

Esters



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In a recent article^a, I discussed the fundamentals of Schiff bases. In this issue, I would like to discuss the basics of esters. An organic ester is any compound of the formula $A-(C=O)-O-B$, where A and B may be any alkyl (methyl, ethyl, isoamyl, etc.), aryl (phenyl, naphthyl, etc.), or heterocyclic (maltyl, etc.) radical.

Special cases arise when A is hydrogen, in which case the ester is a formate; when A is $A-O-$, in which case the ester is a carbonate; and when A and B are connected, in which case the ester is a lactone. Other special cases occur when sulfur atoms replace one or both oxygen atoms of the ester group.

Esters comprise the largest and arguably the most important class of compounds used in flavors and fragrances. For example, nearly half of the 3,102 materials described in Stephen Arctander's monumental "Perfume and Flavor Chemicals" and 25 of the 60 materials listed in the new GRAS 20 can be classified as esters. Their importance probably comes from the wide range of pleasant, fruity and floral notes they possess.

An ester can be thought of as the reaction product of a carboxylic acid, $A-(C=O)-O-H$, and an alcohol, $B-O-H$, with concomitant formation of water. In fact, many esters can be and are made in this manner, called direct or Fischer esterification. Usually a catalytic amount of a mineral acid, such as sulfuric or phosphoric acid, or a sulfonic acid, such as toluenesulfonic or methanesulfonic acid, is used to speed the reaction; however, in esterifications with formic acid, it is strong enough to require no catalyst. The reaction is an equilibrium and is driven forward, that is toward ester plus water, by physical removal of the water. The removal is accomplished by boiling the mixture of reactants, whereupon some of the water is vaporized along with volatile reactants and/or ester; when the vapors are condensed, the water forms a separate phase. The non-aqueous portion of the condensate is returned to the reaction pot. The separation and return steps normally are affected continuously in a decanter. A solvent, such as toluene or cyclohexane, is often employed when the reaction mixture by itself would boil at a prohibitively high temperature (prohibitive because of an equipment limitation or because of decomposition/development of an off-odor). In addition, use of a solvent often aids in the separation of the aqueous phase in the decanter, especially in cases in which the acid or the

alcohol (or both) is low boiling and water-soluble. Alternatively, the esterification may be run under vacuum to lower the boiling point of the reaction mixture. Some reactants, for example, geraniol, are sensitive to acid and require an alternative catalyst. Tin catalysts are very mild, yet very efficient, but they must be used and disposed of with caution, as they also are very toxic to aquatic life.

One of the reactants is commonly used in excess, the faster and better to consume all of the other reactant. If the alcohol boils similarly to the ester, it is advantageous to employ excess acid to consume all of the alcohol; the excess acid may be removed by washing it out with a dilute aqueous base at a temperature low enough to avoid reacting with the ester. Conversely, if the acid boils similarly to the ester, it is advantageous to employ excess alcohol, and remove the excess by distillation at the end of the reaction. If both reactants boil similarly to the ester, they may be taken in stoichiometric quantities and reacted to (near) completion, or a different way to make the ester may be used. Direct esterification is usually the method of choice, because it employs the cheapest starting materials and is the most atom-efficient approach, that is, it gives the least waste.

But some esters cannot be made by direct esterification. Examples are esters of tertiary alcohols, such as dimethylbenzylcarbinol, and esters of aromatic alcohols, such as maltol. In these cases, the synthesis may be accomplished by using an acid anhydride in place of the acid. The anhydride reacts with the alcohol and the byproduct is the acid corresponding to the anhydride, instead of water. The byproduct acid may be removed by fractional distillation or by washing at low temperature with dilute aqueous base. No catalyst is needed, although heating is generally required for tertiary or phenolic alcohols. This process may be thought of as a chemical removal of water. It also may be employed in place of direct esterification—the advantages are faster reaction and milder conditions; the disadvantages are higher material costs and more waste.

Other methods of ester synthesis include the three species of transesterification: alcoholysis, wherein an ester containing the residue of one alcohol is reacted with a different alcohol; acidolysis, wherein an ester containing the residue of one acid is reacted with a different acid; and ester-ester interchange, wherein the alcohol and acid residues in two esters change partners. All three species are equilibrium reactions. Often, with a judicious choice of

^a"Schiff Bases", by Conrad Schmidt, *Perfumer & Flavorist*, January/February 2002, Page 32.

reactants, or of reaction conditions, the equilibrium may be driven to the product side. The catalyst is usually dispersed sodium metal, sodium methylate or potassium carbonate. Titanium and tin catalysts also have been used. Enzymes have been used more recently. Transesterification is less commonly employed than direct esterification in making flavor and fragrance materials. The largest scale industrial transesterification process is the condensation polymerization of ethylene glycol with dimethyl terephthalate to give poly (ethylene terephthalate), or polyester. The most important transesterification to the flavor and fragrance industry is the reaction of methanol with fats to give glycerine and fatty acid methyl esters (FAME). The FAME are fractionated and hydrogenated to give fatty alcohols. The fatty alcohols, ranging from about C6 (hexyl alcohol) to about C20 (arachidyl alcohol), are used in flavor and fragrance products as such, and as derived esters, especially acetates.

Any number of other chemistries may be used to make esters, but generally the methods employ expensive reagents and are not used in the flavor and fragrance industry.

An ester is named by substituting the “-ol” or “-anol” with “-yl” in the name of the imputed alcohol starting material and combining this name with the name of the imputed starting acid, after substituting the “-ic acid” with “-ate.” Thus, the ester of *tert*-butylcyclohexanol with acetic acid is named “*tert*-butylcyclohexyl acetate.” If the alcohol has “alcohol” in its name, the only change to this part of the ester’s name is to drop that word. Thus, the ester of methyl alcohol with caproic acid is named “methyl caproate.”

The first priority of analysis of an ester or other material should be to confirm its identity. A technique such as infrared spectrophotometry (IR), gas chromatography/mass spectrometry (GC/MS), or nuclear magnetic resonance spectroscopy (NMR) could be used. In practice, a “weight of evidence” approach is widely used — if the results of all tests are within expected ranges, the identity is (nearly) certain. Purity is determined by capillary gas chromatography. More or less separated components of the sample are detected as they exit the instrument, and the area of each of these — “peaks” is electronically integrated; each peak’s proportion of the total area is taken to be its proportion of the sample. The implied assumption is that the instrument has the same response to each component. For the commonly used flame-ionization detector (FID), the assumption is close for many materials, but the lower-carbon acids and alcohols give a weak response (ethylene glycol and formic acid barely show up), and water doesn’t appear at all. Techniques, such as using an internal standard, can be used to correct for variable responses, but

most of the time they are ignored. The experienced analyst probably has learned the hard way that this assumption must be kept in mind. Polar (polyethylene glycol) and non-polar (polydimethylsiloxane) columns are used. Polar columns give better peak shape, and therefore more-accurate integration, of likely ester impurities (the alcohol and acid from which the ester was made) — however, sometimes one of them elutes at the same retention time as the ester; that is, it is not separated. Using both types of columns minimizes the chances of an impurity being missed because of co-elution. A non-polar, polydimethylsiloxane column with some cyanopropyl groups gives better peak shape of polar materials, such as alcohols and acids, than a pure polydimethylsiloxane column does, but it seems not to be widely used.

The refractive index — the ratio of the speed of light in a vacuum to the speed of light in the sample — is a commonly measured physical property. Despite

the imposing definition, the measurement is easily taken on a refractometer, and the result can be highly accurate. Liquids are measured readily; solids generally are melted and the measurement is made on the melt. The refractive index is a function of wavelength of the light used, and of the temperature of the sample. The standard temperature is 20°C. Most refractometers have built-in correction for wavelength, and recent instruments have temperature control, but older instruments require external temperature control, usually a circulating constant-temperature bath. A “poor man’s” method is to measure at ambient temperature and add 0.0004 for each Celsius degree above 20; while this is a fair approximation for many materials, the analyst must be mindful that it is only an approximation.

A second physical property commonly used to characterize flavor and fragrance materials, including esters, is specific gravity. The specific gravity is the ratio of the density of the sample to the density of water. Each density will vary with temperature, so the temperature of each must be controlled. Various standards are observed; for example, the US federal government specifies 60°F (15.56°C) for the alcohol-content determination of beverages. The standard in the US flavor and fragrance industry is 25°C for each material.

Another usual determination is acid value. A weighed sample of the ester is dissolved in neutralized aqueous alcohol, and is titrated back to neutrality with dilute base. The acidity is calculated as the mg of potassium hydroxide required per g of sample, and is called the acid value. As usual, there are some materials that must be handled differently. Salicylates and other materials that are weakly acidic require use of a pH meter or of an indicator that changes color at a lower pH than the phenolphthalein usually em-

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ployed. Formates require speedy titration at ice temperature to avoid saponifying the ester and giving a spurious result.

A once-common analytical method is determination of the saponification value. In this process, a sample of the ester is reacted with excess alcoholic potassium hydroxide; the excess base is then titrated. The base added, minus the excess base titrated, equals the quantity of base consumed by reaction of the ester, plus any free acid present. The saponification value is calculated as mg of potassium hydroxide per g of sample. The difference between the saponification and acid values is inversely proportional to the molecular weight of the ester.

Last, but certainly not least, odor, appearance, and for some applications, taste, are evaluated. These subjective tests are the final, and highest hurdle. Chances are that each of us has seen materials that passed the objective tests with flying colors, only to be “shot down” on odor. (In fact, I am working on “fixing” such an ester as I write this.) An off-odor in an ester sometimes can be traced to an off-odor in one of the starting materials, which points out the importance of testing these also. Most often, the specification for appearance is clear and colorless. (The term “clear” is often misused. It refers to transparency, not to color.) The odor and taste of a sample are compared to those of a standard, such as a target sample from a customer or a retained sample of a previously accepted lot, but when a material is new to the lab, recourse must be had to published descriptions.

Once the testing has been completed, the results must be compared to specifications. The Food Chemicals Codex (FCC) is a published compendium containing specifications on many chemicals used in flavors. Most esters listed have a minimum purity of 98 percent and a maximum acid value of 2. In fact, most ester samples that have an acid value above about 1 have such an off-odor from that much acid that the material fails on odor. Many companies have their own specification or claim FCC specifications, but reject some materials that meet these because the materials are different from what they have gotten in the past, usually because the purity is lower than in the past. This would seem to be a laudable trend, in that higher-purity

material means better-characterized material, and, presumably, less chance for any safety problem arising from impurities.

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