The Mechanism of the Copper-Catalyzed Addition of Diazoalkanes to Olefins. II. Electronic Effects

William R. Moser*

Contribution from Monsanto Research SA, Zürich, Switzerland.

Received September 9, 1968

Abstract: The homogeneous catalyzed decomposition of ethyl diazoacetate in cyclohexene utilizing various substituted (triaryl phosphite)copper(I) chloride complexes afforded a linear correlation of the *exo*- and *endo*-cyclopropane products with the normal σ-substituent constants. The negative ρ value so obtained was verified by the use of (tris(ω-chloro-*n*-alkyl) phosphite)copper(I) chloride complexes. Bonding of the electronically varying group directly to the metal atom as in the triisopropyl copper(I) chloride, bromide, cyanide, and iodide, afforded scattered results.

In the previous paper[1] a soluble carbene–metal complex with a specific stereochemistry was proposed as the final excited complex in the copper-catalyzed addition of ethyl diazoacetate to olefins. These conclusions, based on the steric effect of the metal's ligand, are further supported by this investigation concerning the electronic effect of the ligand.

The mechanism of the electronic effect of the ligand on homogeneous metal catalysis is still unclear.[2] Subtle changes in ligands attached to a catalyst commonly causes drastic changes in the product distribution.[3] This investigation will attempt to cast some light on this phenomenon as well as to demonstrate that the steric and electronic effect of a metal's ligands act independently.

Results

For the purpose of this investigation, we have synthesized several copper(I) complexes of the type **3** ($(RO)_3P\cdot CuCl$) in which the electrical composition of a single ligand on the metal was variable. The basic system and method of proof of a carbene–metal intermediate remains the same as in the preceding paper.[1] Thus, the observation of systematic changes in the *exo*-**4** and *endo*-**5** cyclopropanes as a function of the electrical composition of the phosphite ligand in complex **3** will be taken as evidence that the carbethoxymethylene group, the metal atom, and the olefin are all in the final transition state leading to products. The reproducibility of the observed isomer ratios[1] (0.5% of the given value) and the stability of these isomers to the reaction conditions were, likewise demonstrated before.[4]

Hammett Treatment of Ligand Reactivity

A series of *ortho*-, *meta*-, and *para*-substituted (triaryl phosphite)copper(I) chloride complexes were synthesized and utilized in the decomposition as depicted in eq A. These catalysts were soluble throughout the reactions, and provide smooth evolution of nitrogen. In Figure 1, the log of the *exo*/*endo* isomer ratios of cyclopropanes **4** and **5** obtained from these decompositions utilizing these catalysts were plotted against the σ constants of the corresponding *ortho*, *meta*, and *para* substituents.

The excellent fit to the normal Hammett parameters is interesting because this is the first case in catalytic reactivity where one has observed a good correlation of reactivity with the normal Hammett σ constants when substitution directly on metal was studied. Other studies have examined the effect of substitution on the reacting organic substrate, but even in those cases, the correlation of reactivity and electronic properties of the substituent was poor.[5]

For the purpose of examining the quality of the fit in Figure 1, the two points appearing at -0.170 and -0.367σ, resulting from the *ortho*-substituted derivatives, should be disregarded for the moment. The substitution ranged from *p*-CH_3O ($\sigma = -0.268$) to *p*-CH_3CO ($\sigma = +0.502$), and the reaction constant, ρ, calculated from this plot was -0.18. Although the ρ value is not large, it is consistent with similar values[6] which several other noncatalytic studies provide for systems where the electronically changing group was partially isolated.

Thus, as the electron-withdrawing ability of the substituent on the ligand increases, a decrease in the *exo*/*endo* isomer ratio in eq A was observed. This result should aid in the construction of a stereochemical model for the transition state for this reaction. Furthermore, it is seen from the *para* and *meta* substituents that the electronic effect of the ligand on reactivity are both linear and predictable when the steric effects are held constant.

As pointed out in the previous paper,[1] substitution in the *ortho* position increases the steric requirements

---

*Address inquiries to: Corporate Research Laboratories, Esso Research and Engineering Co., Linden, N.J.

(1) W. R. Moser, *J. Am. Chem. Soc.*, **91**, 1135 (1969).

(2) (a) R. Cramer, *Accounts Chem. Res.*, **1**, 186 (1968); (b) J. P. Collman, *ibid.*, **1**, 136 (1968); (c) G. Wilke, *et al.*, *Angew. Chem.*, **78**, 157, 170 (1966); (d) G. N. Schrauzer, P. Glockner, and S. Eichler, *ibid.*, **76**, 28 (1964).

(3) (a) P. Heimbach and W. Brenner, *ibid.*, **79**, 814 (1967); (b) R. F. Heck, Symposium on Allyl and Olefin Complexes of Metals, Scheffield, April 10, 1967; (c) W. Kirmse and K. Horn, *Ber.*, **100**, 2698 (1967).

(4) To be published elsewhere.

(5) (a) M. Schlosser and V. Ladenberger, *Ber.*, **100**, 3901 (1967); (b) E. Muller, H. Kessler, H. Fricke, and W. Kiedaisch, *Ann.*, **675**, 63 (1964); (c) G. L. Closs and R. A. Moss, *J. Am. Chem. Soc.*, **86**, 4042 (1964).

(6) (a) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley & Sons, Inc., New York, N. Y., 1963, p 214; (b) A. Streitwieser, *J. Am. Chem. Soc.*, **78**, 4935 (1956); (c) K. Kindler, *Ann.*, **452**, 90 (1927); **464**, 278 (1928); (d) I. Meloche and K. J. Laidler, *J. Am. Chem. Soc.*, **73**, 1712 (1951); (e) A. T. Blomquist and I. A. Berstein, *ibid.*, **73**, 5546 (1951).

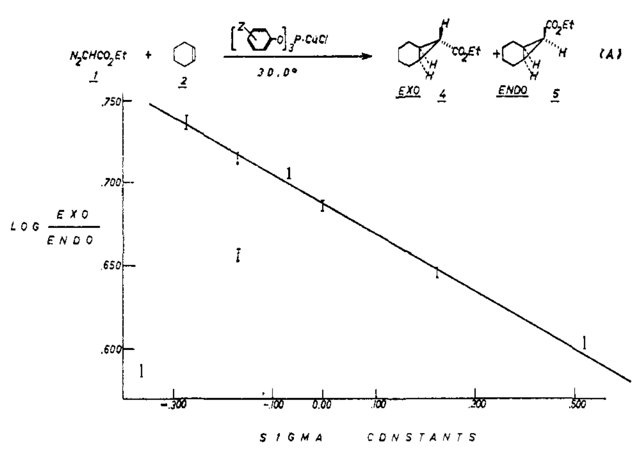


Figure 1.

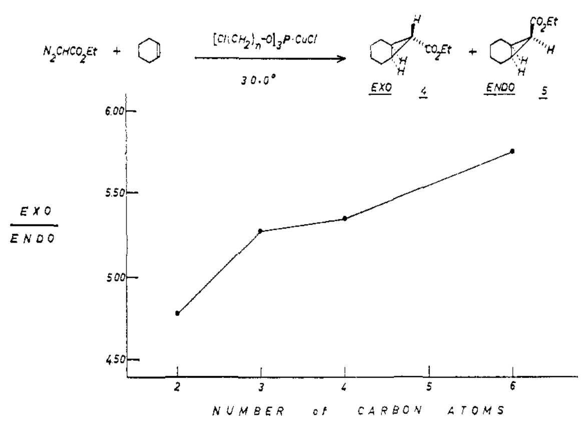


Figure 2.

at the reactive center; thus, no correlation of the substitution to reactivity should be obtained, and they fell below the line in Figure 1 at -0.170 and -0.367σ. The direction of the steric effect under controlled electronic conditions was utilized to support the conclusion that the steric effect acts independently in catalytic processes in general.

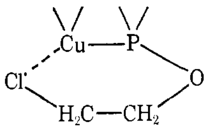
Table I

Acid	pK	Acid	pK
$ClCH_2CO_2H$	2.85	$CH_3CH_2CHClCO_2H$	2.86
$ClCH_2CH_2CO_2H$	3.98	$CH_3CHClCH_2CO_2H$	4.05
$ClCH_2CH_2CH_2CO_2H$	4.52	$ClCH_2CH_2CH_2CO_2H$	4.52

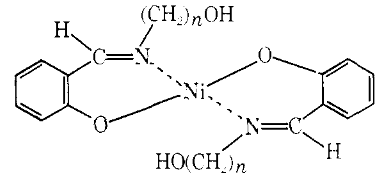
Electronic Effect of ω-Chloroalkyl Phosphite Ligands on Reactivity

Several (tris(ω-chloroalkyl) phosphite)copper(I) chloride complexes **6** were synthesized and utilized in the decomposition depicted in eq B (Figure 2). As Figure 2 shows, regular increases in the *exo/endo* isomer ratios of the cyclopropane products **4** and **5** were observed as the electronegative chlorine atom became more removed from the metal atom. Applying consistent nomenclature with the Hammett treatment, the reaction constant, ρ, has a negative value, *i.e.*, negative slope, which indicates that the *exo/endo* isomer ratio decreases as the ligand on metal becomes more electron withdrawing. It is obvious that the order of electron-withdrawing capacity falls in the series: 2-chloroethyl > 3-chloropropyl > 4-chlorobutyl > 6-chlorohexyl. Thus, the closer the chlorine atom is to the metal center, the greater is the partial positive charge on the metal. As the positive charge on the metal increases, the *exo/endo* isomer ratio decreases. Again, this fact must be accounted for in the formulation of the stereochemistry of the transition state. The changes in the *exo/endo* isomer ratios parallel those changes observed in the pK[7] of ω-chloroalkanoic acids listed in Table I. It should be pointed out that the magnitude of the differences in pK in this study is only slightly larger than the differences observed in the *exo/endo* isomer formation produced by the chloro phosphite ligands. The increase in the strengths of these acids indicates an inductive decrease in the electron density near the ionizable hydrogen, thus aiding its ionization. The electronic effects in the present study are most likely inductive effects through bonds as opposed to either a field effect through space or a chelating effect which directly changes the partial electronic charge on the metal. Either case would predict a specific effect for those ω-chloroalkyl catalysts which would form a six- or seven-membered associated or coordinated ring as shown below with the 2-chloroethyl catalyst.

$[Cl(CH_2)_nO]_3P\cdot CuCl$
6



7



8

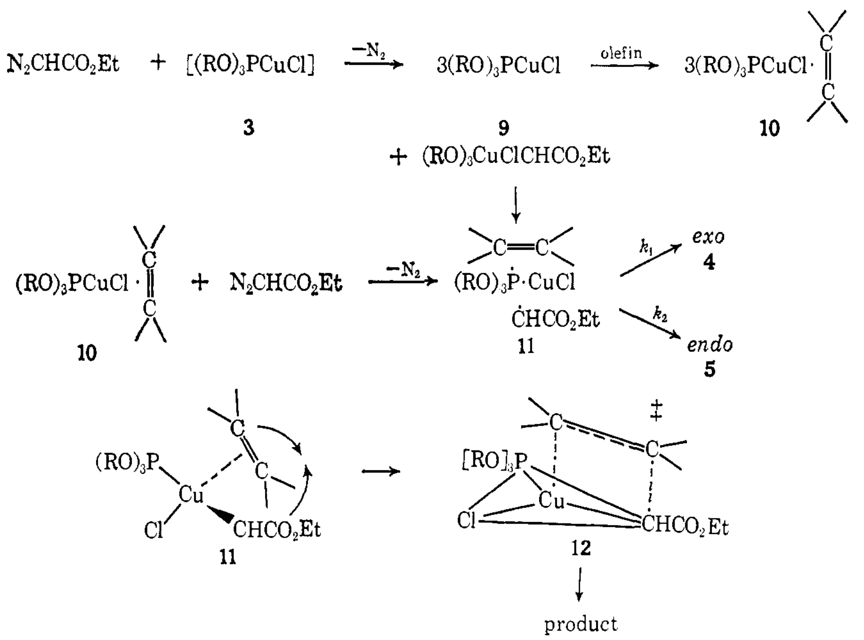
Previous studies[2d] showed that the formation of favorable ring sizes could specifically alter the course of catalytic reactions. Utilizing the *n*-alkoxy complexes **8** it was shown that the complex where $n = 4$ caused an abnormal change in the amounts of both benzene and cyclooctatetraene formed when the complex was used in the cyclization of acetylene. The other derivatives produced amounts of cyclic products which did not widely differ from one another. The absence of such a specific effect in the present study points to a purely electronic effect *via* electron-inductive removal through the ligand chain.

Investigating Figure 2, it is seen that the value of the *exo/endo* ratio for the 6-chlorohexyl catalyst (5.76) is very close to that observed for the saturated *n*-pentyl phosphite (5.97) and *n*-hexyl phosphite (5.90), as well as the higher *n*-alkyl phosphite catalysts reported previously.[1] This means that the inductive withdrawal of electrons in the case of chain lengths higher than 5-chloropentyl or 6-chlorohexyl is very small, and that the main factor determining the *exo/endo* ratio was a pure steric bulk effect. However, in this series of reactions

---

(7) R. C. Weast and S. M. Selby, Ed., "Handbook of Chemical Physics," 48th ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1967–1968, p D-90.

Scheme I



the electronic effect is clearly predominating over a steric effect in the case of the lower members, 2-chloroethyl through 4-chlorobutyl, since a pure steric effect would predict[1] a decrease in the *exo/endo* ratio as the chain length, *i.e.*, steric size, of the phosphite ligand in the catalyst increases. The opposite order was experimentally observed, namely the order predicted by electronic effects.

Effect of Intimate Electronic Variation at the Central Metal Atom

In the case of the substituted(triaryl phosphite)copper(I) chloride complexes **3**, the electronically variable *meta* and *para* substituents were partially insulated from the reactive metal ion center *via* an oxygen and phosphorus atom. Under these conditions the above reported correlation with normal Hammett σ constants was observed. Thus, it was interesting to determine the effect of placing the substituent directly on the metal ion.

The soluble complexes, (triisopropyl phosphite)copper(I) chloride, bromide, iodide, and cyanide, were synthesized and allowed to react with ethyl diazoacetate in pure cyclohexene. The respective *exo/endo* isomer ratios (**4**/**5**) obtained using these catalysts were: 6.68 (Cl), 4.50 (Br), 7.61 (I), and 5.94 (CN).

The *exo/endo* ratio obtained utilizing the complex salts CuCl, CuBr, CuCN, and CuI were 3.5, 5.9, 7.4, and 8.5, respectively.[8]

Visual inspection shows that these data are not correlated with any type of σ constants, electronegativity, or any other known physical or electronic property. This scatter is typical for several other metal complexed reactions[3b, c] where the electronically varying part of the ligand was directly attached to the metal. We think that this observation could be useful, because the basic difference in these two systems and the *meta*- and *para*-substituted phosphite system is the degree of resonance contact which the substituent has with the reactive metal center. An analogous case is the correlation of the ionization constants of benzoic acids with normal Hammett σ constants, and the lack of it for the nuclear bromination of monosubstituted benzenes. This difference is likewise attributed[9] to a difference in the degree of resonance contact. Hence, the key to solving the general problem of ligand effects on reactivity may lie in the identification of a special type of resonance interaction. However, this specific resonance effect is not of the σ^+ or σ^- nature[10] since these types of treatments did not afford a correlation of the above data.

Discussion

Mechanism and Stereochemistry of the Transition State. Of the several mechanisms for the formation of the cyclopropane products **4** and **5** from the decomposition of ethyl diazoacetate in cyclohexene, the overall path depicted in Scheme I best explains the experimental data.

D'yakonov and coworkers[11] have shown kinetically that the catalytic species in this type of reaction is not the starting copper complex but an intermediate derived therefrom. Concerning the first step in the scheme, it is quite reasonable that the coordinatively satisfied tetrameric[1,4] copper complex **3** is cleaved by diazoalkane to form 3 mol of the coordinatively unsaturated monomer **9**, and 1 mol of the monounsaturated carbene–metal complex. Since this reactive monomer **9** is formed in a huge excess of cyclohexene,

---

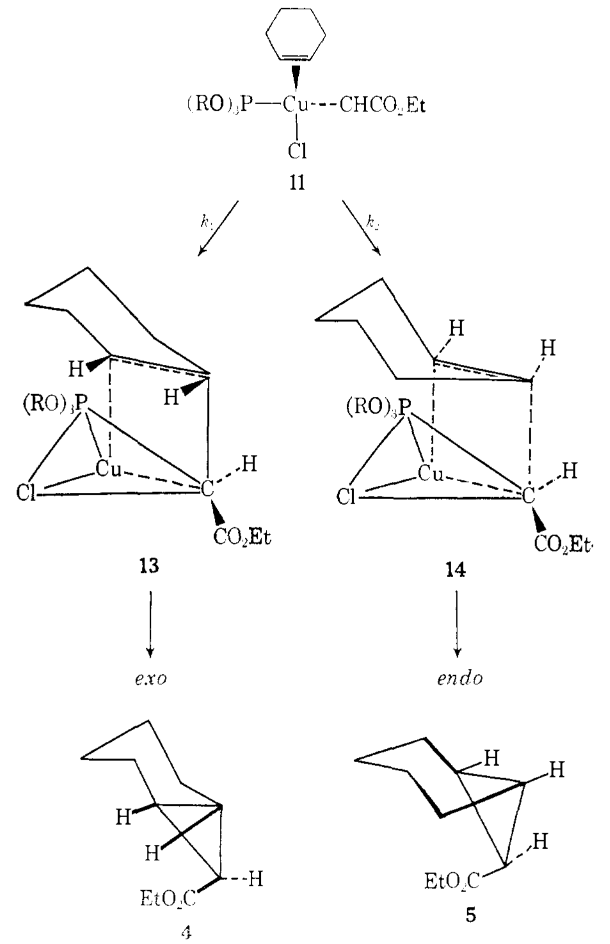
[8] The solubilities of CuCl, CuCN, and CuI in cyclohexene were low, although the chloride and bromide salts were completely taken into solution shortly after the initiation of the reaction.

[9] Reference 6a, p 195.

[10] (a) H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, **80**, 4979 (1958); (b) H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953).

[11] A. G. Witenberg, I. A. D'yakonov, and A. Zindel, *Zh. Org. Khim.*, **2**, 1532 (1966).

Scheme II



and copper(I) forms strong olefin complexes, the next most reasonable step is to coordinate with either 1 or 2 mol of cyclohexene to form the intermediate complex **10**. This complex cannot form the product directly: therefore, it is reasonable that it reacts further with ethyl diazoacetate to form the final intermediate **11** before product formation. This intermediate **11**, depicted in Scheme I, is tetrahedral and coordinatively saturated since the central metal atom is copper(I). The most common coordination number of copper(I) complexes is four and tetrahedral.[12] In this complex **11**, the olefin as well as the carbene (carbethoxy-methylene) would be coordinated *via* a donation–back-donation type of bonding. This requires the donation of two electrons in a sp^2 orbital from a singlet carbene and a back-donation of electrons from the d_{zz} orbital of the metal into the vacant p_z orbital of the carbene carbon. Stable carbene complexes of this type with various other central metal atoms have been reported[13] and the X-ray study indicates sp^2 hybridization of the carbene carbon and a $d\pi$–$p\pi$ bonding contribution.[14]

By a single molecular motion, this complex **11** can rock up to either a transition state **13** leading to the *exo*-cyclopropane **4** or another **14** leading to the *endo*-cyclopropane **5**. Our conception of the most reasonable transition-state stereochemistry is depicted in Scheme II. This configuration of the reacting molecules meets the requirements afforded from the preceding paper,[1] namely: the final transition state leading to products must contain the olefin, metal, and carbethoxymethylene group and must be asymmetric. The intermediate leading to the transition state is reasonably tetrahedral and the products should be obtained from a unimolecular decomposition. An increase in the size of the phosphite ligand must specifically favor the *endo*-product formation. The homogeneous conditions require soluble intermediates; thus the system may be treated as a standard coordination chemistry, solution reaction. Surface-induced modes of ring closure are excluded. The major determinant of the isomer ratio is the interaction of the carbethoxy group with the backbone of the six-membered ring to form *endo*-product **5** or with two *cis*-hydrogens to form *exo*-product **4**. The effect of the phosphite ligand is to introduce a second perturbation which causes changes in the relative stabilities of the transition states **13** and **14**. From this present study one can add another requirement for the stereochemical arrangement of the transition state. As the electron-withdrawing capacity of the ligand increases, the final complex must afford a rationale for the observed relative favoring of the *endo* isomer formation in comparison to *exo*. An investigation of the two transition states, shown in Scheme II, shows that the arrangements are compatible with these data. As one increases the electron-withdrawing capacity of the phosphite ligand, the partial positive charge on copper increases. In general, the effect of increasing the charge on the central metal atom of a coordinated complex, while holding all other parameters constant, is to decrease the length of all metal–ligand bonds. In transition states **13** and **14** a decrease in the metal–ligand bond length[15] causes an increased interaction between the phosphite ligand and olefin in the *exo* product forming transition state **13**, while the same bond length decrease in the *endo* isomer forming transition state **14** affords no increased interaction. The net predicted result from these models is a relative increase in the formation of the *endo* over the *exo* isomer as the electron-withdrawing ability of the ligand increases. The Hammett plot of the *para*-substituted (aryl phosphite)copper(I) chlorides and the (ω-chloroalkyl phosphite)copper(I) chlorides afforded results which are consistent with this prediction. Therefore, we think that these stereochemical arrangements of the intermediate molecules are reasonable working models for the conversion processes. If the above-mentioned concept of the mode of the electronic interaction is correct, it is quite interesting. The primary effect from the ligand is linear and purely electrical in nature; however, the result of this electrical effect is to induce slight differences in steric crowding of the two transition states **13**

---

(12) F. A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry," 2nd ed, Interscience Publishers, New York, N. Y., 1966, p 894.

(13) (a) E. O. Fischer and A. Maasböl, *Angew. Chem.*, 76, 645 (1964); (b) O. S. Mills and A. D. Redhouse, *ibid.*, 77, 1142 (1965); (c) F. D. Mango and I. Dvoretzky, *J. Am. Chem. Soc.*, 88, 1654 (1966); (d) P. W. Jolly and R. Pettit, *ibid.*, 88, 5044 (1966).

(14) E. O. Fischer and A. Maasböl, *Ber.*, 100, 2445 (1967).

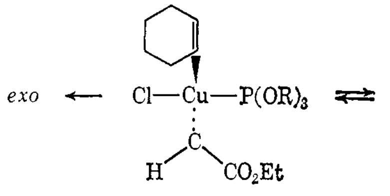
(15) A unique fit of the ^{31}P nmr chemical shifts to the normal Hammett σ constants was obtained for the free phosphites indicating that the electronic changes on the phosphorus nuclei were linear. It is reasonable that this effect would also be transmitted to the copper atom linearly. Although these electrical effects on copper would necessarily be small as well as the resultant changes in ligand–metal bond lengths in the copper complexes, one believes that the relatively small magnitude of change in the *exo*/*endo* isomer ratios is compatible with a small change in the ligand–metal bond length.

and **14**. Therefore, this final pure steric effect leads to the observed differences in the isomer ratios. In essence, the electronic effects in catalytic reactions are better described as combined stereoelectronic effects.

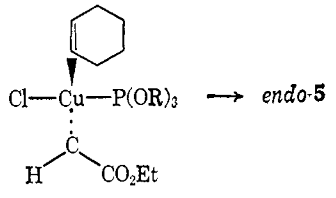
Other Mechanistic Possibilities[16]

There are three other mechanisms for this reaction which also have some merit. One could obtain the same stereochemical results as discussed in this paper as well as that on the steric effects[1] by invoking a bimolecular, product-determining collision of 1 mol of the diazoalkane with complex **10**. In this manner the transition states **13** and **14** could be attained without the intermediacy of **11**. Since one was able to measure only the relative reactivities, *i.e.*, *exo*/*endo* isomer formation, instead of the specific rate constants for this reaction, the bimolecular scheme cannot be excluded. However, most important to the argument to be made here is the fact that the above-mentioned concepts of stabilizing or destabilizing the intermediate complexes through the steric or electronic composition of the ligand apply to either the bimolecular or unimolecular mode of cyclopropane formation. Our working model for the most reasonable final complexes before the irreversible formation of the cyclopropanes *via* either a bi- or monomolecular mode are species **13** and **14**.

The second possibility involves a finite preequilibrium step in the scheme whereby the olefin arranges itself in the least-hindered position in respect to the phosphite ligand and carbethoxy groups. These complexes (**15** and **16**) would decompose independently to the *exo* and *endo* isomers. Again, the concepts of the steric and electronic effects mentioned earlier apply in determining the equilibrium position of these complexes as well as their cyclopropane forming transition states which also should look like **13** and **14**. Although we feel that the restricted rotation in an olefin–metal complex as inferred in complexes **15** and **16** is basically wrong, the data presented here cannot treat this problem. Cramer[17] has presented evidence that ethylene oscillates at the rate of 30 cps in rhodium–ethylene complexes which may have no bearing in this case since the complexes are quite different and the olefin has greater steric requirements.



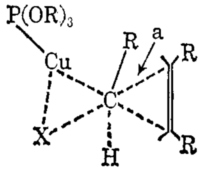
15



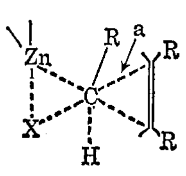
16

One favors the unimolecular route through **11** instead of the other two good alternatives, since **11** is coordinatively saturated and should have some finite stability and we feel that a freely rotating olefin–metal complex is a better model than the rigid one for monoolefin–metal complexes.

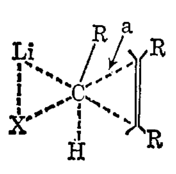
A mechanism similar to that proposed[18] for the Smith–Simmons reaction or the organolithium-induced addition of alkyl dihalides to olefins[19] is disfavored because these mechanisms do not account for the above-mentioned ligand effect.[1] Although these two proposed transition states as well as the general carbene addition mechanism will be treated in detail in a separate paper, we feel that the ligand effect observed there could not be explained by a stereochemical formulation **17** similar to **18** and **19**. If the ligand exerts an influence on reactivity resulting from its steric size, that perturbation must be at a point near a in the above complexes. We further believe that the complexes **11**, **13**, and **14** are more reasonable from both a bonding and coordination chemistry viewpoint. Due to the same reasoning, one feels that the unique optical induction studies[20] of Nozaki and coworkers are better explained *via* complexes similar to those presented in this paper. The three-centered mechanism utilized by Nozaki is basically the same as that proposed for the Smith–Simmons reaction.



17



18



19

Experimental Section

Materials. a. Ethyl diazoacetate was prepared according to a modified procedure[1] of Smith and McKenzie.[21]

b. Tris-(ω-chloroalkyl) phosphites were prepared by standard methods.[22] Optimum yields were obtained when phosphorus trichloride was added to an excess of the corresponding alcohol in ether at +3–5° using triethylamine as base. Other bases afforded poorer yields and impure products.

---

[16] A referee has suggested the possibility that $(RO)_3PCuCl$ promotes the decomposition of the diazo compound to a similar carbene to that derived from the purely thermal decomposition of ethyl diazoacetate ("thermal carbene") since the observed isomer ratio for this reaction (*exo*/*endo* 7.14) was very similar to the ratios obtained utilizing the copper complexes. This concept requires that the copper catalyst be in the near vicinity of the carbon–carbon bond forming process in order to explain the observed ligand effect. This suggested cage reaction has merit, and we believe that the carbene complex is more similar to the "thermal carbene" than the "photolytic carbene." However, the difference in the proposed, discrete metal–carbene complex and the suggested "thermal carbene" associated complex is a matter of the carbene–metal bond lengths. Although the difference is small, we favor the discrete intermediate because it makes sense on a coordination chemistry basis.

(17) R. Cramer, *J. Am. Chem. Soc.*, **86**, 217 (1964).

(18) E. P. Blanchard and H. E. Simmons, *ibid.*, **86**, 1337 (1964); H. E. Simmons, E. P. Blanchard, and H. E. Smith, *ibid.*, **86**, 1347 (1964).

(19) (a) W. T. Miller and D. M. Whalen, *ibid.*, **86**, 2089 (1964); (b) G. Köbrich and K. Flory, *Tetrahedron Letters*, 1137 (1964); (c) G. Köbrich, K. Flory, and W. Drischel, *Angew. Chem.*, **76**, 536 (1964); (d) D. F. Hoeg, D. I. Lusk, and A. L. Crumbliss, *J. Am. Chem. Soc.*, **87**, 4147 (1965).

(20) H. Nozaki, H. Takaya, S. Moriuti, and R. Noyori, *Tetrahedron*, **24**, (1968).

(21) L. I. Smith and S. McKenzie, *J. Org. Chem.*, **15**, 77 (1950).

(22) G. M. Kosolopoff, "Organophosphorus Compounds," John Wiley & Sons, Inc., New York, N. Y., 1950, p 184; (b) A. Arbuzov, *Ber.*, 38, 1171 (1905).

c. Substituted triaryl phosphites were prepared using dimethylaniline in the case of phosphites with electron-donating groups, and triethylamine for phosphites with electron-withdrawing groups or *ortho* substitution.[1] The tris(*p*-methylphenyl) and tris(*p*-chlorophenyl) phosphites were prepared by the high-temperature method[23] of Walsh.

d. Trisubstituted (phosphite)copper(I) halide complexes were prepared[24] by mixing equimolar amounts of the appropriate phosphites and solid copper(I) halides in either pentane or benzene. The reaction was completed when all of the solid salts were dissolved. Correct copper analyses were obtained on all catalysts utilizing the method of Wilcocks and Belcher.[25] Infrared and nmr spectra were measured on several of the catalysts.

Analysis. The gas chromatographic analysis (glpc) were carried out on an F & M Model 720, dual-columned instrument utilizing thermal conductivity detectors. The column employed mainly for the ester separations was a 2 m × 0.64 cm copper tube filled with 10% *m*-bis(*m*-phenoxyphenoxy)benzene plus 10% Apiezon L on Chromosorb W (BPPB). Other columns utilized were: 5% polypropylene glycol adipate (PPGA) on Chromosorb W, 4 m × 0.64 cm, and 15% Carbowax 20M, 2 m × 0.64 cm. In all cases the analysis could be obtained at temperature less than 125°. Yields were determined utilizing internal standards and applying the appropriate response factors.

Catalytic Activity of Complexes. All solvents were passed through aluminum oxide and were degassed just before use; in addition, cyclohexene was distilled from sodium to remove peroxides and stored at −20°.

a. General Procedure for the Cyclohexene–Ethyl Diazoacetate Reaction. The catalyst (5.0 mmol, except when otherwise stated) was dissolved[8] in 20 ml of cyclohexene and placed in a constant temperature bath at 30.0 ± 0.1°. Ethyl diazoacetate (20 mmol) in 20 ml of cyclohexene was added from a constant dropping funnel at a rate of five drops/min. The nitrogen evolution began within 1–2 min and was formed in quantitative amounts. The solution was dark brown after *ca.* 1 ml of the diazoalkane solution had been added; 10–15 min after the addition was completed, a sample was removed and distilled without heating under 10^{-4} mm Hg. Final traces of volatile materials were removed by a final short heating period to 150–200°. The distilled solutions were then analyzed by glpc on the BPPB column at 125° or the PPGA column at 98°. The analysis of a second sample 3–6 hr after the completion of the addition of the diazoalkane showed no change in the product ratio, thus no isomerization of the products by the catalyst was observed. The yields of the cyclopropanes varied between 30 and 70%; the balance was mainly diethyl fumarate and maleate. The unsaturated esters were identified by comparison of the infrared spectra and glpc retention times with authentic materials. The cyclopropanes were identified by a comparison of the mixture melting points and infrared spectra of their acid derivatives with authentic material.[26] The substitution utilized in the Hammett study was *p*-CH_3O, *p*-CH_3, *m*-CH_3, *p*-H, *p*-Cl, and *p*-CH_3CO. The *ortho*-substituted derivatives were *o*-methyl- and *o*-*t*-butyl-*p*-methyl.

Acknowledgments. The author wishes to thank Mr. F. Pfyffer and Mr. W. Scherrer for carefully performing much of the experimental part of this work.

---

[23] E. N. Walsh, *J. Am. Chem. Soc.*, **81**, 3023 (1959).

[24] (a) A. Arbuzov, *Ber.*, **38**, 1171 (1905); (b) Y. Nishizawa, *Bull. Chem. Soc. Japan*, **34**, 1170 (1961).

[25] I. M. Kolthoff and R. Belcher, "Volumetric Analysis," Vol. III, Interscience Publishers, New York, N. Y., 1957, pp 350–352.

[26] Authentic samples of the acid derivatives of **4** and **5** were kindly supplied by Professor H. Musso; H. Musso and U. Biethan, *Ber.*, **97**, 2282 (1964).

On the Mechanism of Acid-Catalyzed Enolization of Ketones[1]

Gustav E. Lienhard and Tung-Chia Wang

Contribution from the James Bryant Conant Laboratory, Harvard University, Cambridge, Massachusetts 02138. *Received August 9, 1968*

Abstract: The rate constants for the catalysis of the enolization of cyclohexanone and of the hydrolysis of 1-methoxycyclohexene by a number of general acids have been determined in water at 25°. The rate constants for ketonization of cyclohexanone enol have been calculated from those for enolization and the equilibrium constant for enolization. The rate constants for ketonization catalyzed by hydronium ion, carboxylic acids, and triethylenediammonium ion are approximately the same as the corresponding rate constants for hydrolysis of 1-methoxycyclohexene. Because the rate-determining step in the hydrolysis of enol ethers is known to be proton transfer to the β-carbon, this result shows that in the transition state of the rate-determining step of acid-catalyzed ketonization, proton transfer to carbon occurs with the bond between the enol oxygen and its hydrogen atom *substantially intact*. Consequently, acid-catalyzed enolization occurs by preequilibrium protonation of the carbonyl oxygen followed by rate-determining proton transfer from carbon to the general base. The approximate equality of rate constants does not hold for the conjugate acid of *p*-toluidine because the rates of enolization were measured by iodination, and *p*-toluidinium ion catalyzes iodination by a special mechanism: formation of the Schiff base salt of cyclohexanone and its enaminization.

The rate laws for the enolization of simple ketones in water contain the summation (ketone)Σk_a(HB) in which HB represents hydronium ion and other acids, such as carboxylic acids.[2] Several plausible mechanisms can be written to account for this acid catalysis; these mechanisms differ from one another in the extent to which the carbonyl oxygen is protonated in the transition state of the rate-determining step and also in the identity of the base that abstracts the proton from the α-carbon atom (see the Discussion for these mechanisms and for references to earlier work on this problem). This paper reports a study of the kinetics of the enoliza-

---

[1] This research was supported by a grant (GB 4848) from the National Science Foundation. Address inquiries to G. E. L.

[2] (a) R. P. Bell and O. M. Lidwell, *Proc. Roy. Soc.* (London), **A176**, 88 (1940); (b) R. P. Bell, G. R. Hillier, J. W. Mansfield, and D. G. Street, *J. Chem. Soc.*, *B*, 827 (1967).