

Catalysis of Olefin and Carbon Monoxide Insertion Reactions

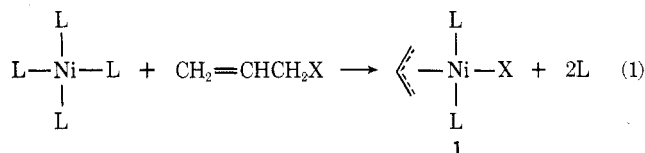
Gian Paolo Chiusoli

Centro Ricerche di Chimica Organica Montedison, Novara, Italy

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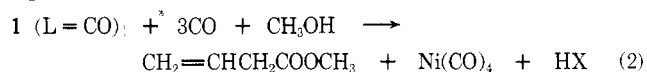
During recent years insertion reactions on transition metal complexes have attracted the attention of organometallic chemists, both academic and industrial.¹⁻³ These reactions pose fundamental problems, and they have striking commercial potentialities.

Insertion reactions of allylnickel complexes have provided insights of particular value. Allylnickel complexes can be made by the oxidative addition of allyl halides ($\text{CH}_2=\text{CHCH}_2\text{X}$) to zerovalent nickel complexes, in the fashion of eq 1, in which L is a lig-

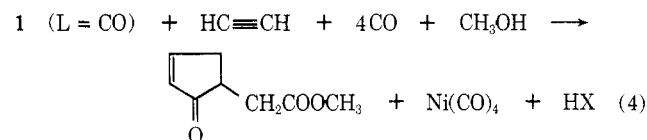
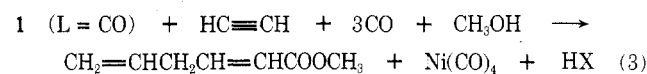


and such as CO or triphenylphosphine.³ This reaction occurs at room temperature and atmospheric pressure, as do the further reactions to be described.

If the allylnickel complex obtained in eq 1 is exposed to CO in methanol solution, further reaction to form methyl vinylacetate occurs as represented by eq 2.¹⁻⁴



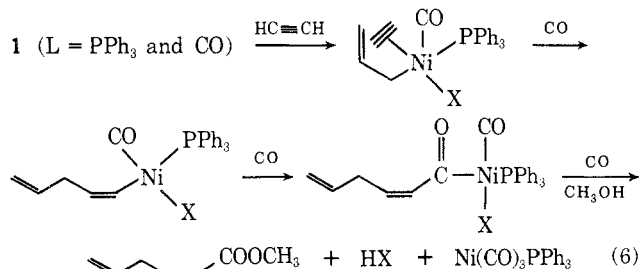
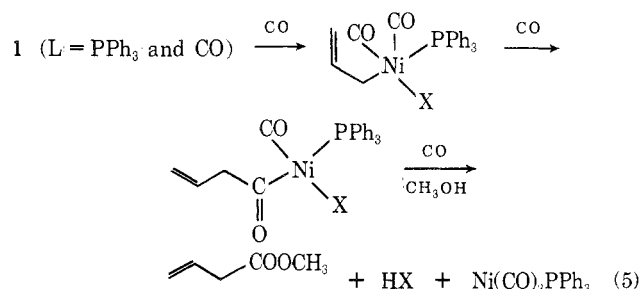
Other examples, also from our laboratory, are reported in eq 3 and 4. In reaction 3, acetylene inserts



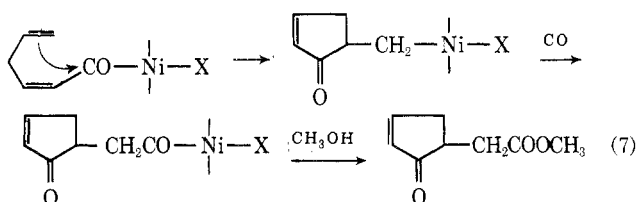
first into the allyl-nickel bond, carbon monoxide is inserted in a second step, and finally reaction with methanol cleaves the complex, forming methyl *cis*-2,5-hexadienoate. These reactions can be regarded as cooligomerizations involving multiple successive insertions.

We have shown that carbon monoxide or acetylene occupies a coordination site left free by the allyl group on passing from the π to the σ form⁴ (eq 5 and 6). The final cleavage generating zerovalent nickel (reductive elimination) leads to methyl esters in the presence of methanol.

In the methanol cleavage step of reaction 6, the methanol competes for the acyl group with the ter-



minal double bond of the coordinated chain. If the reaction is carried out with a low concentration of methanol in inert solvents, the attack of the terminal double bond on the nickel-bonded carbon predominates (reaction 4), and a cyclopentenone ring is formed. This step is followed by another carbon monoxide insertion before final attack by methanol. The ring-closure process can be schematized as in reaction 7.



Multiple insertions of this general type conform to the pattern of Scheme I, in which M_1 , M_2 , etc., are inserting molecules such as CO and acetylene in the examples of eq 1-3. (For simplicity the insertion of a group of the same growing chain as in reaction 4 is not considered in Scheme I.)

A remarkable feature of these reactions is that, despite the presence of several kinds of insertable molecules in solution, one kind is chosen with high selectivity at each step of the addition process. The sequence of involvement of these molecules depends

(1) G. P. Chiusoli, "XXIII Congress of Pure and Applied Chemistry, Special Lectures, Boston 1971," Vol. VI, Butterworths, London 1971; G. P. Chiusoli, *Gazz. Chim. Ital.*, **89**, 1332 (1959); G. P. Chiusoli and L. Cassar, *Angew. Chem. Int. Ed. Engl.*, **6**, 124 (1967).

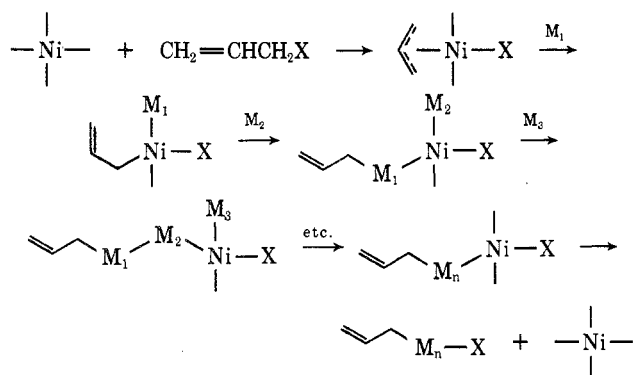
(2) R. F. Heck, *Advan. Chem. Ser.*, **No. 49**, (1965); *Accounts Chem. Res.*, **2**, 10 (1969).

(3) P. Heimbach, P. W. Jolly, and G. Wilke, *Advan. Organometal. Chem.*, **8**, 29 (1970); E. O. Fischer and G. Bürger, *Z. Naturforsch. B*, **16**, 702 (1961).

(4) F. Guerrieri and G. P. Chiusoli, *J. Organometal. Chem.*, **15**, 209 (1968).

Gian Paolo Chiusoli was born in Treviso, Italy, in 1923, and was graduated from the University of Padua. He is presently director of basic organic research in Montecatini Edison Research Center of Novara and Lecturer of Industrial Organic Chemistry in the University of Parma. His main research interests are organic syntheses via organometallic complexes, homogeneous catalysis, syntheses on ion pairs, and heterocyclic systems.

Scheme I



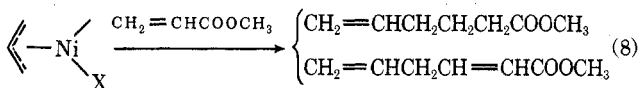
on their structures and on the reaction conditions. Another factor is the identity of the metal-bonded group. Allyl groups are mainly attacked by electrophiles and acyl groups by nucleophiles, while allyl groups show borderline behavior somewhat dependent on the substituents which the allyl group bears.

Other factors are the effective charge on the metal and the concentrations of the molecules to be inserted. Different molecules of appropriate electronic and geometric character can compete for insertion, and it should be possible to favor one of these by facilitating its coordination. There is thus the possibility of directing the process toward different structures by changing the building blocks.

Our efforts to determine what types of molecules possess the characteristics necessary for selective catalytic multistep reactions are the focus of this Account.

It turns out that these reactions require precise geometric arrangements. Steric factors play a very important role, and the synthesized molecules generally appear in one predominant stereochemical configuration.

Our first attempt to cause a double bond to react with an allyl group was carried out on olefins activated by electron-withdrawing substituents. Having in mind the tendency of the nickel-coordinated allyl group to react as a nucleophilic species and the known Michael-type reactions of carbanions with activated olefins, we expected this reaction to occur easily, provided that the activated olefin could take the same coordination site that inserting molecules occupy in the previously described reactions. Actually the insertion⁵⁻⁷ goes very well in certain solvents, according to eq 8, written for the case of an allylnickel complex and methyl acrylate.



Reaction stops, however, after insertion of methyl acrylate because of the nature of the nickel-bonded carbon, which is α to the carboxyl group. At room temperature and atmospheric pressure there is no tendency to insert a molecule of carbon monoxide. A proton is taken up if the medium is protic, with formation of methyl hexenoate in very low yield, whereas hydrogen is lost from the carbon β to the carboxyl

(5) G. P. Chiusoli, *Chim. Ind. (Milan)*, 43, 365 (1961).

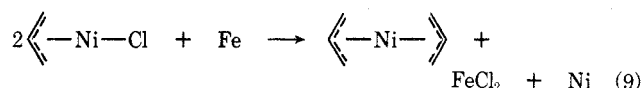
(6) M. Dubini, F. Montino, and G. P. Chiusoli, *Chim. Ind. (Milan)*, 47, 839 (1965); M. Dubini and F. Montino, *J. Organometal. Chem.*, 6, 188 (1966).

(7) G. P. Chiusoli and G. Bottaccio, *Chim. Ind. (Milan)*, 44, 131 (1962).

group in an aprotic medium. This reaction is likely to involve an intermediate nickel hydride which in part hydrogenates the α,β double bond first formed—incidentally, a trans double bond—with formation of some of the hexenoate as a secondary product.

An accurate balance of conditions is necessary to obtain this type of reaction. If a bis(π -allyl)nickel halide is caused to react in methanol, where it gives a monomeric cationic complex, the reaction with acrylate takes place only to a very slight extent. A possible interpretation is that the cationic character of the complex favors the coordination of methanol rather than the activated olefin, renders back-donation more difficult, and also favors nucleophilic attack of methanol on the allyl group. In benzene, where dissociation of the halide ion is hindered and formation of the monomeric species is effected by the activated olefin, the yield is quite satisfactory.

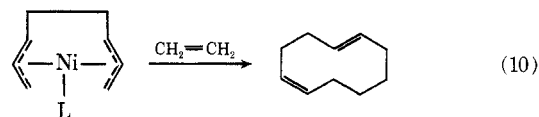
It is possible to achieve insertion in a protic medium, however, by adding a reducing agent such as powdered iron.^{5,8} In this case the reactive species could possibly form according to eq 9.



In fact, the reaction of bis(π -allyl)nickel, prepared by disproportionation of allylnickel chloride with pyridine, goes in an analogous way.

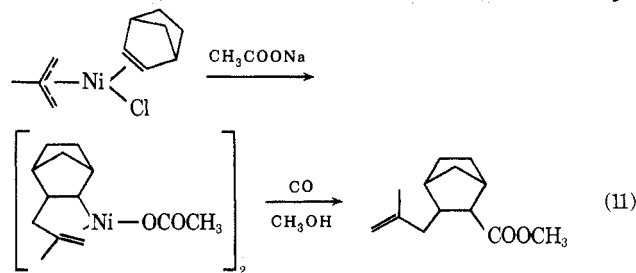
These experiments allowed us to form a picture of the influence of various factors and especially of the solvent on the ability of olefins to coordinate and to insert.

Other useful information came from the literature on reactions of nickel complexes, particularly from Wilke's group.⁹ It has been reported, for example, that ethylene can be inserted into a bis(π -allyl) complex derived from two molecules of butadiene.



Olefin and Carbon Monoxide Insertion

We were interested, however, in a reaction including also carbonylation to carboxylic acids or their derivatives. In this field the closest example is the reaction of methallylnickel acetate with norbornene and carbon monoxide, reported by Porri and coworkers.¹⁰ The reaction gives π -2-*exo*-methallyl-3-*exo*-carboxymethoxynorbornane (reaction 11). Methallyl-



(8) G. P. Chiusoli and G. Cometti, unpublished results.

(9) G. Wilke, *et al.*, *Angew. Chem., Int. Ed. Engl.*, 2, 105 (1963); 5, 171 (1966); P. Heimbach and G. Wilke, *Justus Liebig's Ann. Chem.*, 727, 183 (1969); M. F. Semmelhack, *Org. React.*, 19, 115 (1972).

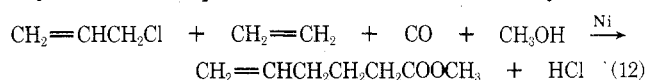
(10) M. C. Gallazzi, L. Porri, and G. Vitulli, Abstracts of papers presented at the Xth Congress of the Italian Chemical Society, Padua, June 17-21, 1968, Section XVI-2; M. C. Gallazzi, T. L. Hanlon, G. Vitulli, and L. Porri, *J. Organometal. Chem.*, 33, C45 (1971).

nickel chloride is first allowed to react with norbornene, and then with sodium acetate to form a dimeric complex. Passage of carbon monoxide into a methanolic solution of the complex results in formation of the ester.

This reaction was carried out on a strained olefin, however, which is known to coordinate very well.

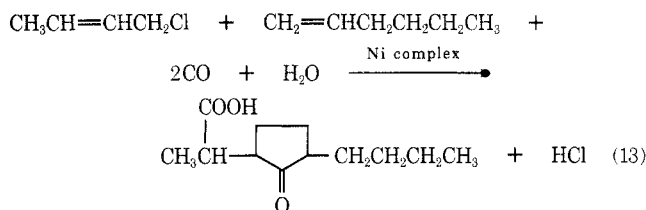
We tried to attack the problem of the direct insertion of simple double bonds, reasoning that the crucial point is to create conditions such that the double bond could win the competition with carbon monoxide for the appropriate coordination site.

The tendency to coordinate carbon monoxide is weakened by a low partial pressure of carbon monoxide, by higher temperatures, and by greater polarity of the medium, which favors formation of a cationic complex of nickel. The latter has a lower tendency to back-donation. Under these conditions, in fact, olefins react with the allyl group by insertion. Thus, ethylene under a pressure of 20–30 atm reacts at 40° with tetracarbonylnickel in a methanolic solution of allyl chloride (eq 12).¹¹ This reaction is catalytic and



parallels the analogous one with acetylene which gives methyl hexadienoate (eq 3). Yields vary from 40 to 60%. Several by-products are formed, including the coupling product of two allyl groups, 1,5-hexadiene, the carbonylation product of an allyl group, vinylacetic acid, and products deriving from the insertion of more than one molecule of ethylene and carbon monoxide such as $\text{CH}_2=\text{CHCH}_2\text{CH}_2\text{CH}_2\text{COCH}_2\text{CH}_2\text{COOCH}_3$, $\text{CH}_2=\text{CHCH}_2\text{CH}_2\text{CH}_2\text{COCH}_2\text{CH}_2\text{COCH}_2\text{CH}_2\text{COOCH}_3$, and others, to be seen later.

With α -substituted olefins, the main product of the olefin insertion no longer was the open-chain acid or ester as in reaction 12, but a cyclopentanone derivative resulting from four successive insertions, double bond insertion, carbonylation, a new double bond insertion causing cyclization, and a new carbonylation, followed by final cleavage of the complex by water or alcohols. The process is depicted in eq 13, written for the case of crotyl chloride and 1-hex-

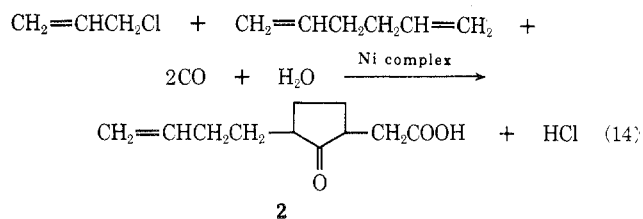


ene. The reaction is catalytic. It takes place at atmospheric pressure and at a temperature of 40–70°, but gives rather poor yields (<5%).

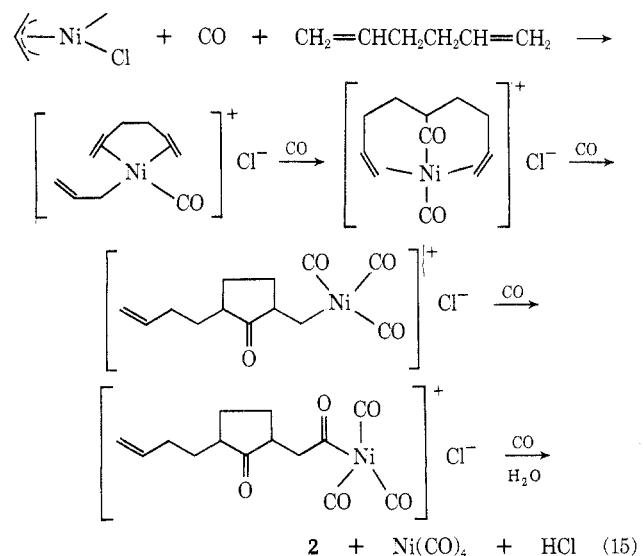
The tendency to give cyclopentanonic products and the low yield are both attributed to the slower hydrolysis of nickel-bonded acyl groups when substituents α to the acyl group are present. This enables the double bond of the coordinated chain to attack the acyl group in competition with the solvent. Simultaneously other reactions also occur. Thus among the products we find 3-pentenoic acid and higher acids.

(11) G. P. Chiusoli and G. Cometti, *J. Chem. Soc., Chem. Commun.*, 1015 (1972); G. P. Chiusoli, G. Cometti, and V. Bellotti, *Gazz. Chim. Ital.*, in press.

The origin of the latter becomes evident if one starts with allyl chloride. Even in the presence of 1-hexene the reaction takes another course, giving rise to a new cyclopentanonic structure, resulting from the insertion of 1,5-hexadiene, which is formed by coupling two allyl groups under the same reaction conditions.



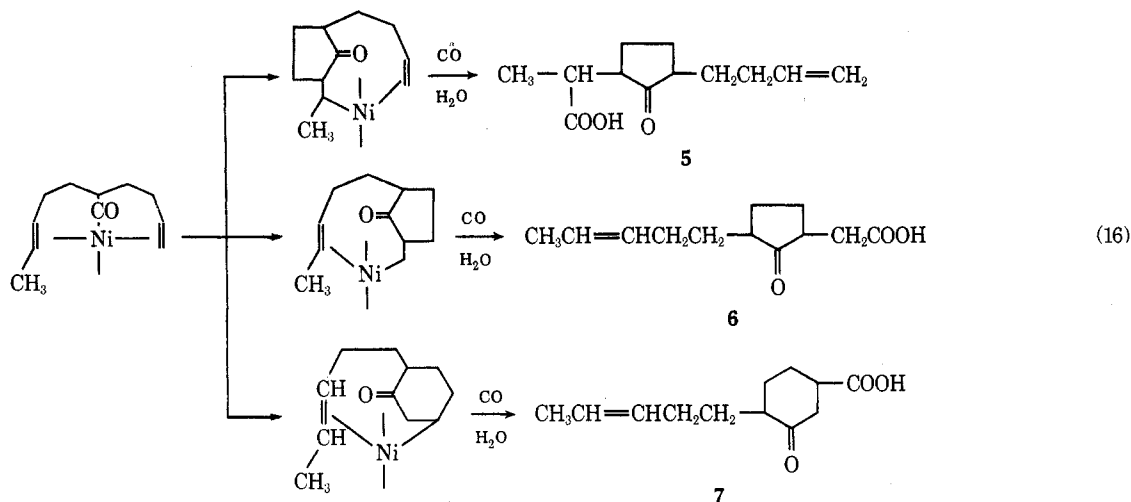
This reaction gives better yields (up to 40%) and is strongly favored by the polarity of the medium and by salts such as KPF_6 , KF , and SnCl_2 , which can enhance the cationic character of the catalytic complex.¹¹ Equation 15 shows our interpretation of the course of the reaction, exemplified for the case of allyl chloride and hexadiene.



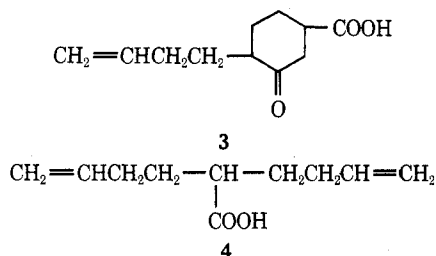
As in the preceding cases, the first step is the oxidative addition¹² of zerovalent nickel to allyl chloride. The resulting complex has cationic character in the solution used for the reaction. This enables hexadiene to coordinate as a chelating ring. One of the two double bonds should occupy a coordination site left free by the allyl group on its passage to the σ form. At this point the first insertion of carbon monoxide takes place with formation of an intermediate which has not been isolated. This intermediate should offer two pathways to cyclization, which are equal in the scheme but are different if a substituent is present on one of the two double bonds, as we shall see in a moment. The cyclization is followed by a new insertion of carbon monoxide and by final cleavage of the complex according to the scheme already shown in other cases. The product essentially is one of the two possible diastereomers. This means that also the cyclization is highly stereoselective.

The use of bis(π -allyl)nickel bromide, in place of allyl bromide and tetracarbonylnickel, with carbon monoxide and 1,5-hexadiene in methanol gives sup-

(12) J. Halpern, *Accounts Chem. Res.* 3, 386 (1970); J. P. Collman, *ibid.*, 1, 137 (1968); A. J. Deeming and B. L. Shaw, *J. Chem. Soc. A*, 1562 (1969).



port to this interpretation.¹¹ Beside the product shown in eq 15, considerable amounts of a cyclohexanonic isomer (3) and of an open-chained compound corresponding to an intermediate stage in the addition process (4) are also obtained. The tendency to



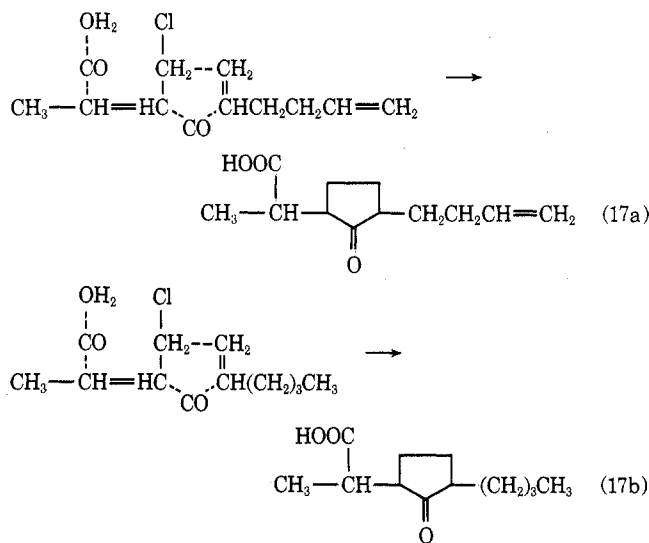
form the latter two products, whose presence is insignificant in the reaction with tetracarbonylnickel, is probably related to the lack of nickel-coordinated carbon monoxide groups. The complex would be less stable, and both penetration of the solvent into the coordination sphere (to cleave the complex before cyclization has occurred) and extension of the cyclizing chain to form a larger ring would be favored.

If the reaction is carried out using crotyl chloride instead of allyl chloride, the main reaction products are two, as already mentioned, corresponding to the possible pathways to cyclization (eq 16). There is also a third isomer, which corresponds to the formation of a cyclohexanonic ring. The three isomers have been obtained in the ratio 6:5:7 = 72:27:1 using KPF_6 as added salt. Compound 6 is a single diastereoisomer of the two possible. Compound 5 is a mixture of two diastereoisomers, one of which can be made to predominate (90:10) depending on reaction conditions. Thus cyclization appears to be stereoselective, whereas double bond insertion between two carbonyl groups is stereoselective to a lower extent.

The ratio between cyclopentanonic and cyclohexanonic structures indicates that the first are strongly preferred. The ratio between the two types of isomers deriving from ring closure at the allylic and at the second double bond of the diene, respectively, indicates that the terminally unsubstituted double bond is clearly preferred.

It is interesting to compare the amount of the product resulting from ring closure at the originally allylic double bond with that obtained with simple 1-olefins such 1-hexene, which in the absence of another double bond can only give the ring closure at

the allylic double bond. In the absence of a chelation effect, one should obtain the same amount from one molecule of 1-hexene and half a molecule of 1,5-hexadiene (in a first approximation the conformation of the alkyl chain is neglected). To test this point we have caused a mixture of 1-hexene and 1,5-hexadiene in the mole ratio 2:1 to react with crotyl chloride. We have not considered the main product, which is the one derived from the ring closure at the second double bond of hexadiene, as mentioned before, and have only compared the other isomer with the product from 1-hexene. The first (eq 17a) is seven times the second (eq 17b). Chelation thus appears to play a very important role in determining the insertion of a double bond.



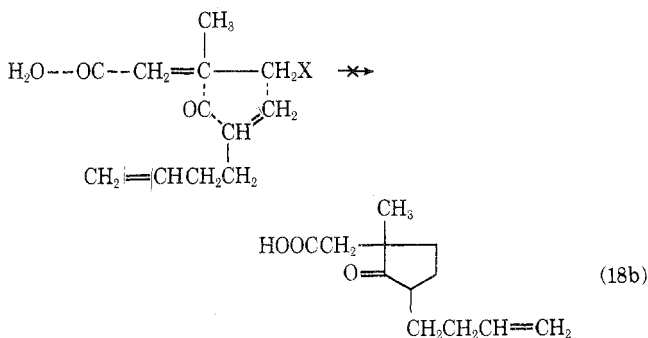
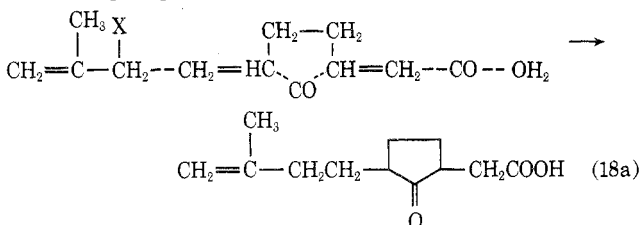
Steric Effects

There are other requirements, however, that must be met to obtain a satisfactory reaction. At least one double bond has to be vinylic. If methallyl chloride, $CH_2=C(CH_3)CH_2Cl$, is caused to react with dimethallyl, $CH_2=C(CH_3)CH_2CH_2C(CH_3)=CH_2$, in place of hexadiene, no insertion occurs under the same conditions—diluted solution of methanol or acetone-water, 45°, and atmospheric pressure—as for the reaction of hexadiene. The failure of dimethallyl to react should be attributed either to its lower ability to coordinate in comparison with 1,5-hexadiene or to steric hindrance to carbonylation.

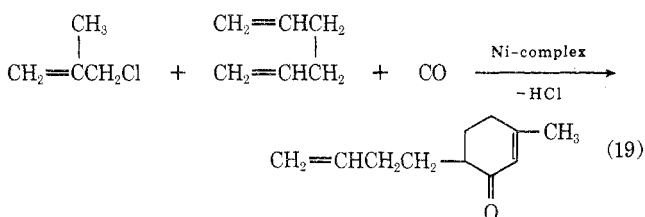
An analogous effect is found in terminally substituted hexadienes. 2,6-Octadiene is practically inert under the conditions of reaction of hexadiene, thus revealing a sensitivity to the effect of substituents which is not equalled by any of the analogous reactions studied so far.

The failure of 2,6-octadiene to react is clearly due to the difficulty of the first attack of the allyl group on the double bond. In fact, a branched isomer of 2,6-octadiene, 3-methyl-1,5-heptadiene, reacts without difficulty, although to a lower extent than with 1,5-hexadiene.

As to the type of substituents on the allyl group, it should be noted that electron-withdrawing substituents cause cleavage of the nickel complex with formation of olefins according to a reaction we described some years ago.⁷ Alkyl or aryl substituents can be present. Two types of products resulting from the two possible ways of cyclization are formed, depending on whether the substituents on the allyl group favor cyclization at the allylic double bond or not. For example, methallyl chloride gives the acid product of cyclization only at the side of the diene double bond (eq 18a) because cyclization at the side of the methallylic double bond to give a cyclopentanone ring (eq 18b) is even less favored than the anal-

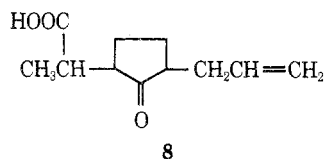


ogous one on the crotyl group. On the other hand, cyclization to give a cyclohexanone ring can occur, but in this case carbon monoxide has to attack a tertiary carbon atom. This attack being not favored, hydrogen elimination occurs with formation of a ketone (eq 19).



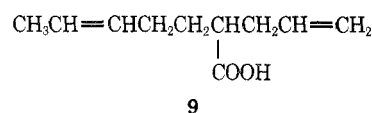
Geometry of the Chelating Molecule

Another important factor influencing the olefin insertion is the size of the chelating ring. To our surprise 1,4-pentadiene has not displayed a reactivity analogous to that of 1,5-hexadiene, although it does permit the closure of a five-membered ring. The only

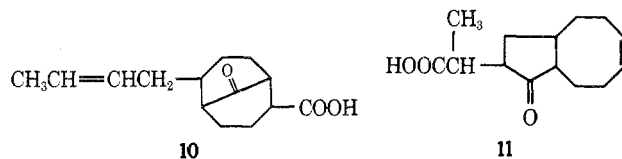


cyclopentanonic acid (8) derived from pentadiene and crotyl chloride, obtained to a limited extent, corresponds to the reaction of only one double bond of the diene. The poor yield may be due to the low chelating ability of the pentadiene system.

Most of the cyclopentanonic product consists of compounds resulting from reaction of the crotyl group with its branched dimer mentioned before, but the main carboxylic acid formed is 3-pentenoic acid, the direct carbonylation product of crotyl chloride. Compound 9, derived from the insertion of one double bond of pentadiene without subsequent cyclization, is also formed.



Cycloolefins like cyclooctene or cyclohexene do not react significantly, but *cis,cis*-1,5-cyclooctadiene easily gives rise to products derived from transannular cyclization or from cyclopentanone ring closure at the side of the originally allylic double bond. Thus crotyl chloride gives mainly 10 along with 11. Both

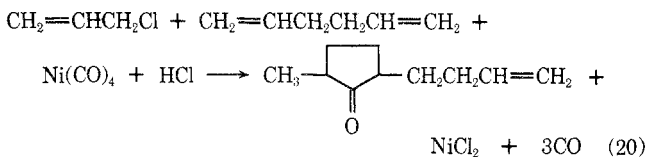


products are accompanied by minor amounts of diastereomers arising from dissymmetry at the tertiary carbon atom α to the carboxylic group. Their structures are being investigated by X-ray methods¹³ and will be reported later.

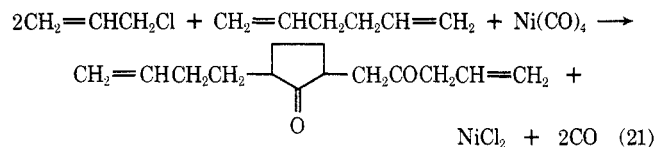
On passing to dienes with an increasing number of methylene groups between the two terminal double bonds, the observed behavior approaches that of simple olefins; thus 1,6-heptadiene and 1,7-octadiene give low yields of compounds which result from a cyclization involving one double bond of the diene and one of the allyl group. The behavior of these two dienes is attributed to their low chelating ability. The size and geometry of the chelating system thus appear to have remarkable effects on reactivity.

Neutral Products from Stoichiometric Reactions

Up to now we have considered carboxylic acids or esters which constitute the main products of the catalytic synthesis. Neutral products are also found, corresponding to eq 20 and 21. These are stoichiometric syntheses which are responsible for destruc-



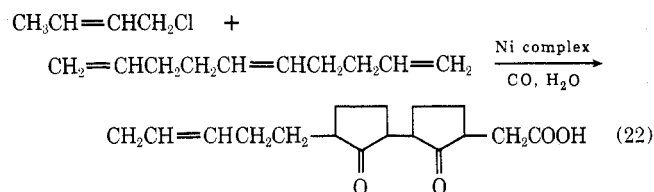
(13) G. D. Andreotti, G. Bocelli, L. Cavalca, and P. Sgarabotto, to be published in *Cryst. Struct. Commun.*



tion of the catalyst by transformation into a Ni^{II} species.

Double Cyclopentanone Ring Closure

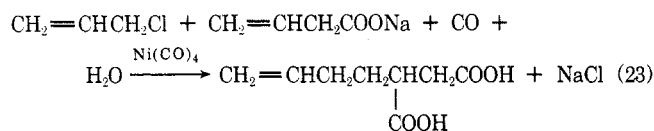
It should be possible to continue the carbon monoxide and double bond insertion along a polyene chain, in which the hexadiene unit regularly repeats. This is the polybutadiene system. We have examined shorter chain compounds as models of more extended systems. *trans*-1,5,9-Decatriene gives reaction 22.



Part of the product consists of compounds with only one cyclopentanonic ring.

Insertion by Chelation of Unsaturated Acids

Another way in which we achieved insertion of a double bond takes advantage of a chelation effect.¹⁴ For this purpose we used olefins containing salt-forming carboxylic groups at an appropriate distance from the double bond. This enabled the double bond to be coordinated as part of a chelating molecule. Suitable acids are the β,γ -unsaturated ones: α,β - or γ,δ -unsaturated acids are not effective. The synthesis is represented by eq 23, which is written for the



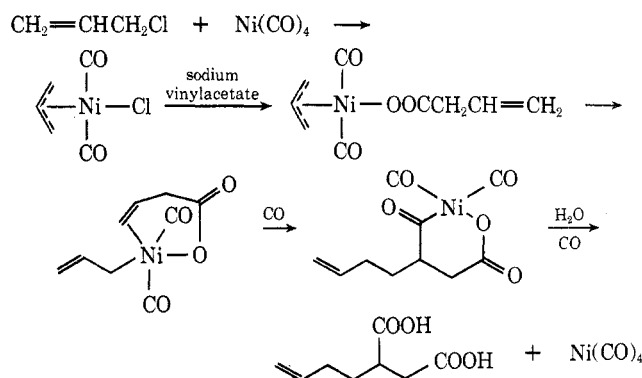
case of allyl chloride and sodium vinylacetate. The reaction is carried out in an aqueous or alcoholic solution at a temperature of about 45° simply by mixing together the reagents under a carbon monoxide atmosphere.

Since under the same reaction conditions allyl chloride is carbonylated to vinylacetic acid, it is also possible to start with allyl chloride without adding sodium vinylacetate, provided that an acceptor of the liberated hydrogen chloride is present, such as magnesium oxide.

Another aspect to be noted is that the reaction is highly regiospecific, the products formed being those derived from the addition of the allyl group to the carbon atom in position 4 and of carbon monoxide to the carbon atom in position 3. We have interpreted this synthesis as in Scheme II.

Beside the oxidative addition of nickel to allyl halide, it involves coordination of the double bond of the transient nickel vinylacetate complex at a coordination site left free by the allyl group on passing

Scheme II



from the π to the σ form, insertion of the double bond and of carbon monoxide, and finally cleavage of the complex by water or alcohols. This interpretation is supported by the fact that reaction of allyl vinylacetate with tetracarbonylnickel gives the same butenylsuccinic acid.

Reaction 23 could also be directed to form butenylsuccinic anhydride. In this case only allyl chloride was used with magnesium oxide as neutralizing agent.

We could show that the anhydride is formed as a product of competition among all the nucleophilic species present in the reaction solution for the nickel-bonded acyl group. The acetate group, which is bonded to nickel, is in the best competitive site because it is coordinated adjacent to the acyl group.

The alkenylsuccinic synthesis allows the preparation of many acids and esters not easily accessible by other ways. In fact it is possible to vary the allyl halide on one side and the β,γ -unsaturated acid on the other, provided that steric effects do not hinder the reaction. These effects are, however, very important; a simple methyl group on the terminal carbon of vinylacetic acid decelerates the reaction remarkably.

Concluding Remarks

To sum up: in the course of stepwise additions on the metal the single blocks are selectively chosen according to the type of the C-metal bond and to the type of substrate. The reactions of the metal-carbon bond can be varied by using appropriate substituents and solvents in order to favor the insertion of one molecule or group in preference to others. The substrate to be inserted can also be favored by taking advantage of chelation effects, of the charge of the metal, and/or of steric and electronic effects caused by substituents. The rate of cleavage of the catalytic complex can also determine the course of a reaction.

From the synthetic point of view, the insertion reactions of olefins on nickel complexes afford a variety of acids and ketones simply by slightly changing the reaction conditions. Much remains to be done, however, toward understanding the catalytic process and the factors affecting it, before a better control of organic syntheses by stepwise additions on transition metal complexes is achieved.

I am indebted to my coworkers, whose dedication and experimental ability made possible the work on which this Account is based.

(14) G. P. Chiusoli, G. Cometti, and S. Merzoni, *Organometal. Chem. Syn.*, 1, 439 (1972).