to that proposed for the formation of authigenic clay minerals (nontronite and illite-smectite) in marine muddy sediments of Kaneohe Bay, Hawaii (*7*) derived from tropical weathering of basalts. This implies that reverse weathering reactions similar to those proposed by Michalopoulos and Aller may be more characteristic of nearshore muddy sediments than indicated by studies in the early 1970s of sediments in temperate environments (*8*). If so, the large quantities of degraded tropical weathering products entering nearshore environments portend substantial formation of authigenic clay minerals. Mackenzie and Garrels (*1*) pointed out that only 7% of the mass of sediments accumulating on the sea floor needs to undergo diagensis (formation of new clay phases or reconstitution of detrital phases) to resolve the mass balance between rivers and oceans. However, before reverse weathering reactions can be viewed as a significant component of elemental cycling in the ocean, it must be demonstrated that these reactions have a global significance. To do so requires more studies of the kind carried out by Michalopoulos and Aller, particularly in muddy nearshore environments of the tropical environment.

What happens to the large quantities of degraded aluminosilicates transported to these environments by tropical rivers? They are not found in shallowly buried sediments, indicating their potential for taking part in early and rapid diagenetic reactions. It is very likely that the ultimate resolution of the geochemical balance for the ocean will involve hydrothermal and low-temperature alteration of the basaltic oceanic crust and sedimentary sinks for the major and minor elements, including the incorporation of elements in newly formed or reconstituted clay mineral phases.

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Metal-Carbon Bonds in Nature

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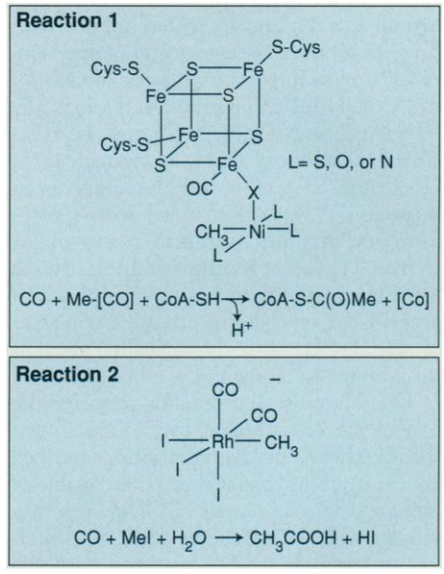
Synthetic organotransition-metal catalysts (species possessing a direct metal-carbon or metal-hydrogen bond) are frequently used in industrial processes to convert hydrocarbon fragments into industrially useful chemicals (*1*). Transition-metal alkyl (M–CR_3) species may, in many instances, play an important role as intermediates in these reactions. In contrast, biology tends to utilize CO_2 or CO to form metabolically useful compounds. There is, however, one biological system, which is fondly referred to as "nature's organometallic catalyst," namely vitamin B_{12} (*2*), that makes use of a M–CR_3 species. Vitamin B_{12} contains cobalt in a substituted corrin macrocycle (a flexible porphyrin relative) and contains an axial Co(III)–alkyl (CR_3). The macrocyclic environment imparts special properties to the cobalt center that allow it to function as nature's Grignard reagent (CR_3^- source), radical ($CR_3\bullet$ source), or Meerwein's reagent (CR_3^+ source). The reaction-type promoted by this site depends on the mechanism of Co–C bond cleavage. The accessibility of several different oxidation states (+1, +2, +3) allows the versatile behavior of this site. On page 628 of this issue, a report by Kumar *et al.* (*3*) presents strong evidence for the occurrence of a second organometallic intermediate in biology that consists of a reactive Ni–CH_3 fragment, which serves as a precursor to acetic acid through its reaction with CO and CoASH (acetyl-CoA synthase reaction 1). Unlike vitamin B_{12}, the nickel ion in this enzyme, carbon monoxide dehydrogenase (CODH), is coupled to an iron-sulfur Fe_4S_4 cluster (Fig. 1).

Iron sulfur clusters are ubiquitous in nature, and analogs are accessible by means of synthetic methods (*4*, *5*). Up until the early 1980s, these clusters were thought to function solely as electron transfer and storage sites, delivering electrons to enzymes that promote substrate reduction (the most difficult being N_2 reduction to ammonia). Later, it was shown that clusters of this type can serve as enzyme active sites (such as Aconitase) and bind and activate substrate (*6*). Examples of Fe_4S_4 clusters linked to a more reactive substrate binding site M (*7*), by what is referred to as a bridging ligand X (M–X–Fe_4S_4), are found in an increasing number of biological systems [for instance, M= Fe(siroheme) in sulfite reductase] (*8*, *9*). If the two sites are chemically linked, they can communicate so that substrate binding at the M site triggers facile multielectron transfer, thereby avoiding toxic or unstable intermediates. In some cases the M site is incorporated into the cubane core (MFe_3S_4) in place of one of the irons (*10*).

With CODH (*4*, *11*) the properties (such as Mössbauer spectra) of the Fe_4S_4 core are not dramatically affected by the presence of the M = Ni site, suggesting that the nickel is bound externally to the cluster core. This led Lindahl, Ragsdale, and Münck to propose the cluster core structure shown in the figure (*12*). Synthetic modeling studies appear to support this structure (*13*). The identity of the bridging ligand X is unknown. Evidence for coupling between the Ni site and the Fe_4S_4 cluster derives from studies in which isotopic labels (^{61}Ni, ^{57}Fe, ^{13}CO) incorporated into the CO derivative perturbed the electron paramagnetic resonance (EPR) signal associated with this cluster site (*14*). Resonance Raman and infrared studies established that CO binds to one of the iron sites (*15*, *16*). Reaction of the CO-bound derivative with a methylated corrinoid (Me-[Co]) species results in methyl transfer to the nickel site with the formation of a CH_3-bound intermediate (see figure). Evidence



Proposed intermediates for the biological acetyl-CoA synthase reaction (reaction 1) and the Monsanto acetic acid process (reaction 2).

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for CH_3 binding to the Ni site is presented in this issue of *Science* (*3*).

To complete the biological reaction, CoASH reacts with the intermediate shown in the figure to form the thioester CoAS-C(O)Me (reaction **1**). The mechanism by which this C–C bond-forming process occurs is still under scrutiny (*16, 17*). The simplest explanation would involve the formation of an intermediate acyl [M-$C(O)CH_3$] (M = Fe or Ni) species, and evidence does indeed point to an acyl intermediate in reaction **1**. It is not clear whether an Fe^- or Ni^- acyl intermediate is involved. With synthetic organometallic systems, CO insertion into M–CH_3 bonds, to form M–$C(O)CH_3$, is one of the most fundamental reaction types (*1*). These reactions generally occur at mononuclear (single metal) sites that contain electron-accepting supporting ligands such as PR_3, C_5H_5 (Cp), or CO. Acyl formation occurs by means of methyl migration to the carbon of an adjacent CO. The best known example of this is the Monsanto acetic acid process (reaction **2**), the catalyst of which is shown in the figure. An obvious distinction between the biological system CODH and synthetic catalysts is the absence of electron-accepting PR_3, Cp, or CO ligands, because they are not biologically available. Instead, nature is limited to ligands L-S, N, and O, which are not typically found to encourage acetate formation. A few rare examples of synthetic models for the CODH Ni site containing biologically relevant ligands (S, N, or O) have been reported, however (*18–21*). Mononuclear (S, N)-ligated Ni–CH_3 species have also been shown (*17, 18, 21*) to react with CO to form acyl complexes, and then to convert to thioesters upon addition of thiols. This is directly relevant to the proposed pathway of acetyl-CoA synthase reactivity. Complexes of Ni(I)–CO with biologically relevant ligands are also known (*18, 20*).

The question that remains concerns the role of the Fe_4S_4 cluster in CODH. Given the synthetic model reactions described above, it would appear that Ni is capable of undertaking the entire CODH reaction scheme without the aid of an Fe_4S_4 cluster. In fact, synthetic Fe_4S_4 clusters are unstable in the presence of CO under reducing conditions (*22*). It has been proposed (*16, 17*) that the more oxidized Fe_4S_4 cluster serves as a CO binding site, and that CO insertion, involving the Fe_4S_4–CO intermediate shown in the figure, is promoted by redox changes at the cluster site. This has yet to be synthetically modeled. Synthetic models have shown, however, that in order for thioester formation to take place at a Ni center, the Ni ion must be reduced by $2e^-$ [from Ni(II) to Ni(0)] (*17*). It is therefore possible that the Fe_4S_4 cluster in CODH serves to facilitate the removal of these two electrons, a step that appears to be critical to the stability of the Ni site. The reconciliation of the mononuclear pathway of acyl formation observed with synthetic systems, and the binuclear pathway proposed to occur with CODH (*16, 17*), awaits further study.

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Calcium Sparks in Vascular Smooth Muscle: Relaxation Regulators

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Many smooth muscle cells periodically exhibit spontaneous transient outward (hyperpolarizing) currents, or STOCs (*1*). Each of these events results from the opening of 10 to 100 potassium-selective channels, triggered simultaneously by a rise in cytoplasmic calcium concentration ($[Ca^{2+}]$). Because these STOCs can be suppressed by agents that interfere with the release of Ca^{2+} from intracellular stores, the triggering Ca^{2+} for the STOCs has been presumed to come from inside the cell (*1, 2*). It has so far been impossible to detect the rise in Ca^{2+} that activates the STOCs—presumably because the Ca^{2+} increase is highly localized and brief, and thus invisible in whole-cell Ca^{2+} recordings or Ca^{2+} images with low time resolution. Now, Nelson and co-workers report in this issue of *Science* the first sighting of these local increases in Ca^{2+} in the cytoplasm of single smooth muscle cells (*3*). This first glimpse of these "Ca^{2+} sparks" is exciting for understanding how STOCs are generated, but perhaps even more exciting is the demonstration that sparks are quite likely responsible for a specific cell function—a vasodilatory influence on small cerebral arteries.

The Ca^{2+} sparks of smooth muscle are not quite the same as those in cardiac muscle, the tissue in which sparks were first reported (*4*). The Ca^{2+} sparks in both muscle types do have a similar duration (~100 ms), magnitude (a few hundred nM), and spatial extent (2 μm diameter at half-maximal $[Ca^{2+}]$). In both tissues, the Ca^{2+} sparks arise from the opening of one or several ryanodine receptors and reflect the activation of an elementary Ca^{2+}-release unit. In cardiac muscle, the sparks are recruited throughout the cell to produce the global rise in $[Ca^{2+}]$ that causes the synchronous activation of the contractile system and the consequent ejection of blood from the heart (*5*). However, the Ca^{2+} sparks in smooth muscle are generated in isolation principally near the cell surface, presumably reflecting the fact that in smooth muscle the sarcoplasmic reticulum (SR), enriched in ryanodine receptors, is near the cell surface (*6*). These ryanodine-sensitive release units are thus perfectly positioned to receive signals from the plasma membrane and to send signals in the form of localized Ca^{2+} increases. In cardiac muscle, the ryanodine receptor amplifies Ca^{2+} signals arising from the plasma membrane. The studies of Nelson and co-workers, however, show

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