that α -pinene exists predominantly in the *bridged half-chair type conformation* as given under:



BORANE [or CAMPHANE] GROUP

The 'borane group' is also referred to as the 'camphane group' because of the presence of the saturated bicyclic hydrocarbon (*viz.*, borane or camphane). Interestingly, it fails to occur in the *natural plant products*; and, therefore, need to be prepared synthetically right from 'camphor', that eventually constitutes and designates as the most important example of this *particular group/class of compounds*. Thus, we may have the following valid conversions:



That is, conversion of camphor to camphane via reduction-hydrolysis-dehydration and reduction.

Wolff-Kishner Reduction (or Huang-Minlon Modification):** It also provides an alternative means of preparing **camphane** from **camphor** as given under:



Thus, nitrogen gas (N_2) escapes from the reaction mixture to give camphane at the end.

NOTE: ' Camphane' is a saturated hydrocarbon. It is obtained as a solid substance having a sharp mp 156°C, and is found to be optically 'inactive'.

The most important member of the 'Borane Group' is the classical example of 'Camphor' which shall now be discussed as under:

^{*} Arbusov and Naumov : In : Banthorpe DV and Whittaker D, Chem Rev, 66 : 643-654, 1966.

^{**} Kishner N : J Russ Phys Chem Soc, 43 : 582,1911; Huang-Minlon, J Am Chem Soc 68 : 2487,1946

Terpenoids 181



Explanation: The various steps involved may be explained as under:

- 1. Acetoacetic ester on treatment with freshly prepared sodium ethoxide followed by methyl iodide loses 2 moles of methyl iodide to yield α, α -dimethyl acetoacetic ester.
- 2. The resulting product undergoes **Reformatsky Reaction** with ethyl-bromoacetate to produce an **organozonic derivative of** α -bromo ester.
- 3. Treatment of this product with an acid gives a *diethyl ester derivative*, which upon reaction with **phosphorus tribromide (PBr**₃) followed by KCN yields a **diethyl cyano ester derivative**.
- 4. Finally, this product on treatment with an alkali and then with an acid yields the *racemate* of **camphoronic acid (I).**

10. Structure of Camphoric Acid [C₁₀H₁₆O₄]

The structure of **camphoric acid** may be duly established by means of its elucidation as stated under:

- (a) Molecular Formula: Its molecular formula has been duly established to be $C_{10}H_{16}O_4$.
- (b) **Saturated Dicarboxylic Acid : Camphoric acid** essentially has a **gem-dimethyl moiety** and an altogether *separate methyl group*; therefore, it should have essentially **3-methyl groups**. Thus, one may express the formula of **camphoric acid** as:



which eventually leads to C_5H_{10} as its saturated parent hydrocarbon. Furthermore, the *molecular* formula C_5H_{10} relates to C_nH_{2n} which designates a saturated hydrocarbon, and thereby suggests that camphoric acid is a cyclopentane dicarboxylic acid.

(c) Oxidation of Camphoric Acid to Camphoronic Acid : The careful oxidation of camphoric acid to camphoronic acid may be expressed as under:



186 Chemistry of Natural Products

All the above scientific arguments lead to the fact that the following **structure (VII)** for **camphor**, which closely corresponds to the **structure (VI)** above should be the most *probable* and *correct structure*.

Actually, it was Bredt (1893) who duly proposed the following reactions to explain logically the intricate relationship amongst the following *three* compounds:



Bredt, later on, proposed judiciously the following structure (VIII) for **camphor**, that eventually explains all the foregoing arguments; however, he rejected **structure** (**VIII**) in favour of **structure** (**VIII**) for camphor.



Why is the proposed structure (VIII) for Camphor rejected? The simple concrete reason for the outright rejection of **Bredt' structure for camphor (VIII)** being supported by the fact that when camphor is distilled with iodine gives rise to the formation of **carvacrol (IX)**. Thus, the critical formation of **(IX)** may only be explained judiciously with the above structure of **camphor (VII)** and 'not' with **structure (VIII)**.





'isoborneol' when subjected to *dehydration reaction* usually gives 'camphene', which on oxidation yields 'camphor' as shown below:



18. Commercial Manufacture of Synthetic Camphor [or Borneol Camphor]

The large-scale (commercial) manufacture of purely synthetic camphor is largely obtained using α -*pinene* as the starting material (which is available mostly from the '*turpentine oil*'). In fact, a series of Wagner-Meerwein Rearrangement* (WMR) effectively come into play that cause an altogether complete change in the C-skeleton.

Following are the various sequential steps of reactions for the **commercial synthesis of camphor** as detailed under:



Explanation : These steps may be explained as under:

- 1. α -Pinene when treated with HCl at 10°C gives pinene hydrochloride (as an *intermediate*) which undergoes the first WMR to yield bornyl chloride.
- 2. The resulting product is treated with *sodium acetate* for the **second WMR** to occur and yields **camphene**, which with interaction of CH_3COOH/H_2SO_4 undergoes the **third WMR** to produce **isobornyl acetate**.
- 3. This product when treated with an **alkali**(**NaOH**) loses a mole of acetic acid (CH₃COOH) to give **isoborneol**, which upon reaction with *nitrobenzene* undergoes **oxidation** to yield **camphor**.

^{*} Wagner G : J Russ Phys Chem Soc., 31 : 690, 1899; Meerwein H : Ann, 405 : 129, 1914