Homogeneous Catalysis (II): Anchored Metal Complexes

Homogeneous catalysts have many potential advantages over the heterogeneous catalysts that are so widely used throughout the petroleum and chemical industries. One advantage is the conservation of increasingly expensive raw materials because of the catalyst's high selectivity. Another is the savings of significant amounts of energy because of the low temperature and pressure possible with homogeneous processes.

The core of a homogeneous catalyst is a transition metal atom. The complete catalyst complex comprises the transition metal and several coordinatively bound chemical groups or ligands. Most reactions of interest take place with the catalyst molecules and reactants in the liquid phase. When the products are evolved as a gas, there is little difficulty in obtaining chemicals uncontaminated by the catalyst. When the products are also in the form of a liquid, however, an expensive, time-consuming separation process is necessary because the transition metals are often rare and relatively expensive. Losing the catalyst when products are extracted is therefore not economically tolerable. One approach to this problem is to immobilize or anchor the homogeneous catalyst complex on a solid support, such as a polymer or a ceramic. In principle, such catalysts retain the activity and selectivity of homogeneous catalysts while remaining anchored to their support during a reaction. In some cases, catalyst activity and selectivity can also be modified by the anchoring process itself.

Early research on immobilized homogeneous catalysts took place in industrial laboratories. While much of it therefore remained unpublished as proprietary, around 1969 patents began being issued to the Mobil Oil Corporation and to British Petroleum Company Ltd.

To form immobilized complexes, many researchers are using a two-stage synthesis procedure that allows them to place the metal atom at any desired distance from a porous silica support having a large surface area. One reason for wanting to do this is that, when the metal lies close to the surface, the catalyst structure is subject to some of the problems of heterogeneous catalysts. In particular, the catalyst activity can be poisoned by adsorbed molecules physically blocking the active sites. Tying transition metal complexes to surfaces by long and "flexible" ligands not only makes such physical blocking less likely, but also allows for wider flexibility in tailoring the stereochemical and electronic environments of the metal center. In this way, a wider variety of reactions can be catalyzed.

Larry Murrell and his co-workers at the Exxon Research and Engineering Company, Linden, New Jersey, and Robert Pitkethly, Keith Allum, P. J. Robinson, and their associates at British Petroleum, Sunbury-on-Thames, Middlesex, are among researchers that have been adopting this two-stage approach to anchoring transition metal complexes to silica. There are basically two ways to effect this immobilizing process. The anchored entity consists of the transition metal complex together with an attaching group called a bifunctional anchoring ligand. The chemist can either first attach the anchoring ligand to the surface and later bond the metal complex to the anchoring ligands, or he can first prepare the entity consisting of the metal complex and the anchoring ligand and then attach this entity to the surface.

The Exxon researchers have investigated several anchoring ligands, such as trichlorosilyated phosphines [$(C_6H_5)_2P(CH_2)_nSiCl_3$]. In the attachment reaction, a silicon atom in the anchoring ligand bonds to oxygen atoms from two adjacent silanol (SiOH) groups on the silica surface, releasing hydrogen chloride molecules in the process. The value of the integer n determines the length of the ligand and hence the distance of the catalyst from the surface.

Binding of the metal complex to the anchoring ligand occurs at the phosphorus atom of the ligand. In one example, $L_2Rh(CO)Cl$, where L is the anchoring ligand, the rhodium is bound by two phosphorus atoms, one from each ligand (Fig. 1). Surprisingly, the researchers have found that four configurations of the anchored catalyst are possible when the anchoring ligands are attached to the silica prior to the addition of the metal complex, whereas only one configuration is possible in the alternative procedure. The latter is preferable because the catalyst retains only that specific configuration with the desired catalyst behavior. At British Petroleum, investigators have carried out similar experiments with sulfur- and nitrogen-, as well as phosphorus-containing anchoring ligands. Research groups at both places have discovered that anchored catalysts of this type have quite high activities for hydrogenation (addition of hydrogen) and hydroformylation (addition of carbon monoxide and hydrogen to create a formyl group) of hydrocarbons, such as the conversion of an olefin (alkene) to an aldehyde.

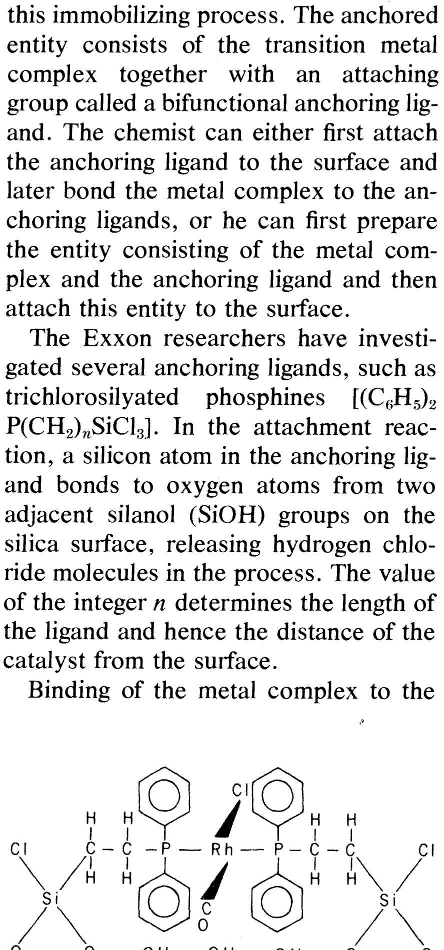

Fig. 1. Schematic diagram of the arrangement of a $[(C_6H_5)_2P(CH_2)_2SiCl_3]_2Rh(CO)Cl$ anchoring ligand-rhodium homogeneous catalyst complex immobilized on a silica support. Anchoring takes place when the silicon atoms in the anchoring ligands bind to oxygen from surface silanol groups, releasing HCl molecules. The rhodium is bound between two phosphorus atoms, one from each anchoring ligand. The chlorine, rhodium, and carbonyl are in a plane parallel to the silica surface. [Source: Larry Murrell, Exxon Research and Engineering Company]

The question of whether to use a ceramic or a polymer support has not been settled, and the notion that each is appropriate for some reactions seems to best characterize the issue. At Mobil's Central Research Division, Princeton, New Jersey, researchers did reach the pilot-plant stage of a hydroformylation process, using a catalyst comprising rhodium complexes immobilized on a polymer support. According to D. Duayne Whitehurst, who along with Werner Haag is one of the principal developers of the new catalyst at Mobil, further development of a commercial-scale plant was halted because the existing and projected markets were not large enough to justify construction of a new facility, although the anchored catalyst would have been the catalyst of choice.

In addition to the Mobil group, several researchers including Robert Grubbs at Michigan State University, James Collman at Stanford University, John Bailar, Jr., at the University of Illinois, and Charles Pittman at the University of Alabama, Tuscaloosa, have demonstrated many features of polymer-anchored homogeneous catalysts of the following type. The polymer is polystyrene cross-linked with divinylbenzene. [Polystyrene consists of a carbon-hydrogen chain with repeating $CH(C_6H_5)CH_2$ units.] The amount of cross-linking is a variable and may range from 1 percent divinylbenzene to much higher values. Anchoring of a complex such as $RhH(CO)[P(C_6H_5)_3]_3$ proceeds in two steps. First, diphenylphosphine $[P(C_6H_5)_2]$ groups are bound to some of the phenyl groups of the polymer. The distance between the neighboring complexes that result depends on the concentration of the added phosphine. Depending on the distances between such complexes, one, two, or three of the polymer-bound diphenylphosphine groups are replaced by the triphenylphosphine groups of the rhodium complex, and the complex becomes immobilized. It is also possible to first synthesize a vinyl metal-ligand complex and then polymerize it to form the polymer, according to Pittman. However, this route is more complicated.

Pittman's group has also demonstrated the possibility of carrying out sequential reactions by anchoring two different homogeneous catalysts to the same polymer. Such a procedure would be advantageous, for converting various diolefins to aldehydes by hydroformylation. Selective hydrogenation of the diolefin to remove only one of the two double bonds would be the first reaction, and would be followed by hydroformylation of the species containing just one double bond.

The polymer does more than just immobilize the homogeneous catalyst; it can also affect the activity and selectivity of the catalyst. According to Pittman, this effect occurs because there is an equilibrium between rhodium complex species with different numbers of phosphine groups, and each complex exhibits a different catalytic activity. Geometric constraints, imposed by the polymer, as well as the ability of segments of the polymer to move and certain entropy effects, can change this equilibrium. At low phosphine concentrations, for example, the phosphines will be widely spaced on the polymer and the rhodium complexes will have access to fewer than the normal number of these.

A dramatic illustration of the possible effect of immobilizing on catalyst activity is given by the anchored homogeneous catalysts that the Union Carbide Corporation has developed for polymerizing olefins such as ethylene.

Organochromium compounds, such as chromocene $[(C_5H_5)_2Cr]$, that are bound to porous silica supports, rather than to polymers, are an example of these anchored catalysts. The silica surface is normally covered by silanol groups. In the anchoring reaction, the chromium atom of the chromocene replaces the hydrogen in the silanol group on the surface—that is, no anchoring ligand is used. At the same time, a cyclopentadiene (C_5H_6) molecule is released when the chromium-oxygen bond forms. According to Frederick Karol of the Union Carbide Research and Development Department, Bound Brook, New Jersey, the anchored chromocene complex provides such a high catalytic activity that there is no need to separate the catalyst from the polymer products. The concentration of transition metal remaining in the polymer is only about one part per million and does not have a significant effect on commercial uses of the product. In contrast, unanchored homogeneous catalysts of a similar type are not active for polymerization at all.

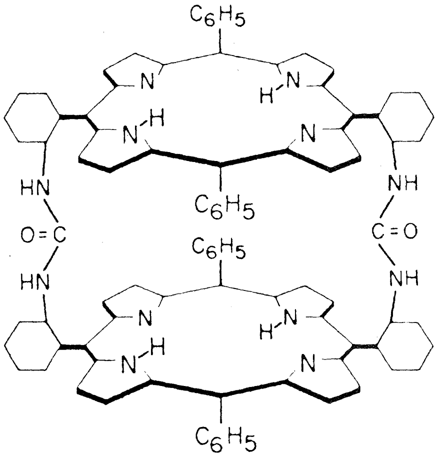

Fig. 2. A face-to-face *trans*-diurea binary porphyrin. The geometry is idealized and double bonds are left out of porphyrin and phenyl rings for clarity. The binary porphyrin is synthesized by treating 5α, 10α-di(2-aminophenyl)-15,20-diphenylporphine with phosgene, followed by addition of a second equivalent of porphyrin. Metal atoms are subsequently introduced by heating the porphyrin with excess $Cu(OCH_3CO)_2$ or $CoCl_2$ in an appropriate solvent. [Source: James Collman, Stanford University]

Solid supports further increase the utility and effectiveness of homogeneous catalysts. Because the metal complexes are bound to the solid support, the concentration of the complexes is not limited by their solubility. When the catalyst concentrations are high, smaller reaction vessels can be used, and thus the cost of a chemical plant becomes lower. But polymers do have some disadvantages. Unlike ceramic supports, polymers are rather flexible, especially if they are not highly cross-linked. Interactions between metal-ligand complexes at different binding sites thus become possible, and these interactions may lead to deactivation of the catalyst. Another difficulty is the sensitivity of polymers to heat. A rapid reaction releases large amounts of energy; the resulting heat can raise the temperature enough to destroy the polymer if care is not taken to provide high-conductivity paths for the heat or to limit the amount generated.

Experiments by Robert Grubbs and Carl Brubaker and their associates at Michigan State University have shown that the use of highly cross-linked polymers can avoid the former difficulty. In experiments involving the catalysis of the hydrogenation of olefins with polymer-anchored titanocene dichloride $[Ti(C_5H_5)_2Cl_2]$, the Michigan State investigators found an increase in activity up to 120-fold, as compared to the unanchored catalyst, provided that the concentration of metal complex was not too high. As the titanocene concentration increased, however, they found that the activity dropped drastically. The decreased activity was attributed to the dimerization of the catalyst species when the concentration was high enough for the titanocene complexes to interact. The dimerization caused the titanium to lose its free coordination sites. Previously, researchers, including Geoffrey Wilkinson of the University of London, had shown that transition metals without free coordination sites cannot catalyze the reduction of olefins. The Michigan State studies therefore established that, on highly cross-linked polymers such as the 20 percent divinylbenzene cross-linked polystyrene they used, isolated, noninteracting catalyst binding sites exist. Furthermore, recent calculations there have indicated that such polymers have surfaces that are nearly as rigid as those of solids, according to Grubbs.

The ultimate tour-de-force in homogeneous catalysis would be to create polynuclear metal cluster complexes and immobilize them on solid supports. Polynuclear metal clusters are like the transition metal complexes that are active as homogeneous catalysts, but they contain three or more metal atoms rather than just one (*Science*, 10 December, page 1150). Chemists hope that the use of such clusters will enable homogeneous catalysts to drive many important reactions, especially those related to more efficient utilization of coal for liquid or gaseous fuels or other chemicals. At present, homogeneous catalysts are not useful for these reactions.

Herbert Kaesz of the University of California at Los Angeles and his associates are doing just this, but in an unusual way. After anchoring ruthenium cluster complexes $[Ru_3(CO)_{12}]$ to silica supports, the investigators anneal the supported catalyst in hydrogen to drive off the carbonyl ligands, leaving small ruthenium particles (150 to 200 angstroms in diameter) evenly dispersed on the silica. In this way, they created a dispersed, small metal particle heterogeneous catalyst of the type that is widely used in the petroleum industry. Kaesz would like to use this approach to synthesize multimetallic clusters—that is, clusters consisting of more than one kind of metal—with compositions and structures that do not occur in bulk metal alloys (*Science*, 30 August 1974, p. 772). Such catalysts are now produced in other ways and are often superior to monometallic clusters, but it is difficult to control the uniformity of the dispersed metal particles.

Taking a clue from certain naturally occurring metalloenzymes, Collman and his colleagues at Stanford are investigating the possibility of immobilizing binary porphyrin complexes on graphite in order to build a reversible oxygen electrode for fuel cells. Another application could be the electrolytic reduction of atmospheric nitrogen for the production of nitrogen-bearing chemicals.

So far, the Stanford group has synthesized several binary porphyrin complexes containing cobalt or copper. The complexes are in the form of so-called face-to-face porphyrins in which two porphyrin rings are held in a parallel configuration (Fig. 2). Two metal atoms, one from each ring, could then act together to bind and reduce oxygen or nitrogen molecules in the gap between the rings. Yet to come are syntheses of iron- or ruthenium-containing complexes for oxygen reduction and molybdenum- or vanadium-containing complexes for nitrogen reduction, as well as attaching such complexes to graphite. Studies of the cobalt- and copper-containing rings have focused on determining which of several possible complexes actually exhibit the face-to-face structure.

As with polynuclear metal clusters, the future importance of immobilized homogeneous catalysts is shrouded by the proprietary nature of much industrial research. In addition, uncertainties surrounding the nature and availability of raw materials and future markets have made it difficult for companies to make decisions about funding of research. Nonetheless, observers detect a growing enthusiasm for ways to tailor the properties of homogeneous catalysts, such as immobilizing them on solid supports. Despite the fact that the first wave of easy experiments has been done and some difficulties have emerged, such approaches to tailoring are just in their infancy.—Arthur L. Robinson

Coronary Bypass Surgery: Debate Over Its Benefits

Cardiologists are becoming more and more adept at diagnosing coronary artery disease (*Science*, 3 December 1976). But once they find that a person's coronary arteries are obstructed, they may be faced with a dilemma about what sort of treatment to prescribe. Many recommend coronary bypass surgery—a procedure in which a vein from a patient's leg is grafted onto the clogged coronary artery to shunt blood past the obstruction into the heart. Others are very cautious about endorsing this procedure and believe drugs may provide benefits that are comparable to those conferred by surgery.

Despite its controversial status, coronary bypass surgery has become a big business in the United States. According to Richard Ross of Johns Hopkins University, about 25,000 operations were performed in 1971 and, by 1973, this number had doubled. He estimates that at least 65,000 operations were performed last year and that each cost at least $10,000. (This price includes the surgeon's fee and charges for hospitalization, laboratory tests, equipment, and medical care.) Thus, about $650 million was spent on coronary bypass operations last year. In contrast, the budget of the National Heart, Lung, and Blood Institute (NHLBI) was $400 million.

In recent years, bypass surgery has become commonplace at many community hospitals, but most of the operations are performed at teaching hospitals and medical centers such as the Cleveland Clinic, the Texas Heart Institute in Houston, and the Mayo Clinic in Rochester, Minnesota. For example, 2,700 operations were performed at the Cleveland Clinic last year and 12,000 were performed there in the past decade, according to Donald Effler, who was formerly at the Cleveland Clinic and is now at Saint Joseph's Hospital in Syracuse, New York.

Most patients who have had this operation are extremely enthusiastic about it, as are many surgeons who perform it and cardiologists who recommend it. Effler, Mason Sones of the Cleveland Clinic, Denton Cooley of the Texas Heart Institute, and other proponents of the operation state unequivocally that it relieves symptoms of coronary artery disease and prolongs lives. Some cardiologists recommend this operation even for asymptomatic patients with coronary artery disease. A number of investigators, however, are asking whether the operation actually improves blood flow to the heart and whether people treated with surgery live longer than those treated with drugs.

Results from numerous studies have established that as many as 90 percent of patients with chest pains (angina pectoris) obtain partial or complete relief after coronary bypass surgery. Angina pectoris occurs when narrowed coronary arteries can no longer sustain an adequate blood flow to the heart. The heart muscle is consequently deprived of oxygen and pain results.

To assess the results of coronary bypass surgery, investigators have looked at changes in blood flow to the heart after the operation. A common way to determine blood flow in coronary arteries is to use contrast angiography. In this procedure, a catheter is inserted into the patient's heart, a radiopaque medium is injected, and x-ray pictures of the coronary arteries are made.

Lawrence Griffith, Stephen Achuff, and their associates at the Johns Hopkins University Medical School used contrast angiography to determine that a significant number of occlusions occur in coronary arteries after bypass surgery, thus impeding blood flow. This result was confirmed by six other groups of researchers. Specifically, the Hopkins group compared patients' coronary arteries before surgery to their arteries 6 months after surgery and found that 40 percent of the arteries had new occlusions. These investigators also looked at the arteries of a group of patients who were not operated on. Only 6 percent of the arteries of this control group had new occlusions after 6 months.

Most of the new occlusions that followed surgery were in the bypassed artery and were upstream from the graft. (Between the point of narrowing in the coronary artery and the point of attachment of the graft.) This is less significant than if they were downstream but it still means that the blood supply to the heart becomes dependent on the grafted vessel remaining open. This may affect only a small proportion of patients since most grafts do remain open. Floyd Loop and his associates at the Cleveland Clinic found that 83 percent of 185 grafts were open 4 years or more after surgery. For those few patients whose grafts close,