Organometallic chemistry in water

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Organometallic chemistry can be carried out in water by using suitable ligands and metals in their higher oxidation states. Several examples from the recent literature are cited to illustrate the principles involved. The advantages of carrying out organometallic reactions in water are highlighted.

ORGANOMETALLIC chemistry has grown tremendously in the last twenty years. The primary reason for such a phenomenal growth is the discovery of new reactions and reagents for organic transformations and development of homogeneous catalysts with unprecedented selectivities using transition metal organometallic compounds. However, the enthusiasm of organic chemists is often dampened by the air- and moisture-sensitive nature of these compounds and the difficulties they pose in handling them. In the recent past several publications have highlighted the fact that organometallic chemistry can be effected in water[1-4]. In this brief overview of the literature, an attempt is made to understand the factors that make M–C chemistry feasible in water, the advantages of developing such chemistry and the exciting possibilities that exist.

Organometallic chemistry in water should not be viewed with suspicion. The first well-characterized organometallic compound was an ethylene complex discovered in 1827 by Zeise[5]. This was water-soluble and crystallized out with a molecule of water in its unit cell[6]. However it is true that most organometallic reactions need to be carried out in the absence of air and moisture even when the final product is not air- and moisture-sensitive. A better understanding of this need is achieved when we classify the organometallic compounds by the type of M–C bonds that are present in them (see Figure 1).

Compounds that contain bonds of type 1 and 2 are, more often than not, low oxidation state compounds. They are stabilized in their low oxidation states by back bonding. Due to their electron-rich nature they are oxidized readily by oxygen. However bonds of type 3 and 4 are formed by metals in higher oxidation states. These molecules are those that contain M–C sigma bonds and it is thermodynamically advantageous to replace them by M–O bonds. Hence they are readily hydrolysed. There are obvious exceptions to these two generalizations. Metal cyclopentadienyls, for example, are extremely robust.

The ability of organotransition metal complexes to function as catalysts primarily stems from the fact that they can oxidatively add a substrate and reductively eliminate a product. Oxidative addition (OA) is the coordination of a substrate to a metal accompanied by a formal transfer of electrons from the metal to the substrate. Reductive elimination (RE), as the name suggests, is the exact opposite of oxidative addition. During a catalytic cycle there are bound to be complexes converting from one of these categories (molecules with bonds of type 1 and 2) to the other (molecules with bonds of type 3 and 4) and hence it becomes imperative that the system be protected against both air and moisture. The catalytic cycle for the isomerization and hydrogenation of an olefin illustrates this principle (Figure 2). In order to have easy oxidative additions, the first step in most catalytic cycles, it is advantageous to start with the metal in a low oxidation state, and this explains why low valent organometallic compounds have been so thoroughly studied.

A possible solution to overcome this difficulty is to look for complexes that would be stable towards oxidation and still be capable of activating organic substrates. There are two ways of making a complex resistant to oxidation. One is to protect it sterically such that it is resistant to oxidation. Such steric protection is likely to make the complex unreactive towards substrates also. The other is to make the complex have a high formal oxidation state. The chemistry of high valent organotransition metal chemistry is relatively unknown[7]. But it is increasingly obvious from the work of Herrmann[8,9] and others[10-16] that high oxidation state organometallic chemistry is not an

Low Oxidation State Organometallics		High Oxidation State Organometallics	
Type 1 η^1	Type 2 η^n n = even	Type 3 η^1	Type 4 η^n n = odd
M = CO M = CR₂ M = CR	$L_nM-\rangle\!\langle$ MLₙ	M – R R = alkyl, H, Aryl, SiR₃	MLₙ MLₙ

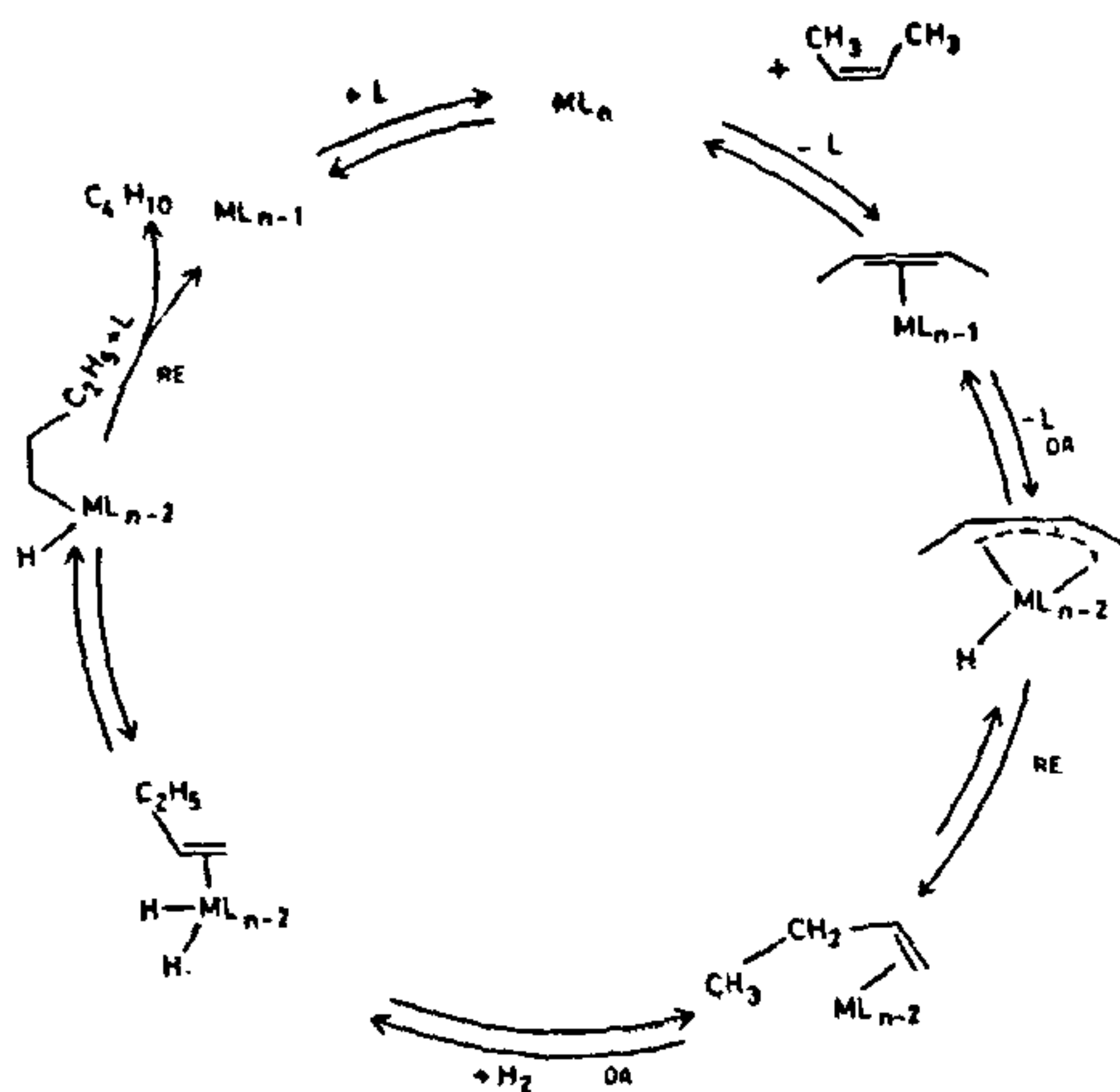Figure 1. Classification of organometallic compounds according to oxidation states.

Figure 2. Isomerization and hydrogenation of an olefin, illustrating the oxidation state changes during a catalytic cycle.

outlandish idea after all. Since this subject has been reviewed recently, only some of the highlights necessary for our discussions would be given. Entry into catalytically active species cannot be done through oxidative additions but could still be done through *in situ* reduction using a metal such as zinc or mercury followed by coordination[17]. So a better way to circumvent this problem of having oxidation-resistant complexes is to look for complexes in high formal oxidation states which would bring about organometallic transformations.

High oxidation state organometallics are common among the 4th and 5th row metals. In these cases the M−C bonds are so robust, that some of them resist oxidation even with H_2O_2. High oxidation state metal fragments do react with organic molecules and carry out stoichiometric transformations. Interestingly, several of these reactions are promoted by acid[18]. Just as CO is a good supporting ligand for the low oxidation state chemistry, O^{2-} appears to be a good supporting ligand for high oxidation state metal fragments[19]. Extended Huckel calculations support the view that interaction of highly oxidized metal fragments with ethylene, for example, is better when the supporting ligand is a pi donor rather than just a sigma donor such as H^- (ref. 20). Since the M = O functionality is known to be stable when M is one of the early transition metals, more examples of high oxidation state organometallics are found with early transition metals.

There are substantial advantages of carrying out organic transformations in water. In the industry heterogenization of homogeneous catalysts has often failed due to problems with heat transfer. If the reaction is carried out with a water-soluble catalyst, separation of the catalyst from the organic products could be easy and at the same time the problems due to heat tranfer would be solved since the solutions can be efficiently mixed. Easy recovery of the catalyst from the product is of tremendous practical value when the catalyst is a precious metal complex. A second major advantage is that substrates such as carbohydrates, polyols, sydnones, etc., which do not dissolve in organic solvents but dissolve in water, can be reacted with the water-soluble organometallic reagents. Sometimes new reaction pathways could be accessed due to the presence of water or the more polar nature of the medium. Last but not the least, for the laboratory chemist, the use of water-soluble and air-stable complexes relieves him of difficult dry box and schlenk-ware techniques.

C–C bond forming reactions in water

Perhaps the most startling example of organometallic chemistry in water is carried out by zinc[21−23] (see scheme 1). The reaction is analogous to Grignard reactions which can be carried out only in the absence of water. On the contrary, these reactions do not take place in the absence of water. Since species such as RZnX are known to be hydrolysed by water very easily, radical intermediates were suspected. However reactions run with radical clock substrates rule out the intermediacy of radicals. It is likely that these reactions are catalysed by the oxidized Zn and not by zinc metal after all. Species such as $(RZn_xCl_yX]^-$ in which the Zn is in the + 2 oxidation state might catalyse the reaction and these intermediates could be resistant to hydrolysis being high oxidation state organometallics.
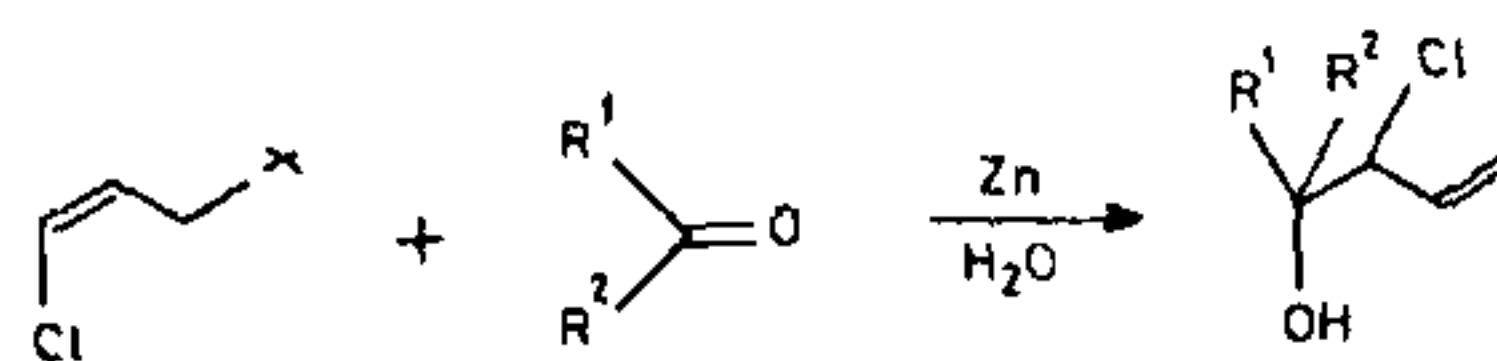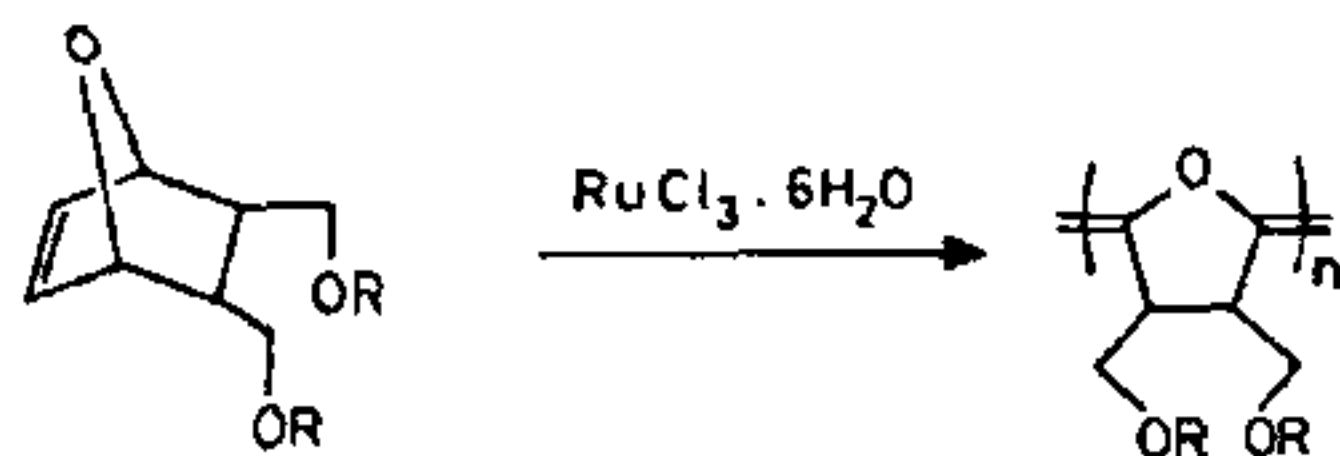

Scheme 1.

A similar example is found in the alkylation reaction promoted by copper(II) perchlorate hexahydrate and copper metal powder in the presence of water[24,25]. The reaction does not proceed with such facility if allyl alcohol is used as an alkylating agent, implying that hydrolysis of the allylhalide or the intermediates involved is not taking place. The reaction is also sluggish if the alkylation is carried out with preformed copper(I) complexes in the absence of water.
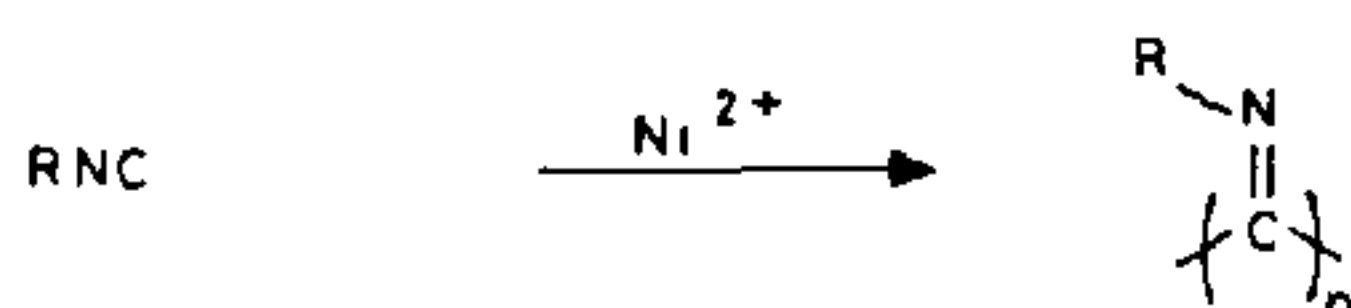
Polymerization reactions in water

Metathesis reactions are also another class of reactions which are known to be carried out with high oxidation

state organometallics[26]. The ring opening metathesis polymerization reaction of polyhydroxy monomers (see scheme 2) has been shown to give higher molecular weight polymers with better polydispersity in water[27,28]. It was shown by Grubbs that the actual catalyst was an aquo complex of Ru^{2+}.
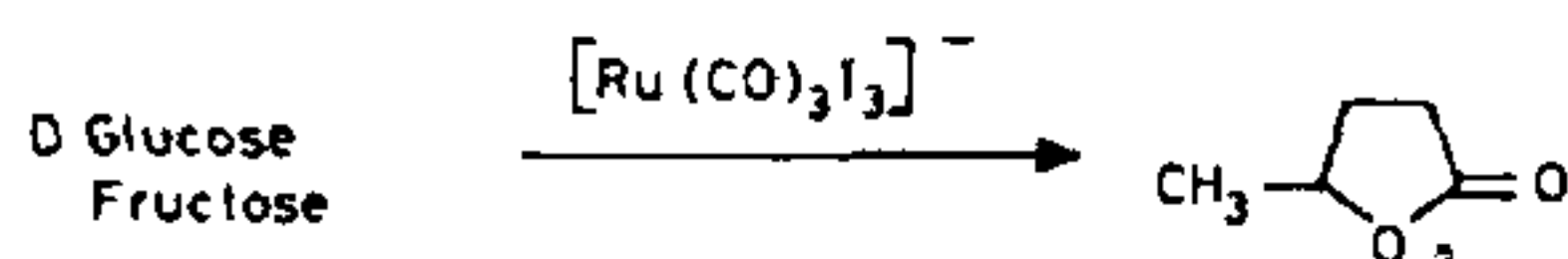

Scheme 2.

Another recent development in aqueous polymerization of substrates using organometallic catalysts or intermediates is the polymerization of RNC (scheme 3) with Ni^{2+} (see refs. 29, 30). In this case the intermediate has been shown to be a Ni^{1+} complex!

Scheme 3.

Reduction reactions in water

Anionic rutheniumiodocarbonyl complexes have been used to carry out dehydroxylation of C_3–C_5 polyols and C_6 sugars with H_2 and CO in aqueous solution[31]. Glycerol is dehydroxylated to N-propanol and its ethers, while glucose and fructose give gamma valerolactone in high yield (scheme 4). These reactions are also promoted by HI. The role of [Ru] in these cases appears to be primarily that of a hydrogenation catalyst. Since the active catalyst is anionic in nature its solubility and reaction in water is facile.
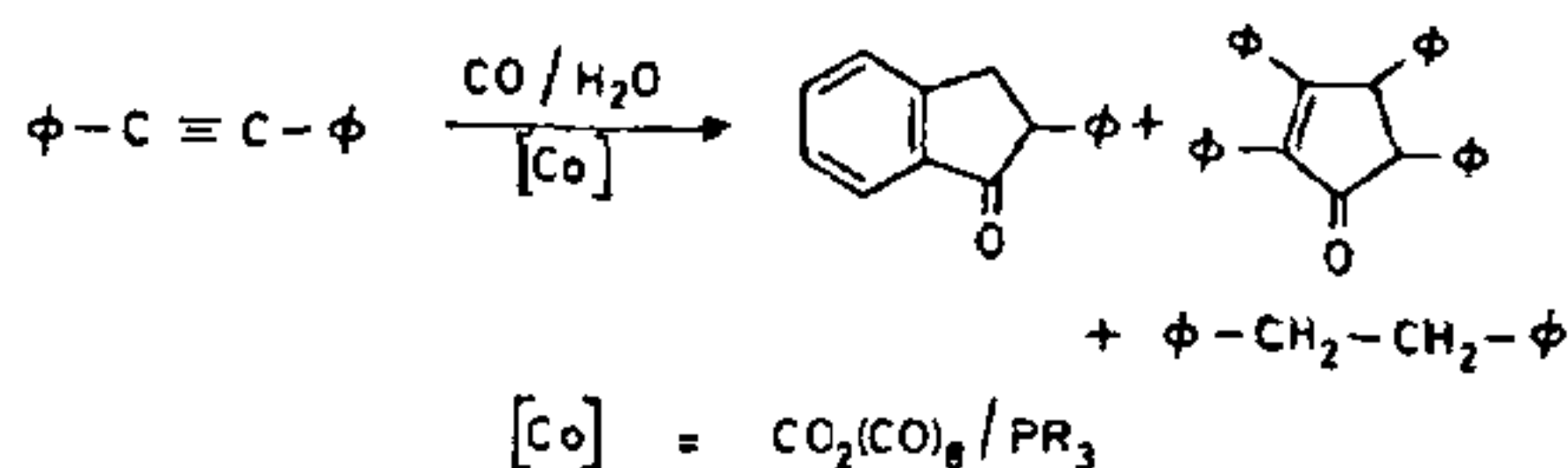

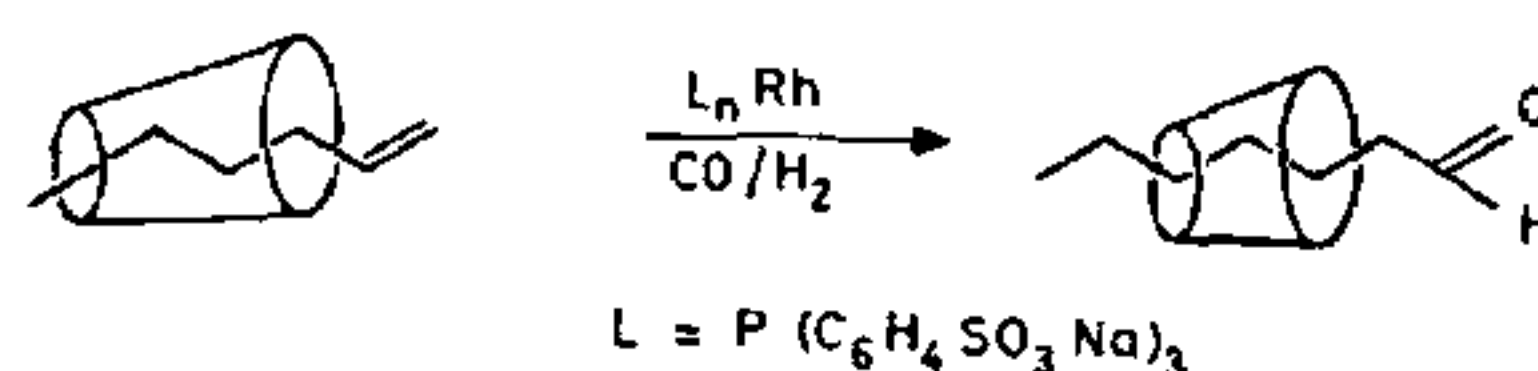
Scheme 4.

Altered selectivities in water

The presence of water can trigger new reaction pathways. A recent example uses water gas as a reducing agent instead of hydrogen and carbon monoxide since the organometallic compound itself functions as a water gas shift reaction (WGSR) catalyst (scheme 5). The cobalt catalysed carbonylation of diphenylacetylene to give the indanone, proceeds only in the presence of water[32]. Furthermore, the selectivity to give the indanone is also dependent on the amount of water.

An easier approach to the reduction of water soluble

Scheme 5.

substrates is the use of complexes which have water-soluble ligands. This method has even been exploited commercially[33]. However, an interesting variation is the use of inverse phase transfer catalysis to achieve unique selectivity[34]. Reductive carbonylation of terminal olefins to give exclusively 1-aldehydes has been demonstrated in the presence of cyclodextrins in water (scheme 6).

$L = P (C_6 H_4 SO_3 Na)_3$

Scheme 6.

Having gone through some of the recent achievements in this field it is only proper that we ask the question, is it possible to modify existing catalysts or design catalysts which will be successful in carrying out reactions in the aqueous medium? The answer to this question is a guarded, yes. Many transformations could be attempted by functionalizing ligands to make them water-soluble. However, will the water-solubilized catalyst behave in the same way? This question must be answered by looking at the intermediates involved. In most cases if a M–C bond which is susceptibile to hydrolysis is involved, making a catalyst with a heavier metal would make the M–C bond more resistant to hydrolysis. If the reactive centre is prone to oxidation on the other hand, a high oxidation state metal with suitable ancillary ligands might be the answer. The greatest strength of the organometallic chemist is the fact that he can modify the organic ligand extensively and at the same time change the metal at his will so that a multitude of possibilities are at his disposal. Hence aqueous organometallic chemistry has a bright future.

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RNA world and ribosomes

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Earlier and recent evidences in favour of RNA as the original genetic material have been documented. Through this the diverse functions of RNAs have been focused on. That the function of ribosomal RNAs in protein synthesis will be the final word for the 'RNA world' has been emphasized through the recent observations of our own and other laboratories.

THE discovery of 'nuclein' by Miescher[1] in 1868 and the proposition of the double helical structure of DNA by Watson and Crick[2] in 1953 are two landmarks of life sciences in the nineteenth and twentieth centuries respectively. The series of discoveries that followed Watson and Crick's fundamental breakthrough finally established the DNA world where the master molecule plays the key role. Some breakthroughs in the recent past, specially the establishment of RNAs acting as catalysts[3] (so-called ribozymes) initiated rethinking in the area. Could it be that the DNA world developed at a later stage, subsequent to the ushering in of the RNA world? The latter term was coined first by Walter Gilbert in 1986 for obvious reasons and is not to be dismissed so early although it is disliked by many, for example Joyce[4]. The arguments in favour and against have led to healthy discussion and 'RNA world' terminology is being tossed about more and more instead of being discarded. It is not easy to look back into the history of the earth since its birth about billions of years ago and a lot of speculation has to be made to establish one theory or the other. Since there is no other alternative we have to take recourse to the present-day information to extrapolate to the past to have an idea about the primordial situation. That is the exercise I plan to do here.

The mechanism of synthesis of DNA is well-established although the same cannot be said of some of the intricacies[5]. However, it is safe to conclude at this stage that it is practically impossible for nature to synthesize DNA today without the help of RNA ingredients. DNA and RNA, as the names signify, differ primarily in the nature of the sugar in their structure and that leads to major differences. The 2'-OH present in RNA enables it to take part in a number of reactions and also leads to its basic instability. The absence of this OH imposes restrictions on the capabilities of DNA but provides remarkable stability to the genetic information it carries. The switch-over from RNA world to DNA world, if any, can be strongly justified on this ground only.

It is difficult to push a similar argument for the exchange of the base uracil in RNA with thymine in DNA. The advantage of introducing a methyl group in uracil does not appear to make much of a difference. The widespread occurrence of thymine in RNA as well