Copper(I) Catalysis in Cyclopropanations with Diazo Compounds. The Role of Olefin Coordination

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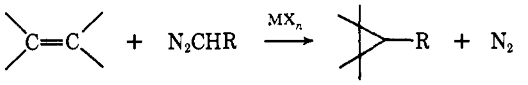
Abstract: Copper triflate is a highly active catalyst for the cyclopropanation of olefins with diazo compounds. Intra- and intermolecular competitions show that copper triflate promotes the cyclopropanation of the least alkylated olefin, in contrast to other copper catalysts which favor the most highly substituted (nucleophilic) olefin. The unique selectivity shown by copper triflate is attributed to coordination of olefins by the highly electrophilic copper(I) species. Olefin coordination is examined in a variety of copper(I) complexes by nmr and shown to be highly sensitive to the presence of coordinating ligands. Two mechanistic schemes for catalytic cyclopropanations can be delineated on the basis of olefin coordination to copper(I). The latter is apparently not important with most catalysts employed heretofore. Kinetic studies with copper(I) triflate show that decomposition of diazo compounds is first order to very high conversions. The inverse dependence of the rate on olefin concentration is attributed to deactivation of copper(I) triflate by multiple coordination of olefins. Nominal catalysis by copper(II) complexes in homogeneous and heterogeneous systems involves prior reduction to copper(I) by diazo compounds followed by catalytic reactions of copper(I).

Various carbenes and carbenoid reagents are available for the cyclopropanation of olefins. Foremost among these precursors are diazo compounds, which can be induced to undergo addition thermally and photochemically to double bonds.[1] The cyclopropanation can also be promoted by catalytic amounts of a variety of metal species. Copper complexes represent one of the most efficient catalysts and have been employed under homogeneous as well as heterogeneous conditions.[2]



(1)

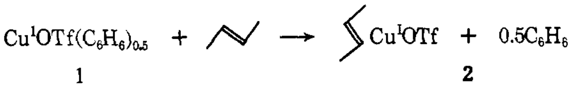
The relevance of metal–olefin coordination in the copper-catalyzed cyclopropanation of olefins with diazo compounds has been discussed.[3–6] The observation of induction periods,[3,7,8] changes in the physical appearance of the reaction mixtures,[2,9–11] and side products derived from the ligands associated with the metal[3,4,12,13] have led to uncertainty as to the identity of the actual copper catalyst. It has also been recognized[14] that alteration of the ligands or changes in the oxidation state of the metal may lead to transformation of the added or nominal catalyst and afford *in situ* the actual catalyst responsible for cyclopropanation. Furthermore, the participation of several simultaneous processes is possible.[12]

The elucidation of the mechanism of this interesting reaction depends on the resolution of several important factors including (a) the catalytically active species, Cu(I), Cu(II) or both, (b) homogeneous *vs.* heterogeneous catalysis, (c) copper–carbene complexes as intermediates, and (d) the role of copper–olefin coordination in determining the site of cyclopropanation.

The metastable character of most copper(I) complexes in solution is responsible for part of the difficulty in the mechanistic study of this process. Coordination of copper(I) with various ligands does inhibit disproportionation (eq 2),[15,16] but also leads to decreased catalyst activity.

$$2\mathrm{Cu(I)} \rightleftharpoons \mathrm{Cu(0)} + \mathrm{Cu(II)} \qquad (2)$$

We recently reported the preparation of a variety of cationic copper(I)–olefin complexes which are readily derived from the benzene adduct of copper(I) trifluoromethanesulfonate.[17]



(3)

The thermal stability and high solubility of these olefin complexes of copper(I) recommended their use directly as homogeneous catalysts for the cyclopropanation of olefins. Trifluoromethanesulfonate (OTf = triflate) like perchlorate is an exceptionally weakly coordinating anion, and the binary metal salts such as those of copper(I) and copper(II) are extensively ionized (as ion pairs) even in nonaqueous solutions.[18] The highly

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[1] W. Kirmse, "Carbene Chemistry" 2nd ed, Academic Press, New York, N. Y., 1971.

[2] (a) V. D. Warnhoff and E. W. Warnhoff, *Org. React.*, **18**, 217 (1970); (b) ref 1, Chapter 3, p 85 ff.

[3] W. R. Moser, *J. Amer. Chem. Soc.*, **91**, 1135, 1141 (1969).

[4] H. O. House, W. F. Fischer, Jr., M. Gall, T. E. McLaughlin, and N. P. Peet, *J. Org. Chem.*, **36**, 3429 (1971).

[5] D. S. Wulfman, B. W. Peace, and E. K. Steffen, *Chem. Commun.*, 1360 (1971).

[6] (a) A. G. Vitenberg, I. A. D'yakonov, and A. Zindel, *J. Org. Chem. USSR*, **2**, 1516 (1966); (b) I. A. D'yakonov and A. G. Vitenberg, *ibid.*, **5**, 1019 (1969); (c) A. G. Vitenberg and I. A. D'yakonov, *ibid.*, **5**, 1023 (1969).

[7] H. O. House and C. J. Blankley, *J. Org. Chem.*, **33**, 53 (1968).

[8] I. A. D'yakonov, A. G. Vitenberg, and M. I. Komendantov, *J. Org. Chem. USSR*, **1**, 1193 (1965).

[9] G. Wittig and K. Schwarzenbach, *Justus Liebigs Ann. Chem.*, **650**, 1 (1961).

[10] M. I. Komendantov, I. A. D'yakonov, and T. S. Smirnova, *J. Org. Chem. USSR*, **2**, 561 (1966).

[11] M. I. Komendantov, I. A. D'yakonov, I. Gokhmanova, and R. R. Kostikov, *ibid.*, **1**, 201 (1965).

[12] D. O. Cowan, M. M. Couch, K. R. Kopecky, and G. S. Hammond, *J. Org. Chem.*, **29**, 1922 (1964).

[13] I. A. D'yakonov and A. G. Vitenberg, *J. Org. Chem. USSR*, **3**, 1115 (1967).

[14] T. Shirafuji, Y. Yamamoto, and H. Nozaki, *Tetrahedron*, **27**, 5353 (1971).

[15] F. A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry," 3rd ed, Interscience, New York, N. Y., 1972, p 905 ff.

[16] Coordination around copper and the counterion will not be included hereafter unless required for discussions.

[17] R. G. Salomon and J. K. Kochi, *J. Chem. Soc., Chem. Commun.*, 559 (1972).

[18] C. L. Jenkins and J. K. Kochi, *J. Amer. Chem. Soc.*, **94**, 843 (1972).

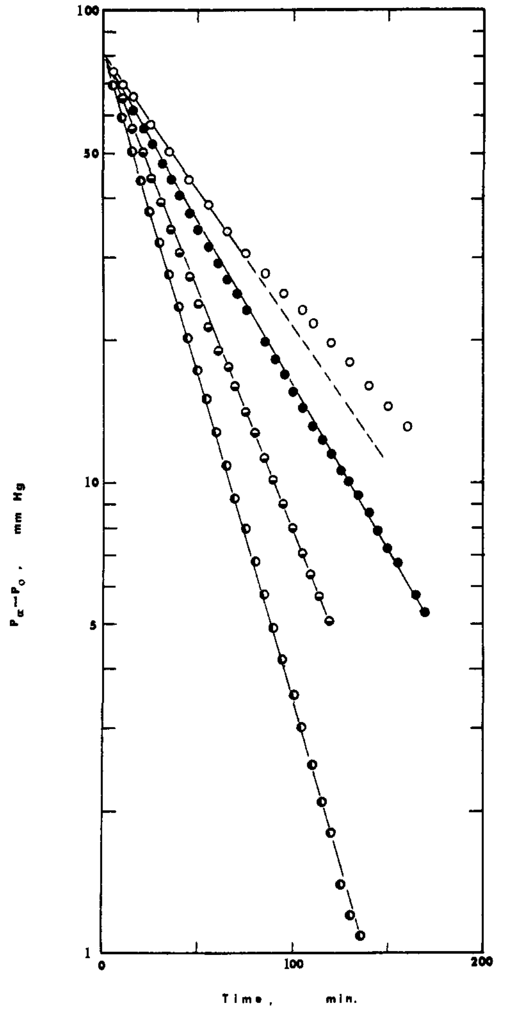


Figure 1. First-order rate of nitrogen evolution from copper(I) triflate catalyzed decomposition of ethyl diazoacetate (9.5 × 10^{-2} *M*) in hexene-1 at −20°: (○) 1.7 × 10^{-2} *M* Cu(I); (●) 2.6 × 10^{-2} *M* Cu(I); (horizonally half-filled circles) 3.5 × 10^{-2} *M* Cu(I); (vertically half-filled circles) 4.3 × 10^{-2} *M* Cu(I).

electrophilic metal ion under these conditions is capable of multiple coordination. If metal–olefin coordination is a factor in the catalytic cyclopropanation of olefins with diazo compounds, its importance should be magnified with these catalysts.

We wish to report unique olefin selectivities in cyclopropanations with diazo compounds using copper triflate catalysts. The use of proton nmr as a probe for olefin coordination to copper(I)[19] allows several mechanistic paths to be distinguished. Furthermore, we find that these metal-catalyzed cyclopropanations can be carried out at very low temperatures with the highly electrophilic copper(I) species.

Results

Homogeneous Copper(I) Catalyzed Cyclopropanation of Olefins. The copper(I) complex **1** is quite soluble in a number of olefins, even at low temperatures. Such solutions react vigorously with ethyl diazoacetate. Thus, *cis*- and *trans*-butene-2 were converted stereospecifically and cleanly to the corresponding ethyl 2,3-dimethylcyclopropanecarboxylates at 0° in greater than 50% yield (isolated by simple distillation). The use of insoluble copper(II) sulfate to catalyze this cyclopropanation has been reported to proceed in only 5–10% yield.[20] The alternative photochemical reaction of ethyl diazoacetate with butenes gave products in lower yields, and contaminated with numerous side products which were difficult to separate.[21]

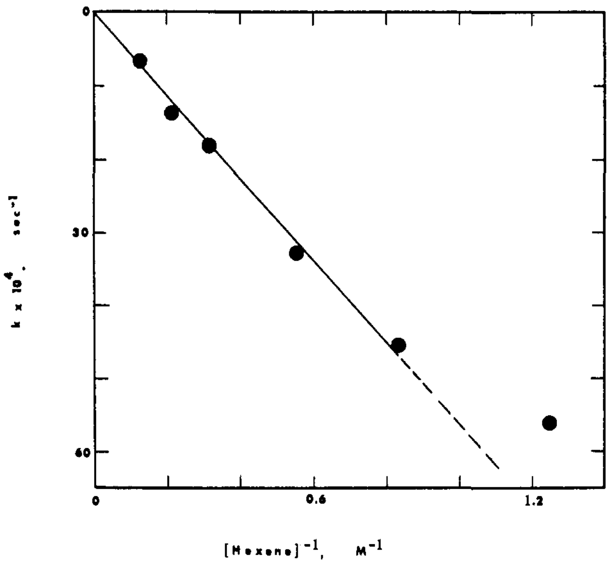
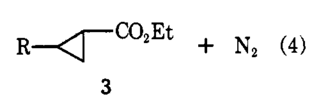


Figure 2. Dependence of the first-order rate constant for nitrogen evolution on hexene-1 concentration from the copper(I) triflate (1.7 × 10^{-2} *M*) catalyzed decomposition of ethyl diazoacetate (4.75 × 10^{-2} *M*) in hexene-1–hexane solutions at −10°.

The addition of catalytic amounts of copper(I) complex **1** to a solution of ethyl diazoacetate in hexene-1 or octene-1 also caused a rapid and quantitative evolution of nitrogen, and the adducts ethyl 2-alkylcyclopropanecarboxylate (**3**) were produced in good yields.



(4)

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R = $CH_3(CH_2)_3$; $CH_3(CH_2)_5$

The nitrogen evolution could be followed at convenient rates at −20° and obeyed first-order kinetics to very high conversions as shown in Figure 1. The pseudo-first-order rate constant increased linearly with the concentration of copper(I) triflate (Table I), and was inversely related to the concentration of hexene-1 (Figure 2). Deviation of the kinetics from a first-order dependence only occurred at low catalyst concentrations (or more accurately, at relatively high ratios of diazoacetate to catalyst). The fall-off after 50% reaction was probably due to partial reduction of copper(I) *via* disproportionation (*vide infra*). The rate of nitrogen evolution can then be expressed by eq 5. The

$$\frac{dN_2}{dt} = k\frac{[Cu^IOTf][N_2CHCO_2Et]}{[\text{hexene-1}]} \qquad (5)$$

temperature dependence of the rate constant is also listed in Table I, from which we extracted values of the

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[19] R. G. Salomon and J. K. Kochi, *J. Organometal. Chem.*, **43**, C7 (1972).

[20] W. von E. Doering and T. Mole, *Tetrahedron*, 10, 65 (1960).

[21] A. P. Meshcherayakov and I. E. Dolgii, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 864 (1960).

Table I. Kinetics of the Copper(I) Catalyzed Cyclopropanation of Hexene-1 with Ethyl Diazoacetate

N_2CHCO_2Et, *M*	Hexene-1, *M*	Cu^IOTf, *M*	Temp, °C	Rate constant,[a] sec^{-1}
9.5×10^{-2}	8.1	0.0261	−20	2.9×10^{-4}
9.5×10^{-2}	8.1	0.0345	−20	4.3×10^{-4}
9.5×10^{-2}	8.1	0.0430	−20	5.5×10^{-4}
9.5×10^{-2}	8.1	0.0690	−20	8.6×10^{-4}
4.76×10^{-2}	8.1	0.017	−18	2.6×10^{-4}
4.76×10^{-2}	8.1	0.017	−14	4.5×10^{-4}
4.76×10^{-2}	8.1	0.017	−10	7.2×10^{-4}
4.76×10^{-2}	8.1	0.017	−6	1.4×10^{-3}
4.76×10^{-2}	8.1	0.017	−2	2.9×10^{-3}
4.76×10^{-2}	8.1	0.017	+2	4.5×10^{-3}

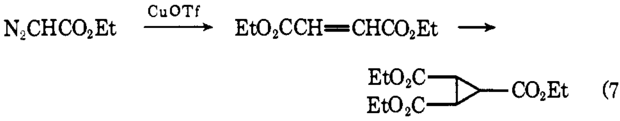
[a] Apparent first-order rate constant.

apparent activation parameters as

$$\Delta H^{\ddagger}_{app} = 19.1 \text{ kcal mol}^{-1} \quad (6a)$$

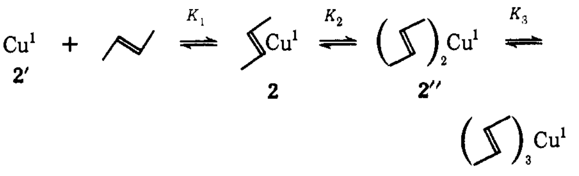
$$\Delta S^{\ddagger}_{app} = -8.90 \text{ eu } (-18°) \quad (6b)$$

The inverse dependence of the rate of nitrogen evolution on the concentration of hexene-1 given in eq 5 is meaningful to the cyclopropanation process only in the concentration range above approximately 1 *M*. In the absence of alkene, no cyclopropanation is possible, of course, and decomposition of diazo ester afforded a mixture of diethyl maleate and fumarate as well as 1,2,3-tricarbethoxycyclopropane and other unidentified products.[22] The yield of cyclopropanation products



(7)

was relatively invariant with hexene-1 concentration (see Experimental Section, Table V). The latter together with the retarding effect of hexene-1 on the rate of nitrogen evolution suggest that the catalytically effective copper(I) species are deactivated by multiple coordination of olefin.[23]

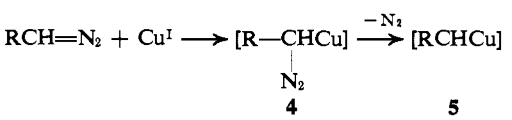


(8)

The formation constants of olefin complexes of copper(I) triflate in solution are not yet available.[24] Isolation studies, however, indicate that they are generally as thermally stable as the corresponding silver(I) complexes.[25]

Copper(I) triflate in the absence of olefins reacts with diazo compounds almost explosively even at −80° in solution. We suggest that it is either the mono- or bis-olefin complex **2** in eq 8 which is the actual cyclopropanation catalyst. Whichever species it may be, the first-order kinetics observed to very high conversions and shown in Figure 1 suggests that it is essentially unchanged during the course of reaction. The singular absence of any induction period even at low copper concentrations indicates a catalytically homogeneous system.

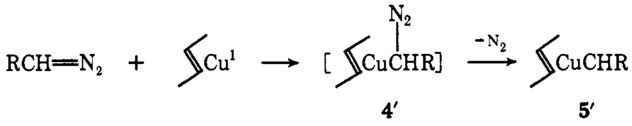
The nmr spectra of solutions containing copper(I) triflate and diazo compounds were examined in order to investigate the possibility of the preliminary formation of a (meta)stable intermediate such as **4** or **5**



$$RCH{=}N_2 + Cu^I \longrightarrow [R{-}\underset{\underset{\textstyle N_2}{|}}{C}HCu] \xrightarrow{-N_2} [RCHCu] \quad (9)^{16}$$

$$\mathbf{4} \qquad\qquad \mathbf{5}$$

or alternatively in the presence of olefin



(10)

Copper(I) triflate (**1**) forms a stable solution in acetone at −76°.[26] Addition of ethyl diazoacetate to this solution resulted in the rapid evolution of nitrogen. In contrast, the addition of diazoacetate to an acetone solution of norbornylene–copper(I) triflate complex gave a homogeneous solution, which was also stable at −76° but evolved nitrogen only when warmed above −45°. Similarly, addition of diazoacetate to a chloroform solution of (*E*,*E*,*E*)-1,5,9-cyclododecatriene–copper(I) triflate[17] afforded a homogeneous solution stable at −76°, and it evolved nitrogen only upon warming above −20°. The temperature of decomposition of ethyl diazoacetate under these conditions is no doubt related to the stability[27] of the copper(I)–olefin complex. However, the nmr spectra of all of these mixtures containing copper(I), olefin, and diazoacetate were identical with those constituted by the superposition of the spectrum of ethyl diazoacetate on that of the copper(I)–olefin complex. Thus, there is no evidence for the formation in appreciable concentrations of either **4**, **5**, or ternary complexes (**4′**,**5′**) containing olefin. If indeed such complexes are formed, as the chemical studies indicate,[3,28–32] they must have only a fleeting existence.[33]

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(22) *Cf.* ref 6.

(23) (a) Nmr experiments[19] indicate that exchange of olefinic ligands and benzene in 1 is rapid. (b) The maximum number of monoolefins which can be coordinated to copper(I) triflate appears to be three.[17]

(24) Studies are in progress.

(25) H. W. Quinn and J. H. Tsai, *Advan. Inorg. Chem. Radiochem.*, 12, 217 (1969).

(26) The presence of copper(II) causes line broadening of the spectrum.

(27) The stability of copper(I)–olefin complexes like the silver(I) analogs[25] decreases with alkyl substitution on the olefinic carbon atoms: R. M. Keefer, L. J. Andrews, and R. E. Kepner, *J. Amer. Chem. Soc.*, 71, 3906 (1949).

(28) P. Yates, *ibid.*, **74**, 5376 (1952).

(29) P. S. Skell and R. M. Etter, *Chem. Ind.* (*London*), 624 (1958); *Proc. Chem. Soc., London*, 443 (1961).

(30) (a) H. Nozaki, S. Moriuti, M. Yamabe, and R. Noyori, *Tetrahedron Lett.*, 59 (1966); (b) H. Nozaki, S. Moriuti, H. Takaya, and R. Noyori, *Tetrahedron*, 24, 3655 (1968).

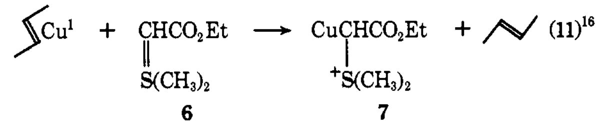
(31) E. O. Fischer and A. Mossböl, *Angew. Chem.*, 76, 645 (1964).

(32) O. S. Mills and A. D. Redhouse, *ibid.*, 77, 1142 (1965).

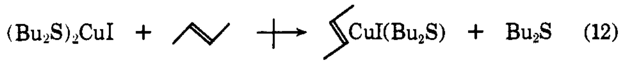
(33) (a) Recently, stable isoelectronic analogs of such complexes, *viz.*, diazoalkane–nickel(0) complexes containing olefins, have been isolated, but on decomposition do not afford cyclopropanation products: S. Otsuka, A. Nakamura, T. Koyama, and Y. Tatsuno, *J. Chem. Soc., Chem. Commun.*, 1105 (1972). (b) A variety of stable carbene complexes of metals are known,[34] but none of copper.

(34) (a) Reference 1, P. Gaspar and B. J. Herold, Chapter 13; (b) D. J. Cardin, B. Cetinkaya, and M. F. Lappert, *Chem. Rev.*, **72**, 545 (1972); (c) P. Hong, N. Nishii, K. Sonogashira, and N. Hagihara, *J. Chem. Soc., Chem. Commun.*, 993 (1972); (d) E. O. Fischer, *Pure Appl. Chem.*, 24, 407 (1970); C. G. Kreiter and E. O. Fischer, *ibid.*, Suppl. (6), 151 (1971).

In order to study copper–carbenoid complexes, we examined by nmr the more stable sulfur analog, ethyl (dimethylsulfuranylidene)acetate (**6**) as a model.[35] The ylide **6** was treated with the copper(I) complex **1** or cyclododecatriene–copper(I) under the same conditions described above. The expected linear dependence of the chemical shift of the methine proton of **6** with the relative concentration of copper(I) is shown in Figure 3. The presence of olefin had no effect on the chemical shift of this proton. Moreover, the resonances associated with the olefinic protons were found at the same frequencies as those of the free olefin (which are different from those of the olefin–copper(I) complex[19]). Thus, **6** reacts with copper(I) triflate to afford a stable α-organocopper sulfonium salt **7** with displacement of the olefinic ligands.



The coordination of olefin to a coordinatively saturated copper(I) species was examined with $(n\text{-}Bu_2S)_2$-CuI, which has also been successfully employed as a cyclopropanation catalyst for diazo ketones.[4] The α-methylene protons of di-*n*-butyl sulfide are shifted slightly downfield (0.16 ppm) on coordination to Cu(I). Addition of norbornylene to a solution of $(n\text{-}Bu_2S)_2CuI$ in carbon tetrachloride caused no change in the nmr spectrum of either the copper(I) complex or norbornylene. There is, thus, no evidence for the (inner-sphere) coordination of norbornylene to $(n\text{-}Bu_2S)_2CuI$ under these conditions. Similar results were obtained with $(CH_3O)_3PCuI$.



We conclude from the foregoing results that no *stable* complexes such as **4** and **5** are formed from diazoacetate and copper(I) triflate. Furthermore, in these studies the competition between olefin and the diazo compound for coordination sites on copper(I) is noteworthy, and to be compared with that of the sulfur analog (eq 11). Finally, it should be emphasized that the presence of strongly coordinating ligands on copper(I) (such as sulfides, phosphites, and phosphines) strongly attenuates its ability to coordinate with olefins.

We relate the high catalytic activity of copper(I) triflate in cyclopropanation to the effective coordination of olefin and diazo compounds. Competition from other bases can diminish the capacity of copper(I) to accommodate additional ligands and reduce its catalytic activity. Indeed, suppression of olefin cyclopropanation by added iodide has been noted in the $(CH_3O)_3$-PCuI catalyzed reaction of dimethyl diazomalonate.[5,36] Likewise, pyridine has been reported to retard the copper acetylacetonate catalyzed decomposition of diazo compounds.[30b] The inverse dependence on the olefin concentration of the rate of cyclopropanation (eq 5)[37] can also be attributed to saturation of the coordination sites on copper(I), leading to the formation of catalytically inactive or significantly less active catalyst–olefin complexes. It should be noted that the observation of such inhibition by olefins is strong evidence for a catalytically active copper(I) species, since copper(II) has very little if any tendency to coordinate with olefins.[38] Catalysis by copper(I) species, when copper(II) compounds are *nominally* employed as catalysts for cyclopropanation, is examined in the following studies.

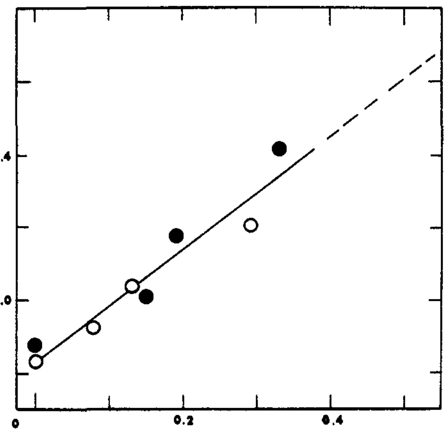
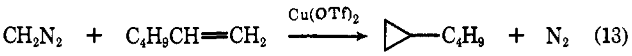


Figure 3. Observed chemical shift of the methine proton in ethyl (dimethylsulfuranylidene)acetate by added (●) copper(I) triflate–cyclododecatriene and (○) copper(I) triflate–benzene in $CDCl_3$ solutions.

Cyclopropanation Using Copper(II) Triflate. Formation of Copper(I) Catalyst by the Oxidation of Diazo Compound. I. Heterogeneous System for Copper(II) Triflate. Copper(II) triflate is insoluble in most hydrocarbon media, but it readily induced at 80° the cyclopropanation of octene-1 with ethyl diazoacetate to ethyl 2-hexylcyclopropanecarboxylate which could be isolated in 91% yield. The cyclopropanation of hexene-1 with diazomethane affords butylcyclopropane under mild conditions.[39] The mixture darkened as the reaction progressed and was almost black when complete. If additional copper(II) triflate was added at this point the darkened reaction mixture rapidly lightened to a clear pale blue solution, from which copper(I) triflate was isolated in good to excellent yields in the form of the crystalline complex with 1,5-cyclooctadiene.[17]



These experiments show that diazomethane is capable of reducing copper(II) triflate in the course of cyclopropanation. The dark coloration can be attributed to colloidal copper(0) since copper(I) can be obtained by syn proportionation with copper(II) in the presence of

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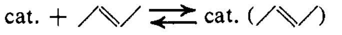
[35] G. B. Payne, *J. Org. Chem.*, 32, 3351 (1967).

[36] Excess iodide would be expected to sequester the copper by coordination with $(CH_3O)_3PCuI$ to give an unreactive diiodocuprate(I), in which further interaction with diazo compounds would be suppressed. The alternative explanation[5] involving the ionization of the neutral complex in these nonpolar solvents is not favored.

[37] A similar dependence has been observed in the copper stearate catalyzed reactions[6] and attributed to the equilibrium:[6c]



[38] There is no evidence for copper(II)–olefin complexes except under special circumstances: R. A. Zelonka and M. C. Baird, *J. Organometal. Chem.*, 33, 267 (1971).

[39] In these studies diazomethane was always introduced with ether for safety.

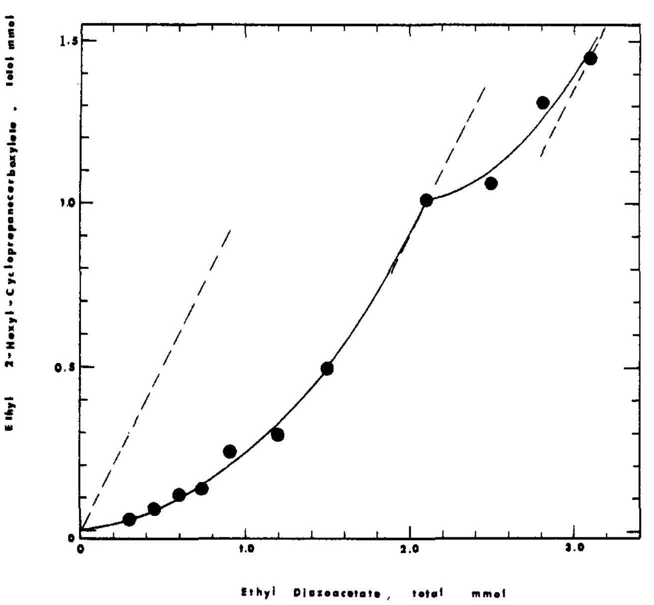
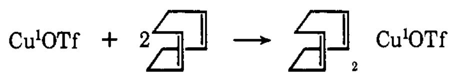


Figure 4. Homogeneous cyclopropanation of octene-1 with incremental amounts of ethyl diazoacetate in the presence of copper(II) triflate (0.68 mmol) in methyl acetate solutions. Dashed lines represent theoretical slopes for quantitative yield of adduct from diazo compound. Additional copper(II) triflate (0.40 mmol) was added after a total of 2.1 mmol of diazoacetate was added.

an olefinic ligand (compare eq 2). The highly colored

$$Cu^{II}(OTf)_2 + RCHN_2 \longrightarrow \underset{\mathbf{8}}{[RCH]_{ox}} + Cu^{I}OTf \rightleftharpoons Cu^0 + Cu^{II} \quad (14)$$

solutions associated with colloidal forms of copper(0)



(15)

have been described previously.[40]

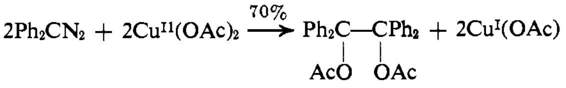
The changing nature of copper(II) triflate during the course of cyclopropanation can also be observed with ethyl diazoacetate. Addition of diazoacetate to a suspension of copper(II) triflate in hexene-1 or tetramethylethylene was followed by an induction period before nitrogen was evolved. Additions of more diazoacetate were followed by successively shorter induction periods. The reduction of copper(II) triflate was not as apparent in this system as it was with diazomethane since the mixture took on the appearance of a dark color only after rather large amounts of diazoacetate had been added relative to copper. We infer that copper(II) is also reduced by diazoacetate (although less readily than by diazomethane)[41] to copper(I) which is the effective catalytic species. However, the rigorous differentiation between a homogeneous and a heterogeneous catalytic process based on copper(I) and copper(II) species, respectively, is extremely difficult to establish, since solubility of copper(I) in imperceptible amounts could be responsible for the apparently heterogeneous process. We examined, therefore, the activity of copper(II) species in a homogeneous medium.

II. Homogeneous System for Copper(II) Catalysis. Homogeneous catalytic systems are often studied as models of related heterogeneous systems. We found that copper(II) triflate, insoluble in olefins, can be dissolved in a mixture of octene-1 and 20% (v/v) methyl acetate. The yield of ethyl 2-hexylcyclopropanecarboxylate (**3**) is given in Figure 4 as a function of the amount of ethyl diazoacetate added to this solution. The yield of **3** was negligible initially. Furthermore, after the addition of 1 equiv (0.7 mmol) of ethyl diazoacetate relative to copper(II) triflate, the yield of **3** was still less than 20%. As the addition of ethyl diazoacetate was continued, the yield of **3** eventually approached quantitative (based on the incremental amounts of ethyl diazoacetate added). The addition of more copper(II) triflate at this point caused a sharp drop in the relative yield of **3**, but with continued addition of ethyl diazoacetate the yield increased again to the limiting value of 100%.

The reaction mixture remained homogeneous at all times during these manipulations. No darkening of the reaction mixture was observed to indicate the formation of copper(0). The colorless copper(I) triflate could be isolated as the crystalline 1,5-cyclooctadiene complex in excellent yields. Clearly, the *nominal* catalyst, copper(II) triflate, does not catalyze the cyclopropanation of octene-1 with ethyl diazoacetate. Rather, the diazo compound is oxidized (*vide infra*) by copper(II) triflate, which is reduced to copper(I) triflate as we have shown to occur under heterogeneous conditions. The latter must be the *actual* catalyst for cyclopropanation. Moreover, the identical selectivities observed in the competitive cyclopropanation of different olefins under either heterogeneous or homogeneous conditions (*vide infra*) strongly suggest that the *actual* catalyst in both of these systems is the same.

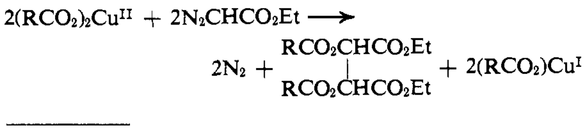
Other workers have reported similar though less conclusive observations. For example, D'yakonov observed the formation of black precipitates and metallic mirrors during the copper(II) sulfate catalyzed reactions of ethyl diazoacetate and suggested that colloidal copper(0) was the actual catalyst.[10,11,42] Wittig observed the precipitation of a finely powdered suspension during the reaction of diazomethane with cyclohexene in the presence of copper(II) chloride.[9] He suggested that copper(I) chloride, the ether insoluble material, was the actual cyclopropanation catalyst.

Oxidation of diazo compounds represented in eq 14 has also been observed with diphenyldiazomethane and copper(II) carboxylates in aqueous dimethylformamide solutions, *e.g.*[14]



$$2Ph_2CN_2 + 2Cu^{II}(OAc)_2 \xrightarrow{70\%} \underset{AcO\quad OAc}{Ph_2C{-}CPh_2} + 2Cu^{I}(OAc) \quad (16)$$

Similarly, the heterogeneous oxidation of ethyl diazoacetate by copper(II) carboxylates produced the corresponding diesters of diethyl tartrate (90%) and copper(I) carboxylate (94%).[13]



$$2(RCO_2)_2Cu^{II} + 2N_2CHCO_2Et \longrightarrow 2N_2 + \begin{array}{c} RCO_2CHCO_2Et \\ | \\ RCO_2CHCO_2Et \end{array} + 2(RCO_2)Cu^{I} \quad (17)$$

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[40] (a) M. Tamura and J. K. Kochi, *J. Organometal. Chem.*, **42**, 205 (1972); (b) *cf.* for silver(0), M. C. Lea, *Amer. J. Sci.*, **37**, 476 (1889).

[41] Diazomethane may also be more readily decomposed catalytically by copper(I).

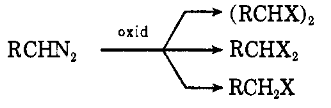
[42] In view of the extremely ready disproportionation of copper(I) in the absence of coordinating ligands, it is difficult, if not impossible, to avoid copper(0). Catalysis by the latter is possible but not demanded by the data.

Since copper(I) stearate appeared to be resistant to further modification by diazoacetate, it was suggested[13] that copper(I) species are the actual catalysts in the homogeneous decomposition (eq 18). Copper(I) stearate is rapidly autoxidized to a green basic copper(II) stearate, which can account for the inhibitory effect of oxygen on the rate of the homogeneous copper(II) stearate catalyzed decomposition of ethyl diazoacetate.[8]

$$2N_2CHCO_2Et \xrightarrow{C_{17}H_{35}CO_2Cu^I} 2N_2 + EtO_2CCH{=}CHCO_2Et \qquad (18)$$

$$2C_{17}H_{35}CO_2Cu^I + {}^1/_2O_2 \longrightarrow (C_{17}H_{35}CO_2Cu^{II})_2O \qquad (19)$$

It has been noted that cyclopropanation of olefins by diazo compounds is consistently effected in higher yields under heterogeneous conditions. Oxidative side reactions of the diazo compounds could account for all of these observations, since such side reactions can proceed to completion more readily under homogeneous compared to heterogeneous conditions. In the latter case, modification of only a small portion of the solid might be needed to produce a soluble highly active catalyst. The reduction of copper(II) triflate shown above under both conditions is supported by a number of other examples in which the side products (**8** in eq 14) derived from the oxidation of diazo compounds have been identified.[14]



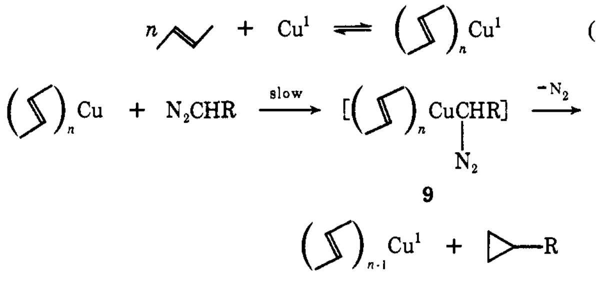
$$\mathrm{RCHN_2} \xrightarrow{\text{oxid}} \begin{cases} \mathrm{(RCHX)_2} & (20a) \\ \mathrm{RCHX_2} & (20b) \\ \mathrm{RCH_2X} & (20c)^{43} \end{cases}$$

$R = EtO_2C, PhCO, RCO$
$X = Cl, SBu, OAc$

Role of Olefin Coordination in the Copper Catalyzed Cyclopropanation of Olefins. I. Mechanisms of Catalyzed Cyclopropanation. The difference in the reactivity of diazo compounds in catalyzed reactions in comparison to the thermally or photochemically induced reactions has led to the postulation of coordination of the diazo compound and/or the derived carbenes to the metal.[29] In addition, changes in the ratios of the stereoisomeric products with variation of the ligands on the catalyst,[3] as well as the induction of optical activity in the products by optically active ligands,[3,30b] have been adduced as evidence for the presence of diazo compound (or derived carbene), metal ion, and olefin in the transition state leading to cyclopropane. Furthermore, the relative reactivity of dimethyl diazomalonate toward increasingly substituted olefins differs in cyclopropanations catalyzed by (MeO)₃PCuI and those induced photochemically.[5,44]

Two basic mechanisms have remained indistinguishable on the basis of the evidence at hand. In Scheme I, the diazo compound reacts directly with a metal–olefin complex or *via* a metastable ternary complex **9**. If the latter is formed, it is only a transient intermediate since it cannot be detected by nmr even at low temperatures (*vide supra*). In either case, according to this mechanism the relative reactivities of different olefins should be heavily dependent on the stabilities of the olefin–copper(I) complexes.

Scheme I



(21)[16]

(22)

Alternatively, a pathway may be considered as in Scheme II, which involves bimolecular transfer of the carbene from a metal complex to a free olefin either with or without direct interaction of the olefin with the metal in the transition state. Since the metal-complexed carbene or carbenoid should be quite reactive, its electronic and steric demands are expected to be product determining. It should be noted that the olefin-free complex **4** and/or **5** could arise by reaction of the diazo compound either directly with the olefin-free catalyst or by displacement of the coordinated olefin from the catalyst since exchange (eq 21) is rapid.[19,46]

Scheme II

$$\mathrm{Cu^I + N_2CHR \xrightarrow{slow} \underset{\mathbf{4}}{\overset{\overset{N_2}{|}}{Cu}CHR} \xrightarrow[{[?]}]{-N_2} \underset{\mathbf{5}}{CuCHR}} \qquad (23)^{16,45}$$

(24)

In each of these mechanisms, olefin can compete with the diazo compound for coordination sites on copper(I). To differentiate between these mechanistic categories, we examined the relative reactivities of different olefins toward cyclopropanation with several diazo compounds and copper catalysts.

II. Relative Rates of Methylene Transfer. The relative reactivities of various substituted olefins toward diazomethane were determined in a 1 : 1 mixture of a pair of olefins. Diazomethane (entrained by dry nitrogen from an ethereal solution) was passed through the olefin mixture at 0–10° in the presence of catalytic amounts of copper(II) triflate or acetylacetonate. The reaction was interrupted before 10% of the olefin had been cyclopropanated, and the mixture of products analyzed quantitatively by gas chromatography using the internal standard method. Competitive cyclopropanation of tetramethylethylene (**10**) and hexene-1 (**11**) with diazomethane catalyzed[47] by copper(II) acetylacetonate resulted in the preferential reaction of

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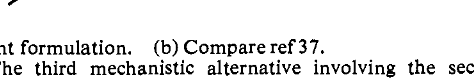
(43) Formally, no change in oxidation state is required to proceed from carbene RCH to RCH₂X. The latter, however, may be formed by two successive free-radical reactions (H atom and ligand transfer) in which case the copper species may suffer reduction: J. K. Kochi, "Free Radicals," Wiley-Interscience, New York, N. Y., 1973, Chapter 11.

(44) The parallel between the reactivity of olefin in the catalyzed process with its stability in the copper(I) halide complex toward diazomalonate has also been interpreted as evidence for a ternary complex leading to products.[5] Steric factors in this carbene precursor, however, may have influenced the reactivity pattern of these olefins, since there is no evidence for olefin complexation with the catalyst used.

(45) (a) Displacement of coordinated olefin by diazo compound is an

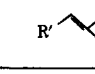
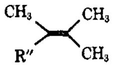


equivalent formulation. (b) Compare ref 37.

(46) The third mechanistic alternative involving the second-order reaction of a coordinated carbene with a coordinated olefin has been discounted by kinetic studies.[6a]

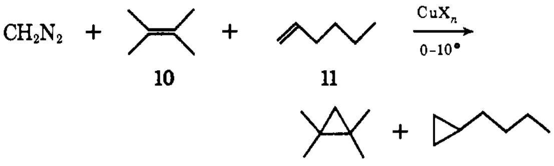
(47) Catalysis is used loosely in this context since copper(II) is reduced prior to catalysis.

Table II. Relative Reactivity of Olefins toward Methylene Transfer

Methylene transfer agent	Olefin			Ref
				
ICH_2ZnI	1.00	5.3[b,e,g]	3.3	i
$Hg(CH_2Br)_2$	1.00	19.1[b,e,h]	122[b,h]	j
CH_2N_2-Cu(*N*-α-phenethyl salcylaldiminate)$_2$	1.00	5.54[c,e,g]	5.77[e,g]	30b
CH_2N_2–Cu(acac)$_2$	1.00	6.0[d,f,g]	6.7[a,g]	This work
CH_2N_2–Cu(OTf)$_2$	1.00	0.52[d,f,g]	0.27[a,g]	This work

[a] R = *n*-butyl. [b] R = *n*-pentyl. [c] R = *n*-hexyl. [d] R = $(CH_3)_2C{=}CH(CH_2)_3^-$. [e] R′ = methyl. [f] R′ = $CH_2{=}CH(CH_2)_3^-$. [g] R″ = methyl. [h] R″ = ethyl. [i] E. P. Blanchard and H. E. Simmons, *J. Amer. Chem. Soc.*, **86**, 1337 (1964). [j] D. Seyferth, R. M. Turkel, M. A. Eistert, and L. J. Todd, *ibid.*, **91**, 5027 (1969).

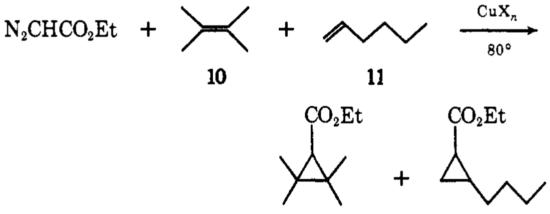
the more highly substituted olefin **10**. The only volatile products consisted of 87% 1,1,2,2-tetramethylcyclopropane (**12**) and 13% *n*-butylcyclopropane (**13**).



10 **11** **12** **13** (25)

On the other hand, **11** was preferentially cyclopropanated with copper(II) triflate to afford 79% **13** and 21% **12**. These results are summarized in Table II and compared with other representative data previously reported for the relative reactivity of olefins in methylene transfer reactions.

A similar variation in the selectivity of olefin cyclopropanation with different copper catalysts was observed in the reaction of ethyl diazoacetate. Ethyl diazoacetate was added under nitrogen to a gently refluxing mixture of catalyst and a large excess of an equimolar mixture of **10** and **11**. The relative yields of the cyclopropanated adducts **14** and **15** obtained with various copper complexes are given in Table III. The results in Table III show that the terminal olefin **11** was preferentially cyclopropanated in the presence of CuOTf, Cu(OTf)$_2$, and Cu(BF$_4$)$_2$, whereas the more highly substituted isomer **10** reacted more readily with $(CH_3O)_3PCuX$, Cu(acac)$_2$, and $CuSO_4$ as catalysts.



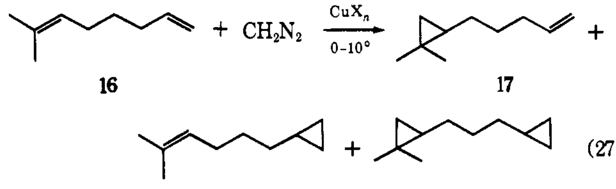
10 **11** **14** **15** (26)

Table III. Effect of the Copper Catalyst on the Selectivity of Olefin Cyclopropanation with Diazoacetate

Copper complex[a]	Cyclopropanated products: Overall yield (%) 14 + 15	Mole fraction 14	Mole fraction 15
CuOTf	84	0.20	0.80
Cu(OTf)$_2$	98	0.21	0.79
Cu(BF$_4$)$_2$	98	0.19	0.81
$(CH_3O)_3PCuI$	36	0.64	0.36
$(CH_3O)_3PCuCl$	60	0.58	0.42
Cu(acac)$_2$	96	0.64	0.36
$CuSO_4$	b	0.64	0.36

[a] Copper compound added initially. [b] No yield, from ref 29.

Intramolecular competition can also be employed to show the selective cyclopropanation of different olefinic bonds. Thus, the diolefin **16** underwent preferential cyclopropanation to the more highly substituted cyclopropane **17** with diazomethane and Cu(acac)$_2$. At low conversions, the cyclopropanated products consisted of 86% **17** and 14% **18**. The addition of diazomethane was continued to about 90% conversion, and the product then consisted of a 1:0.1:0.6 mixture of **17**, **18**, and the dicyclopropane **19**, respectively. On the other hand, the less substituted cyclopropane **18** was formed preferentially with Cu(OTf)$_2$ as catalyst. The products initially were a mixture consisting of 66% **18** and 33% **17**, but continued addition of diazomethane until approximately 50% of **16** had reacted afforded a a 1:2.5:0.4 mixture of **17**, **18**, and **19**, respectively.



16 **17** **18** **19** (27)

III. Mechanistic Distinctions Based on Olefin Selectivities. The enhanced reactivity of olefins which possess alkyl substituents generally observed in copper catalyzed cyclopropanations has been interpreted to result from the electron seeking character of the attacking agent. The preferential cyclopropanation of the least substituted olefins by diazo compounds is unusual, and effected by those copper salts with poorly coordinating ligands such as OTf$^-$ and BF$_4^-$.[48] Olefin coordination should play a proportionately greater role in catalytic reactions involving these copper salts because of their enhanced proclivity to coordinate with additional ligands.[49] Thus, the behavior observed with copper(I) triflate is consistent with a mechanism involving coordination of the diazo compound with an equilibrium mixture of copper(I)–olefin complexes followed or accompanied by rapid intramolecular collapse to products (compare Scheme I). The measured activation param-

(48) For copper(I) tetrafluoroborate, see (a) D. A. McCauley, U. S. Patent 2,953,589; *Chem. Abstr.*, 55, P3050a (1961); (b) M. Dines, private communication.

(49) It is unlikely that the distinction between copper triflate and copper acetylacetonate is due to a difference in the electrophilic character of the carbene complex, since weakly coordinating ligands would be expected to *enhance* the electrophilicity of the carbenoid.

eters (eq 6) under these circumstances represent a composite of a preequilibrium change in free energy for olefin complexation as well as the kinetic process leading to the cyclopropanation itself. Enthalpy and entropy changes for olefin complexation may be compared with values for silver(I),[25] but further speculation is avoided until these values are determined for copper(I) triflate.

The capacity of copper(II) to coordinate with olefins is very slight, at best.[38] Hence, it is difficult to rationalize the behavior of copper(II) triflate and fluoroborate in promoting selective cyclopropanation of olefins (as that observed with copper(I) triflate) to a similar degree of complexation. We are forced, thus, to conclude, as stated earlier, that *nominal* catalysis by copper(II) triflate and fluoroborate actually involve catalysis by the corresponding copper(I) salt.[48]

The relative reactivities of different olefins by Scheme I should depend heavily on the stabilities of the corresponding copper(I)–olefin complexes. It is understandable, therefore, that such sterically and electronically different carbenes as methylene and carbethoxymethylene can exhibit quite similar selectivities. The latter, however, are quantitatively differentiated by various copper catalysts as shown by the selectivities summarized in Table IV. Thus, the relative reactivities of hexene-1 and tetramethylethylene are the *same* toward CH_2 and $CHCO_2Et$ using a copper triflate catalyst. These results are in accord with Scheme I, in which olefin coordination to copper(I) largely determines selectivity, rather than carbene reactivity. On the other hand, copper acetylacetonate in common with the phosphite, halide, and sulfide complexes show opposed selectivities. The greater reactivity of the highly substituted tetramethylethylene with these catalysts indicates that olefin coordination is not important, a conclusion which is supported by the nmr studies. We favor Scheme II for these catalysts in which selectivity is largely determined by electrophilic attack of the transient carbene complex (**4** or **5**) on the olefin. The greater selectivity shown by CH_2 compared to $CHCO_2Et$, despite its greater reactivity (*cf.* 2 and 4, Table IV), may be attributed to steric differences.[50]

Table IV. Olefin Selectivity, Carbenes, and Copper Catalyst

No	Diazo compd	Copper catalyst	Selectivity 11	 10
1	N_2CHCO_2Et	CuOTf $CuBF_4$	79–81	21–19
2	N_2CHCO_2Et	Cu(acac) $CuP(OCH_3)_3I$	36	64
3	N_2CH_2	CuOTf	79	21
4	N_2CH_2	Cu(acac)	13	87

The coordinative interaction of olefins with $(Bu_2S)_2CuI$ with displacement of dibutyl sulfide has been suggested.[4] We previously showed that chemical shifts of 10–50 Hz result in the nmr resonances of the vinylic protons when olefins coordinate with copper(I) triflate or perchlorate.[19] However, we observed no such shifts when the nmr spectra of various olefins were examined in the presence of a molar equivalent of $(Bu_2S)_2CuI$ or $(CH_3O)_3PCuI$. Complexes such as $(CH_3O)_3PCu^{I}I$, $(CH_3O)_3PCu^{I}Cl$, $(Bu_2S)_2CuI$, and $Cu^{II}(acac)_2$ all have strongly coordinating ligands and are expected to interact only weakly with olefins. The greater reactivity of the more highly alkylated olefins in cyclopropanations with these catalysts is not consistent with a mechanism in which the product distribution depends on the stabilities of the olefin–metal complex.[27] The product distribution instead reflects a control determined by the electrophilicity of the methylene transfer agent.[1,51] Moreover, the previous correlation of olefin reactivities with the stabilities of the olefin–metal complexes reported for the $(CH_3O)_3PCuI$ catalyzed cyclopropanation with diazomalonate[5] is reversed with ethyl diazoacetate (see Table II). We attribute the difference between dimethyl diazomalonate and ethyl diazoacetate to greater steric demands of the carbenoid–copper complex derived from diazomalonate in Scheme II, and not to preferential coordination of the less substituted olefin with the metal (Scheme I). The latter appears to be operative only with copper complexes containing weakly coordinating ligands.

Finally, the control of regioselectivity in the cyclopropanation of polyenes by variation of the anionic ligands on the copper catalyst should be valuable for organic synthesis. In addition, the exceptional activity and solubility of these copper species in olefins even below 0° recommend their use as catalysts for cyclopropanation under extremely mild conditions. Allyl-

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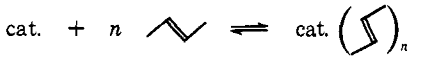
(50) (a) The transition state in Scheme II may be highly congested if the olefin is also partially bonded to copper.[3,4] The lack of observation of an inner-sphere complex between olefin and copper(I) in these complexes does not of course preclude such a formulation of the *transition state*. (b) Compare also ref 44.

(51) (a) A referee has suggested that the preferential cyclopropanation of the least substituted olefin with CuOTf as catalyst and of the most substituted olefin with $(RO)_3PCuX$ as catalyst is better explained as an *unusual* difference in the complexing ability of the metal ion for olefin. Thus, the opposed selectivities observed might be the result of a reversal of coordinating abilities of different complexes of a single metal (*i.e.* due to other ligands) for nucleophilic and nonnucleophilic olefins. We disfavor this alternative explanation. Although it cannot be excluded on the basis of the evidence at hand, several facts militate against its acceptance. Strongly associating counterions such as halide greatly diminish the ability of Cu(I) to coordinate with olefins compared with triflate.[17,51b] Alkyl phosphite ligands also compete with olefin for Cu(I) coordination sites.[51c] Thus olefin coordination by catalysts such as $(RO)_3PCuI$ and $(Bu_2S)_2CuI$, if any, should be very weak compared with CuOTf. The equilibrium



should lie far to the left. We and others[6c] have noted a decrease of catalyst activity due to saturation of catalyst coordination sites by olefin coordination. Olefin complexes of $(Bu_2S)_2CuI$ or of monomeric $(RO)_3PCuI$, if formed, would thus have greatly diminished reactivity toward diazo compounds compared with olefin-free catalyst. Also, we have shown that catalysts such as $(RO)_3PCuI$ and $(Bu_2S)_2CuI$ do not coordinate with olefins in the absence of diazo compounds, which may be due to the inability of olefins to cleave oligomeric catalyst aggregates. It has been suggested[3] that catalyst aggregates may be cleaved by diazo compound to give an olefin-free monomeric intermediate. We expect such an intermediate would be too reactive to equilibrate with olefin. We and others[4] have demonstrated that such carbene–Cu(I)–olefin complexes must have, at most, only a fleeting existence. Selectivity would not, therefore, be determined by the relative stability of olefin catalyst complexes. (b) Olefin complexes of copper(I) halides are known.[52] However, they dissociate readily and the likelihood that they are completely dissociated in solution has been previously noted.[53] (c) R. G. Salomon and J. K. Kochi, unpublished results.

(52) (a) H. L. Haight, J. R. Doyle, N. C. Baenziger, and G. F. Richards, *Inorg. Chem.*, **2**, 1301 (1963); (b) E. O. Fischer and H. Werner, "Metal π-Complexes," Vol. I, Elsevier, Amsterdam, 1966; M. Herberhold, Vol. II, 1972; C. P. Heimbach and R. Traunmuller, "Chemie der Metal-olefin Komplex," Verlag Chemie, Weinheim/Bergstr., Germany, 1970.

(53) (a) E. W. Abel, M. A. Bennett, and G. Wilkinson, *J. Chem. Soc.*, 3178 (1959); (b) G. M. Whitesides, G. L. Goe, and A. L. Cope, *J. Amer. Chem. Soc.*, 91, 2608 (1969).

palladium chloride dimer is a similarly active catalyst,[54] but the reported yields in cyclopropanation are only fair to poor and the selectivity will be predictably different. Palladium diacetate has also been recently reported[55] to be an active homogeneous catalyst for cyclopropanation and coordination of olefin may be mechanistically important. Moreover, it is likely that examples of catalyzed methylene transfer which proceed by both mechanistic categories outlined above will be found with catalysts other than copper.

Summary

Regioselectivity in the copper(I) catalyzed cyclopropanation of olefins exhibits a striking dependence on the nature of the ligands on the catalyst. This dependence results from the ability of various copper(I) complexes to coordinate olefins. For copper(I) salts which coordinate strongly with olefins, regioselectivity is determined by the relative stabilities of the metal–olefin complexes. On the other hand, for copper(I) complexes which do not coordinate strongly with olefins, regioselectivity is controlled by a combination of steric and electronic properties of the carbene and olefin.

The nature and number of ligands (including olefins) associated with copper(I) affect its catalytic activity since diazo compounds must compete with these ligands for coordination to the copper(I) nucleus. Ethyl diazoacetate does not form a stable α-organocopper diazonium salt or carbenoid with copper(I) triflate in the presence of olefins. If such species are intermediates they have transient existence and contrast with the reaction of analogous ethyl sulfuranylidene acetate with copper(I) triflate to form stable α-organocopper sulfonium salts with concomitant displacement of an olefinic ligand.

Copper(II) triflate and tetrafluoroborate can be used effectively under heterogeneous conditions. They are not, however, the active catalysts for cyclopropanation, but are reduced by diazo compounds *in situ* to the catalytically active copper(I) species.

Experimental Section

Elemental microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich. 48106. Cu(I) was analyzed by reaction with excess Fe(III) and back titration of the resulting Fe(II) with dichromate. Nmr spectra were obtained with a Varian A-60A or HR100 spectrometer with a low-temperature probe. Vapor phase chromatography was performed on a Varian A90 or Aerograph Hi Fy chromatograph. Infrared spectra were measured with a Perkin-Elmer 137G spectrometer. Olefins were purified by careful distillation, followed by passage through a column of Woelm Activity I basic alumina under a blanket of dry nitrogen. They were degassed by bubbling a stream of dry nitrogen for 30 min. All reactions were also carried out under a blanket of dry nitrogen. Vapor phase chromatographic (vpc) determinations of product compositions are corrected for differences in detector sensitivity by calibration with standard samples.

Homogeneous Copper(II) Triflate Catalyzed Decomposition of Ethyl Diazoacetate in the Presence of Octene-1. A carefully dried 15-ml round-bottom flask containing a small magnetic stirring bar and fitted with a reflux condenser and with a side neck fitted with a rubber serum cap was charged with $Cu(OTf)_2$ (247 mg 0.68 mmol), octene-1 (5 ml), and methyl acetate (3 ml). Ethyl phenylacetate (90 μl, 0.56 mmol) was added as internal standard. Then portions of diazoacetate were added with a hypodermic syringe to the boiling reaction mixture. Samples (30–40 μl) of the reaction mixture were analyzed by vapor phase chromatography after each addition (10 ft × 0.25 in. 15% FFAP on Chromosorb P 60–80 column at 170°). The results are plotted in Figure 4.

Cuprous Triflate–Benzene Complex (1). The reaction vessel consisted of two 100-ml one-neck, round-bottom flasks connected with a glass tube of 2-cm diameter in the middle of which was a medium porosity sintered glass disk. One of the flasks was charged with 2 g (14 mmol) of cuprous oxide, 80 ml of dry benzene, and 5.5 g (19.5 mmol) of trifluoromethenesulfonic anhydride. A magnetic stirring bar was added and the flask was fitted with a condenser which was connected through a gas outlet adapter to a mineral oil bubbler. The other flask was fitted with a gas inlet adapter which had a second inlet which was sealed with a rubber serum cap. A slow stream of dry nitrogen was pased into the latter flask and out of the former *via* the condenser. The reaction mixture was boiled under gentle reflux with magnetic stirring for several hours until the red Cu_2O had dissolved affording a clear solution. The gas flow was reversed and the hot solution was filtered into the second flask. Upon cooling to room temperature a white complex crystallized from the solution. Reversal of the gas flow allowed back filtration for removal of the mother liquor. The product was washed with two 10-ml portions of fresh benzene which were added with a hypodermic syringe through the serum cap. The washings were removed by filtration. The product was dried under a stream of dry nitrogen. The complex (5.5 g, 77%) thus obtained turns orange-brown upon exposure to air and must be handled in an inert atmosphere.

Anal. Calcd for $C_8H_6Cu_2F_6O_6S_2$: C, 19.09; H, 1.20; Cu(I), 25. Found: C, 18.47; H, 1.23; Cu(I), 24.

Reaction of 2-Butenes with Ethyl Diazoacetate in the Presence of 1. A two-necked, round-bottom, 200-ml flask was fitted with a stopper in one neck and in the other a 25-ml pressure equalizing addition funnel which in turn was fitted with a Dry Ice–acetone cooled condenser which was connected to a nitrogen line provided with a mineral oil bubbler. The addition funnel was modified with an inlet near the top which was sealed with a serum cap. The complex (1) (1.3 g, 5.2 mequiv of Cu^+) was placed into the flask under an atmosphere of dry nitrogen. Then 50 ml (0.6 mol) of either *cis*- or *trans*-2-butene was condensed into the flask through a hypodermic needle through the serum cap. The catalyst dissolved to give a colorless solution. Then 4.5 g (39 mmol) of diazoacetate was added in 0.5-g portions to the addition funnel with a hypodermic syringe. Each portion of diazo ester was diluted with about 4 ml of olefin and then added dropwise with magnetic stirring to the reaction mixture. After completion of the addition, the mixture was allowed to boil under reflux with stirring for another hour. Excess olefin was then evaporated and the residue taken up in ether and 10 ml of a saturated aqueous solution of NH_4Cl to which NH_3 had been added until the pH reached 9. After thorough extraction of the aqueous phase, the organic extracts were washed with another 10 ml of NH_4Cl–NH_3 solution and then with water. After drying ($MgSO_4$) and removal of ether by distillation, the residue was distilled under reduced pressure. *trans*-2-Butene yielded 3.2 g (53%) of pure ethyl *trans*-2,3-dimethylcyclopropanecarboxylate while *cis*-2-butene yielded 3.1 g (51%) of a mixture of isomeric ethyl *cis*-2,3-dimethylcyclopropanecarboxylates.

Reaction of EDA with Norbornylene–Copper(I) Triflate Complex at Low Temperature. A solution of norbornylene–copper(I) triflate[17] (31 mg, 0.1 mmol) in acetone (0.2 ml) was treated with EDA (0.1 mmol) at −76°. No nitrogen evolution was observed. The nmr spectrum of the mixture resembled a superposition of the individual components. Especially noteworthy is the fact that the absorptions associated with the methine proton of the diazo ester were unshifted. Upon warming, these absorptions gradually decreased in intensity but *did not shift* as the diazo compound underwent decomposition. In another experiment, the solution was allowed to gradually warm while the temperature of the cooling bath was monitored. A gentle effervescence began when the temperature of the solution reached about −45°. Upon cooling, the evolution of nitrogen ceased, and resumed upon warming once again.

Reaction of Ethyl Diazoacetate with (*E*,*E*,*E*)-1,5,9-Cyclododecatriene–Copper(I) Triflate at Low Temperature. Ethyl diazoacetate (0.2 mmol) was added to a solution of (*E*,*E*,*E*)-1,5,9-cyclododecatriene–copper(I) triflate[17] (74 mg, 0.2 mmol) in $CDCl_3$ (0.3 ml) at −76°. No nitrogen evolution was observed. The nmr spectrum of the mixture consisted of a superposition of the spectra of the individual components. The solution was allowed to gradually warm while the temperature of the cooling bath was

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(54) R. K. Armstrong, *J. Org. Chem.*, 31, 618 (1966).

(55) R. Paulissen, A. J. Hubert, and Ph. Teyssie, *Tetrahedron Lett.*, 1465 (1972).

monitored. A very gentle effervescence began when the temperature of the solution reached −20°. At 5° the evolution of gas was vigorous.

Reaction of CuOTf with Ethyl (Dimethylsulfuranylidene)acetate. The nmr spectrum of ethyl (dimethylsulfuranylidene)acetate[35] in $CDCl_3$ consisted of an absorption at δ 2.8 due to the single proton on the anionic carbon, the methine proton. Addition of the CuOTf–benzene complex to this solution resulted in the selective downfield shifting of this absorption, as shown in Figure 3. The foregoing experiment was repeated using (*E,E,E*)-1,5,9-cyclododecatriene–copper(I) triflate[17] in place of the complex (**1**). The absorption of the methine proton was shifted downfield as also shown in Figure 3. The absorptions due to protons of the olefin appeared at the same positions as for the free olefin (substantially different from those of the olefin–copper complex).

Nmr Spectrum of $(Bu_2S)_2CuI$–Norbornylene Mixtures. The nmr spectra of norbornylene, Bu_2S, $(Bu_2S)_2CuI$,[4] and of a mixture containing 1 mmol of norbornylene and 0.3 mmol of $(Bu_2S)_2CuI$ in 0.3 ml of CCl_4 were compared. The α-methylene protons in Bu_2S which appear at δ 2.45 (triplet) are shifted downfield to δ 2.62 in the CuI complex. In the presence of approximately 3 equiv of norbornylene [a relatively strongly coordinating olefin toward Cu(I)], this resonance is unshifted from δ 2.62 indicating no displacement of sulfide ligand from the CuI complex. Moreover, the vinyl proton resonance of norbornylene, which is shifted from δ 6.00 to 5.15 by coordination with Cu(I) in its 1:1 complex with CuOTf,[19] appears at δ 6.00 as expected for free olefin. This observation suggests the absence of any olefin coordination by $(Bu_2S)_2CuI$ in solution.[51b]

Isolation of Copper(I) Triflate from the Reaction of Copper(II) Triflate with Diazomethane in Hexene-1. Anhydrous copper(II) triflate[18] (150 mg) and hexene-1 were placed in a 25-ml test tube equipped with a side arm, a magnetic stirring bar, and a one-hole rubber stopper through which an inlet tube protruded almost to the bottom of the tube. A stream of nitrogen was bubbled through a solution of diazomethane in ether and then (containing entrained diazomethane and ether vapor) through the suspension of $Cu(OTf)_2$ in hexene-1 with magnetic stirring and ice–water bath cooling. The reaction temperature was maintained at about 10–20° (at lower temperatures the reduction of the catalyst was less efficient). Addition of diazomethane was continued until the reaction mixture began to turn black. Then more $Cu(OTf)_2$ (20 mg) was added. The black dissolved and the mixture became light green. The mixture was filtered under nitrogen and then an excess of 1,5-cyclooctadiene was added to the clear filtrate. A crystalline olefin complex precipitated from the solution. The solid was collected, washed with pentane, and dried to yield bis(1,5-cyclooctadiene)-copper(I) triflate[17] (210 mg, 0.49 mmol) corresponding to roughly a quantitative yield.

Competitive Cyclopropanations of Tetramethylethylene and Hexene-1 with CH_2N_2. $Cu(OTf)_2$ (0.3 g) or $Cu(acac)_2$ (0.3 g) and 5 ml of a 1:1 mixture of hexene-1 and tetramethylethylene were placed in a 25-ml test tube and equipped with a side arm, a magnetic stirring bar, and a one-hole rubber stopper through which an inlet tube protruded to within 0.25 in. of the bottom of the test tube. A stream of dry nitrogen was bubbled through a KOH dried solution of CH_2N_2 in ether. The entrained diazomethane (and some ether) was bubbled through the magnetically stirred reaction mixture at 0–10° (ice–water bath). Unreacted CH_2N_2 which exited from the reaction vessel was conducted through a 3 ft Tygon tube to the back of a fume cupboard. The composition of the reaction mixture was monitored by vpc on a 12 ft × 0.25 in. 5% bentone 34 and 15% didecyl phthalate on 60–80 HMDS treated Chromosorb W column at 90°. The only volatile products detected were 1,1,2,2-tetramethylcyclopropane and *n*-butylcyclopropane. Relative retention times on this column were: hexene-1, 1.00; 1,1,2,2-tetramethylcyclopropane, 1.19; tetramethylethylene, 1.44; *n*-butylcyclopropane, 2.25.

Intramolecular Competitive Cyclopropanation of 7-Methyl-1,6-octadiene (16) with Diazomethane. The procedure was similar to the above except that 50 mg of catalyst was used to cyclopropanate 0.83 g (1.0 ml) of methyloctadiene[56] in a 15-ml reaction vessel. After less than 10% of diene had been cyclopropanated the solutions remained light and clear. The relative proportions of monocyclopropanated products, 1-(4-pentenyl)-2,2-dimethylcyclopropane (**17**) and 5-methyl-4-hexenylcyclopropane (**18**), were determined by vpc on a 10 ft × 0.25 in. Apiezon J on Firebrick column at 180°. Relative retention times on this column were (*n*-octane) 1.00, (**16**) 1.36, (**17**) 1.60, (**18**) 2.60, and (**19**) 3.01. Addition of diazomethane was then continued until 50–90% of the diene had reacted. The resulting mixtures were again analyzed by vpc for relative yields of the two monocyclopropanated products and the diadduct, 1-cyclopropyl-3-(2′,2′-dimethyl)cyclopropylpropane (**19**), the only volatile reaction products. The results were summarized in the text. Addition of 20 mg more catalyst to the $Cu(OTf)_2$ catalyzed reaction mixture resulted in dissolution of the black sediment to give a clear light green solution. The final reaction mixtures were taken up in 30 ml of pentane and washed with two 20-ml portions of saturated aqueous NH_4Cl–NH_3 (pH 9), two 20-ml portions of water, and 20 ml of saturated brine, and dried (Na_2SO_4). Solvent was removed by distillation through a 10-in. Vigreux column. The reaction products and unreacted diene were separated by preparative vpc. The products were characterized as follows.

1-(4-Pentenyl)-2,2-dimethylcyclopropane (17). Colorless liquid: ir (neat) 915, 995, 1025, 1375, 1450, and 1640 cm^{-1}; nmr (CCl_4) δ 5.4–5.9 (1 H), 4.7–5.2 (2 H), 1.8–2.3 (2 H), 1.1–1.8 (5 H), 1.02 (6 H, s), 0.2–0.5 (2 H).

Anal. Calcd for $C_{10}H_{18}$: C, 86.88; H, 13.12. Found: C, 86.74; H, 13.24.

(5-Methyl-4-hexenyl)cyclopropane (18). Colorless liquid: ir (neat) 820, 1015, 1370, and 1440 cm^{-1}; nmr (CCl_4) δ 5.1 (1 H), 1.8–2.2 (2 H), 1.67 (3 H, s), 1.57 (3 H, s), 0.8–1.7 (5 H), 0.1–0.8 (4 H).

Anal. Calcd for $C_{10}H_{18}$: C, 86.88; H, 13.12. Found: C, 86.87; H, 13.30.

1-Cyclopropyl-3-(2′,2′-dimethyl)cyclopropylpropane (19). Colorless liquid: ir (neat) 1015 and 1450 cm^{-1}; nmr (CCl_4) δ 1.02 (6 H, s).

Anal. Calcd for $C_{11}H_{20}$: C, 86.76; H, 13.24. Found: C, 86.92; H, 13.17.

Competitive Cyclopropanations of Tetramethylethylene and Hexene-1 with Ethyl Diazoacetate. A carefully dried 15-ml flask containing a small magnetic stirring bar and fitted with a reflux condenser was charged with catalyst and 30 mmol each of hexene-1 and tetramethylethylene. The following amounts and catalysts were used: $(CuOTf)_2$–C_6H_6, 0.35 mmol; $Cu(OTf)_2$, 0.7 mmol; $Cu(BF_4)_2$, 0.5 mmol; $(MeO)_3PCuI$, 0.1 mmol; $(MeO)_3PCuCl$, 0.5 mmol; $Cu(acac)_2$, 0.5 mmol. In the case of $(MeO)_3PCuI$ catalysis, the olefins were intentionally *not* freed of peroxides or degassed. The mixture was boiled under reflux with magnetic stirring under a blanket of dry nitrogen while 1.5 mmol of diazoacetate was added dropwise with a hypodermic syringe. The needle was carefully positioned under the reflux so that the refluxing solvent washed the diazo ester from the needle thereby diluting it as it was slowly added over about 30 min. The reaction mixture was then analyzed for product composition and yield (using 0.38 mmol of ethyl phenylacetate added at the end of the reaction as internal standard) by vpc on a 15% FFAP on Chromosorb P column at 170°. Relative retention times on this column were: ethyl 2-butylcyclopropanecarboxylate, 0.42; 2,2,3,3-tetramethylcyclopropanecarboxylate, 0.23; ethyl phenylacetate, 1.00. The results are summarized in Table II.

Nmr Spectra of 1,5-Cyclooctadiene and Norbornylene in the Presence of $(MeO)_3PCuI$. A mixture of 126 mg (0.40 mmol) of $(MeO)_3PCuI$ and 43.5 mg (0.40 mmol) of 1,5-cyclooctadiene was dissolved in 0.5 ml of acetone-d_6 containing 2% tetramethylsilane. The nmr spectrum of this mixture was the same as a superposition of the absorptions of the individual components. A similar mixture was prepared with 0.40 mmol of norbornylene as olefin. Again, the olefin resonances were at the same position as in the absence of the cuprous complex.

Competitive Cyclopropanations of Hexene-1 and Tetramethylethylene with Ethyl Diazoacetate Catalyzed by $Cu(OTf)_2$ in Homogeneous Solution. A carefully dried 15-ml flask containing a small magnetic stirring bar and fitted with a reflux condenser was charged with $Cu(OTf)_2$ (234 mg, 0.66 mmol), 30 mmol each of **11** and **12**, and 2.5 ml of methyl acetate. Then ethyl diazoacetate was added dropwise to the gently boiling reaction mixture. The ratio of ethyl 2,2,3,3-tetramethylcyclopropanecarboxylate to ethyl 2-butylcyclopropanecarboxylate was determined by vapor phase chromatographic analysis of the reaction mixture after addition of 0.94, 1.41, and 1.88 mmol of ethyl diazoacetate. The ratio varied between 0.26 and 0.35. Ethyl phenylacetate was then added as internal standard, and the overall yield of cyclopropane products (44%) was determined. The reaction mixture was taken up

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(56) V. C. Solomon and D. Eros, *J. Amer. Chem. Soc.*, 80, 5455 (1958).

in 2-butanone (3 ml) and treated with an excess of 1,5-cyclooctadiene to yield a crystalline olefin complex[17] (171 mg, 61%).

Kinetics of the Copper(I) Triflate Catalyzed Reaction of Ethyl Diazoacetate with Hexene-1. Apparatus. A 50-ml or 25-ml round-bottom flask with a long neck, which had a small side neck near the top with a 10/30 female joint, and a small side neck fitted with a rubber septum, was fitted with an outlet adapter which had a three-way stopcock, one of the arms of which was sealed with a rubber septum, another served as a vacuum takeoff. The flask was connected to a Dynisco APT85 pressure transducer which was equipped with a stainless steel male 10/30 joint. A B&F Instruments Model 1-110S transducer input conditioner was used to apply the voltage across the arms of a strain gauge and to direct the output signal to a Beckmann Model 1005 recorder (set for 10 mV full scale). The reaction temperature was maintained to ±0.2° with a mechanically stirred ethanol bath which was cooled with cold ethanol circulating through a 10 ft × 0.25 in. stainless steel coil. The circulating ethanol was cooled with a Neslab Instruments Model RTE-3 constant-temperature bath. The reaction mixture was magnetically stirred.

Reagent grade hexene-1 and hexane were purified by passage through a column of Activity I Woelm Basic alumina and degassed with a stream of dry nitrogen for 30 min. Ethyl diazoacetate was obtained from Aldrich Chemical Co. A standard solution of catalyst was prepared by dissolving (CuOTf)$_2$–C$_6$H$_6$ in hexene-1 under nitrogen.

Measurement Procedure. The reaction vessel was flushed with dry nitrogen and then charged with hexene-1 or a hexene-1–hexane mixture and either ethyl diazoacetate or an aliquot of catalyst solution. The reaction vessel was sealed and immersed in the cooling bath and then evacuated (to a pressure of 10–50 mm). Calibration was accomplished by the introduction of several 5-ml portions of dry nitrogen with a hypodermic syringe. The vessel was then reevacuated and after 10–20 min of thermal equilibration either an aliquot of catalyst solution or ethyl diazoacetate was then added through the side neck with a Hamilton microliter syringe. Nitrogen evolution, which commenced immediately, was monitored electronically and recorded automatically. After cessation of nitrogen evolution, the reaction mixtures were washed and diluted with pentane and the resulting solution was washed with 10 ml of 2 *M* aqueous KCN. The organic solution was then concentrated by careful distillation of the solvent(s). Then ethyl phenylacetate was added as internal standard and the resulting mixture analyzed by vpc on a 10 ft × $^1/_8$ in. 20% FFAP on 60–80 Chromosorb W (acid washed) column. Relative retention times on this column were: ethyl 2-butylcyclopropanecarboxylate, 0.41; diethyl fumarate, 0.67; diethyl maleate, 0.85; ethyl phenylacetate, 1.00; *cis*-triethyl cyclopropane-1,2,3-tricarboxylate,[35] 3.5; *trans*-triethyl cyclopropane-1,2,3-tricarboxylate,[35] 3.9. The various products and their yields obtained from the decomposition of ethyl diazoacetate in hexane solutions containing various concentrations of hexene-1 are listed in the Table V. Only *cis*-triethyl cyclopropane-1,2,3-tricarboxylate was formed and none of the trans isomer was detected. Its yield was, therefore, less than 1%. The observed strong preference for the formation of the cis isomer is reasonable, in view of the expected greater reactivity of maleate *vs.* fumarate and of the usual tendency of copper catalyzed cyclopropanations to favor the most sterically hindered product.

Table V. Variation of Product Yields with Concentration of Hexene-1 in Hexane

Hexene-1, *M*	Product yields (%)[a,b] A	B	C	D	Overall yield
0.8	48	7.6	3.8	3	62
1.8	59	4.3	2.3	3	69
3.2	65	2.5	1.5	2	71
4.8	74	2.0	1.1	2	79
8.0	75	1.4	0.8	2	79

[a] All products exhibited identical vpc retention times as those of authentic samples. In addition, the mass spectra of the products, separated from the mixtures by vpc, were identical with those of authentic samples. [b] A, ethyl 2-butylcyclopropanecarboxylate; B, diethyl fumarate; C, diethyl maleate; D, *cis*-triethyl cyclopropane-1,2,3-tricarboxylate.

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Chemistry of Carbanions. XXIII. Use of Metal Complexes to Control the Aldol Condensation[1a]

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Abstract: Preformed lithium enolates may be used as reactants in aldol condensation with other carbonyl compounds provided reaction conditions are chosen that intercept the initially formed aldol products as metal chelates 9. Although lithium may serve as the chelating metal cation in nonpolar solvents at low temperatures, it is experimentally more convenient to add a divalent metal salt such as anhydrous MgBr$_2$, or especially ZnCl$_2$. By adding an ethereal solution of ZnCl$_2$ to a preformed lithium enolate in ether or 1,2-dimethoxyethane solution, subsequent addition of either an aliphatic or an aromatic aldehyde results in the formation of a single aldol product in 80–90% yield. Where diastereoisomers of the aldol product are possible, there is usually a preference for the formation of the threo stereoisomer, the stereoisomer in which the greater number of substituents on the intermediate six-membered cyclic metal chelate may occupy equatorial conformations.

The aldol condensation (eq A)[2] has long presented organic chemists with the enigma of being a very rapid and efficient method for forming new carbon–carbon bonds and yet a reaction whose synthetic utility is severely curtailed in those instances where more

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(2) For reviews, see (a) A. T. Nielsen and W. J. Houlihan, *Org. React.*, 16, 1 (1968); (b) H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, Reading, Mass., 1972, pp 629–682.