

Chemical technology as a source of synthetic fragrance and flavor materials

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Dr. Dorsky joined Givaudan in 1951 as a chemist and has worked on research and development of aroma chemicals, antimicrobials, fragrances, flavors, and cosmetic ingredients. He has been responsible for all chemical research since 1971 and for research and chemical pilot plant and development since 1977.

In the early days of the fragrance and flavor industry, the important materials used in bulk were natural essential oils or relatively pure chemicals isolated or derived from these natural materials. As the industry grew, difficulties inherent in supplying natural products such as variable weather conditions, manipulation of markets by traders, and limited production capability caused problems and encouraged chemists to develop synthetic processes. The rapidly growing chemical industry made available a large number of cheap raw materials and practical technology for producing many important materials synthetically.

Terpenoids

Perhaps the most important example for our industry is the present-day, large-scale production of terpenoids and their derivatives such as methylheptenone, linalool and its esters, geraniol, citronellol, citronellal, hydroxycitronellal, citral, ionones, and methyl ionones. In addition, nerolidol, farnesol, phytol, and a host of formerly exotic materials are now readily available from chemical plants.

Today, the bulk of the chemicals mentioned above is produced synthetically. The essential oils which in past years were the only sources are now secondary or supplementary sources or are only used where their characteristic "natural" notes are desired. Citronella oil has been relegated to a supplementary source position for geraniol and citronellal and their derivatives, while rosewood oil and lemongrass oil remain commercial materials principally for their "natural" qualities.

The original impetus for the production of synthetic terpenoids came from the demand on the pharmaceutical industry for synthetic vitamin A and vitamin E. These products still consume at least half of the production. Both end-use industries benefit from the low manufacturing cost made possible by large-scale production.

Three routes to synthetic terpenoid chemicals are in commercial use today. For each there is a special "raison d'être" based on patents, technology, raw material supply, or market position. All of the processes are economically competitive. In fact, this segment of the industry is highly competitive as there are five large companies producing terpenoid chemicals. In addition, citronella oil is available as an alternative raw material for other potential suppliers.

Hoffmann-La Roche process

This process starts with acetone and acetylene as shown in figure 1. The first reaction product, methylbutynol (1), is converted to methylheptenone (2) by hydrogenation and reaction with methyl isopropenyl ether from acetone and methanol. Ethinylation yields dehydrolinalool (3), a key building block in this route. Hydrogenation of 3 and its esters affords linalool (4) and its esters. Citral (5) is obtained by catalytic rearrangement of 3. The ionones (7, 8, 9) can be made from citral by aldol condensation with acetone or methyl ethyl ketone followed by cyclization. Citral can also be reduced to geraniol, citronellal, and citronellol but usually there are more economical routes to these chemicals.

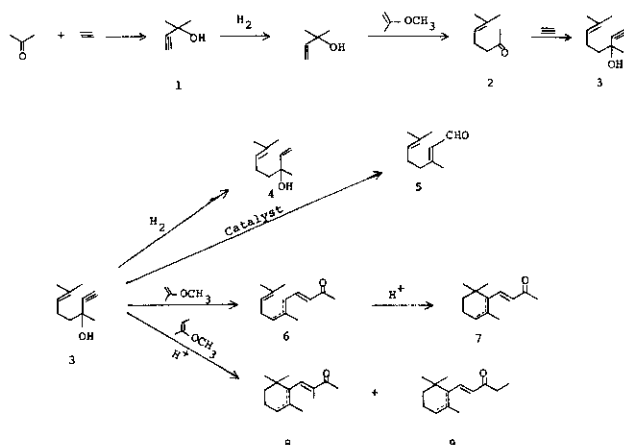


Figure 1

Hoffmann-LaRoche has a patented route to the ionones from dehydrolinalool via trans etherification with methyl vinyl ethers, rearrangement to the pseudo compounds, and finally, cyclization. From methyl isopropenyl ether, pseudoionones (6) and ionones (7) are obtained. Butenyl methyl ether, from methyl ethyl ketone and methanol, yields methylionones as the final product. This reaction can be directed to produce high purity α -isomethylionone (8), the isomer highly preferred by perfumers, or the mixture of normal and isomethylionones (8 and 9) which is obtained by conventional chemistry. Nerolidol and phytol, useful ingredients in fragrances, are derived from linalool. An alternate route to phytol starts with pseudoionone. Phytol is an essential intermediate for vitamin E. β -Ionone (7) is used in the production of vitamin A.

Turpentine, beta-Pinene, Myrcene

Turpentine, rich in beta-pinene, is the starting material for the second commercial route to the terpenoids.

beta-Pinene is a minor component (up to 30%) of turpentine from various sources. It is recovered by efficient fractionation which is required for separation from alpha-pinene, the main component. It is possible to isomerize alpha-pinene to a mixture containing about 5% beta-pinene and to recover beta-pinene from this mixture. This procedure is, however, expensive and is not used unless the supply of natural beta-pinene is insufficient to meet demand.

The chemistry by which beta-pinene is converted to the terpenoids is shown in figure 2. Pyrolysis of beta-pinene (10) in a hot-tube furnace produces myrcene (11) which is converted to geraniol (12) in three steps.

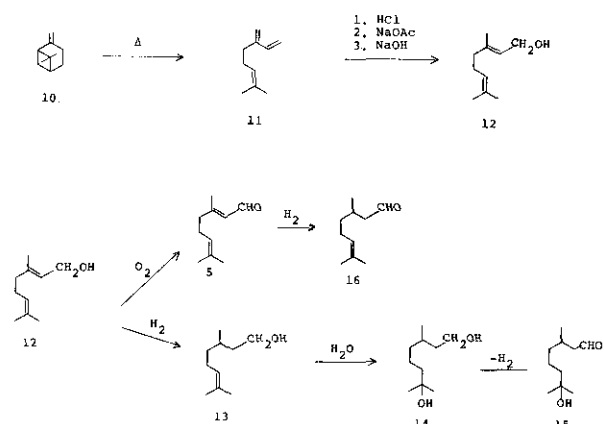


Figure 2

The first step involves addition of anhydrous HCl in the presence of a copper catalyst to form a mixture of chlorides. Heating with sodium acetate produces a mixture of acetates which on saponification with sodium hydroxide yields geraniol (12). It should be noted that synthetic geraniol of commerce is a mixture, usually 65/35,

of geraniol, the trans-isomer, and nerol, the cis isomer.

A small percentage of linalool is unavoidably produced along with geraniol in this process. By modifying reaction conditions and catalysts, the percentage of linalool can be increased substantially. However, it is difficult to make linalool suitable for perfumery by this process because of by-products which spoil the odor.

Geraniol is the key building block in this route just as dehydrolinalool is the key in the Hoffmann-LaRoche process. Oxidation of geraniol in the vapor phase, usually with purified oxygen, yields citral (5), which is used directly in flavors and fragrances or converted to ionones and methylionones. A substantial amount of citral made in this manner has been used for the manufacture of vitamin A and vitamin E. Citronellol (13) and citronellal (16) are made by selective hydrogenation of citral. Hydration of citronellol produces hydroxydihydrocitronellol (14) from which hydroxycitronellal (15) is made by catalytic dehydrogenation. Large amounts of citronellol and synthetic hydroxycitronellal have been manufactured by this route.*

Rhodia process

Isoprene and acetone are the basic raw materials for this process which is outlined in figure 3. Hydrogen chloride is added to isoprene (17) to produce prenyl chloride (18). Reaction with acetone in the presence of amine catalysts yields methylheptenone (2). As in the Hoffmann-La Roche process, dehydrolinalool (3) is made by ethinylation of methylheptenone. Hydrogenation of 3 produces linalool (4) and catalytic isomerization gives citral (5). The reaction of acetylenic and olefinic alcohols with vinyl ethers is covered by Hoffmann-La Roche patents and is not used by Rhodia. Citral is therefore the key building block in this route and can be converted to the ionones and hydroxycitronellal.

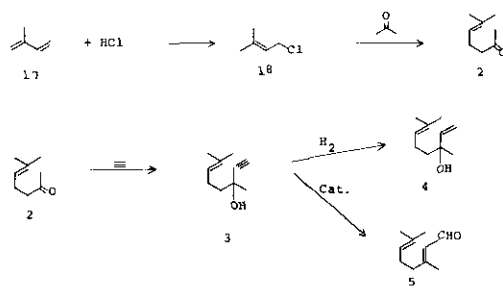


Figure 3

BASF process

The starting materials for this process are three basic petrochemicals: isobutylene, formal-

*Glidden, Union Camp, and Bush Boake Allen operate large plants for producing terpenoids from beta-pinene.

dehyde, and acetone. As shown in figure 4, the reaction of these materials yields a methylheptenone (19) with a terminal olefinic group. It is an isomer of the methylheptenone (2) from which the terpenoid chemicals are produced. It is possible to isomerize 19 to 2 and this opens the route to the desired aroma chemicals. Formaldehyde and acetone react in situ to form methyl vinyl ketone (20) which can also be produced separately and reacted with isobutylene.

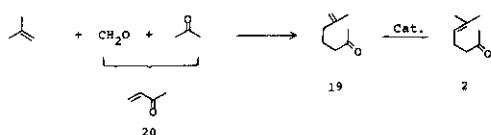


Figure 4

Phenylethyl alcohol

One of the most widely used fragrance materials is phenylethyl alcohol. It is a common base for rose fragrances but also is used extensively in many other applications because it blends so well.

The history of phenylethyl alcohol manufacture in the United States is another example of how changing chemical technology determined the manufacturing procedure for a fragrance chemical. In the early part of this century, phenylethyl alcohol was manufactured by the Bouveault-Blanc reduction of various phenylacetic acid esters with sodium. The basic raw material was readily available at low cost from benzyl chloride and sodium cyanide. Butyl phenylacetate worked particularly well. Subsequently, this process was replaced by the Friedel-Crafts reaction of benzene and ethylene oxide which is now the most important commercial process. The shift to the Friedel-Crafts process occurred only after ethylene oxide became commercially available at low cost. For a short time, commercial quantities of phenylethyl alcohol were produced via the Grignard reaction of phenyl magnesium chloride on ethylene oxides but this process could not compete with the improved Friedel-Crafts reaction.

More recently cheap styrene oxide has been investigated as a raw material for phenylethyl alcohol. Catalytic hydrogenation under controlled conditions yields high quality phenylethyl alcohol. Since other routes to phenylethyl alcohol are under study, it can be predicted that changing technology and raw materials supply will develop serious competition for the Friedel-Crafts process.

Many other examples could be cited but those discussed above serve to make the point that we are part of the dynamic chemical industry where technological obsolescence is built into each new development. The resultant competitive pressure will keep our segment of the industry young and vigorous.