PART – A

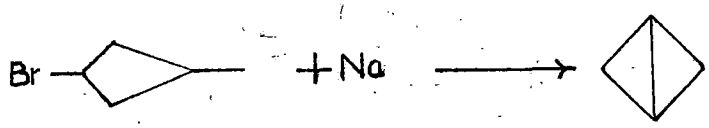
CHAPTER - I

REVIEW

1.1 Preparation of cyclopropanes:

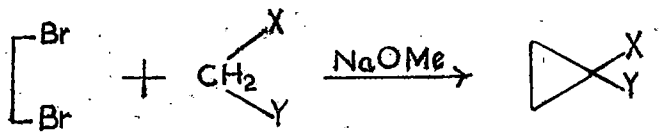
Cyclopropanes are the first member of the alicyclic compounds. Its existence was first reported in 1882 by Freund and since then down to the present days the importance of the ring is gradually expanding. Here is a brief review of the known methods for its preparations:

1. The first known method is a Wurtz type of reaction of 1,3-dihalogen derivatives of paraffins. An interesting application of this method is the synthesis of bicyclobutane[1].



93 96 %

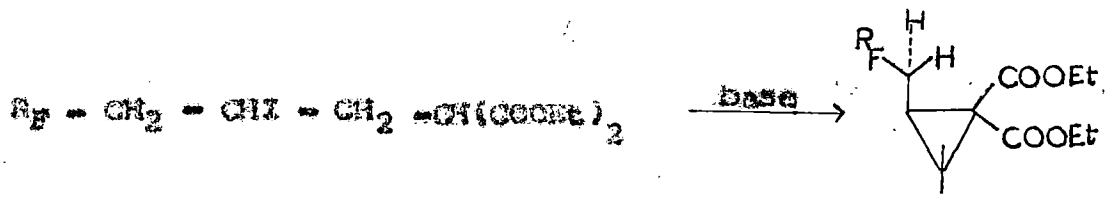
2. Malonic ester type of synthesis with the use of sodium methoxide as base[2,3,4]



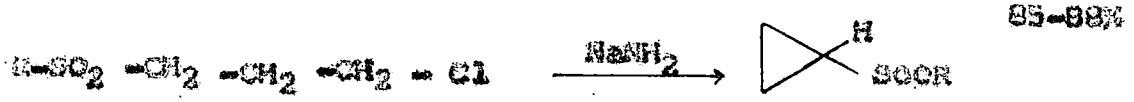
X,Y are esters, keto or nitrile functional groups.

3. There are also some base catalysed elimination reactions which involve cyclisation to produce cyclopropane ring compounds. N.C. Brace[5,6] reported that dehydrohalogenation reaction of 3-perfluoro-alkyl-2-iodo propyl malonic ester in presence of sodium ethoxide in

anhydrous ethanol or sodium hydride in benzene suspension gave 2- (perfluoroalkyl, R_F) methyl cyclopropane dicarboxylic acids and esters in a preliminary fashion[6].

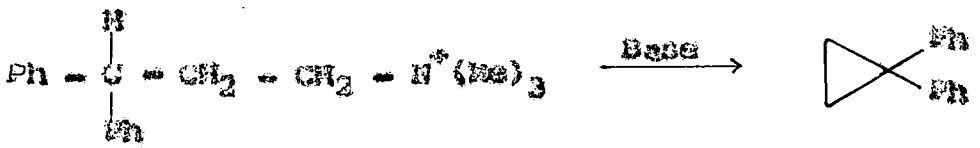


Trus et al[7] also adopted γ-dehydrohalogenation reaction to obtain the several alkyl and aryl cyclopropyl sulfones.



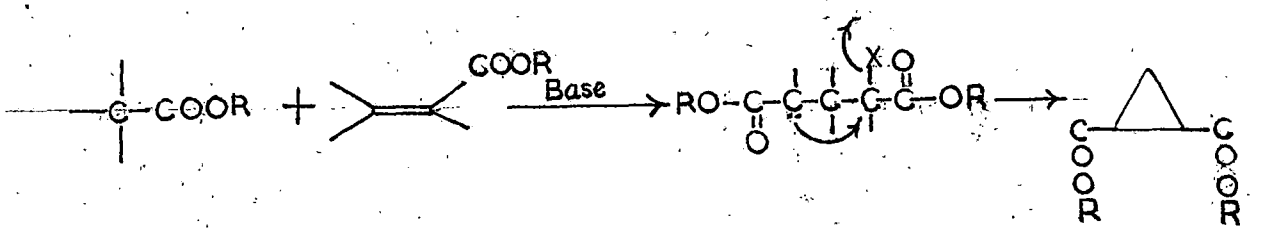
Base catalysed malonate condensation of 1,4-dibromo-but-2-ene is a convenient route to prepare vinyl cyclopropane as reported by Kirstead et al[8].

Hofmann (γ-elimination) reaction[9] has also been used for the formation of cyclopropane derivatives.

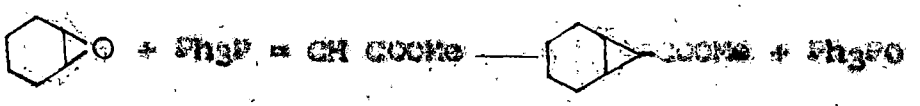


4. Michael type addition reaction coupled with elimination reaction was used by Warner[10] and McCoy[11] to prepare 1,1,2,2-tetra substituted

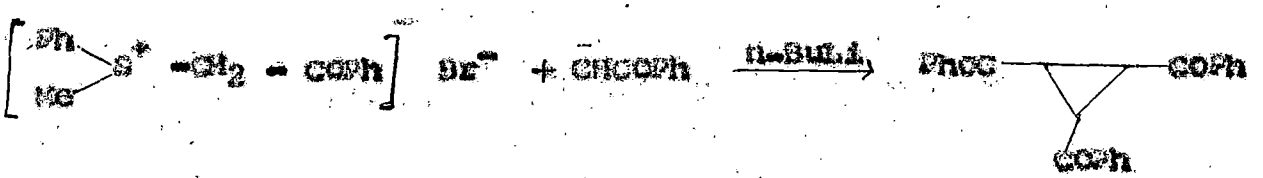
cycloprapane ester derivatives[12,13].

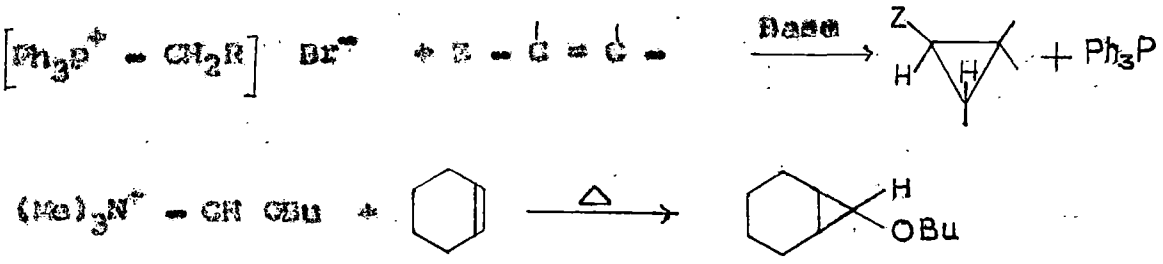


5. With the help of Ylides Wadsworth and Emmons[14] have shown that phosphate carbanion reacts with epoxide to give substituted cyclopropanes. This method has also been employed by D.G. Denny et al[15-17] in preparing cyclopropanes carboxylic acid from carbanion reaction of carbomethoxy methylene triphenyl phosphorane with cyclohexen oxide, 1-octene oxide and styrene oxide etc.

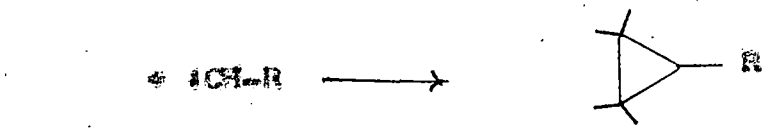


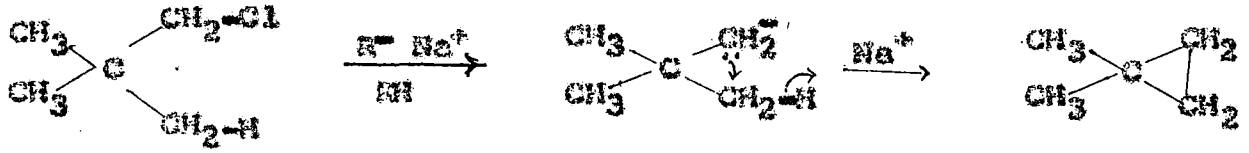
other various ylides, viz. nitrogen[18], sulphur[19] and oxo-sulphur[20] and phosphorane[21] can also take part in cyclopropanation reaction with 2-halogenated or 2,3-unsaturated carbonyl compounds. From the reaction path it is, however, proved that no benzoyl-carbene intermediate is isolated on base treatment of methylphenacyl phenyl sulphonium bromide in transforming into 1,2,3-tribenzoylcyclopropane.





6. Carbene addition methods:- The -elimination of primary alkyl halides by phenyl sodium[22] or amyl sodium[23] gives carbene resulting in the formation of cyclopropane compounds with olefins in low yield. W. Kirmse et al[24] observed that the treatment of tertiary alkyl halide such as neopentyl chloride with sodium[25] or alkyl sodium[26,27] gives 1,1-dimethyl cyclopropane.

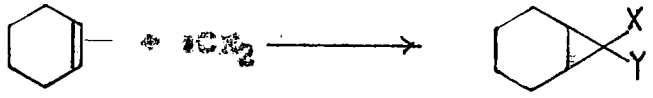


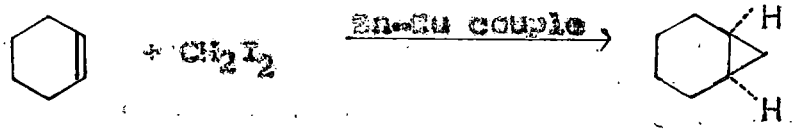


Doering and Hoffmann[28] showed that dihalocarbenes generated from the haloforms could be trapped by addition to olefins to give cyclopropane derivatives. Simmons and Smith[29], however, first used zinc-copper couple in methylene iodide to form iodomethyl zinc iodide,

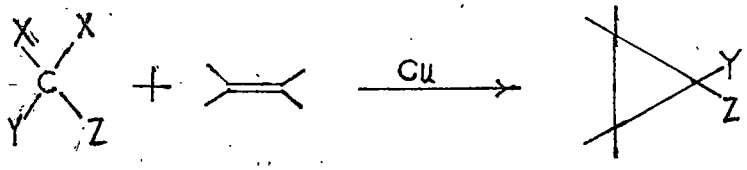
$ZnCH_2I$, which is trapped in olefins to produce cyclopropane compounds in fair yield. ICH_2MgI and Et_2AlCH_2Cl can convert olefins into cyclopropane in good yield.

$$CHX_3 + {}^-O^- \longrightarrow \bar{C}X_3 \xrightarrow{-X^-} :CX_2$$





Kawabata et al[30,31], however, modified a method to formulate a stereoselective path in the mode of cyclopropenation for the reaction between haloalkanes with terminal olefins such as 1-hexene, 1-octene and styrene etc. They also found that the exo isomer predominated over the endo product in case of cyclic olefins such as cyclohexene. They further improved the method with the use of cuprous bromide in DMSO[32].



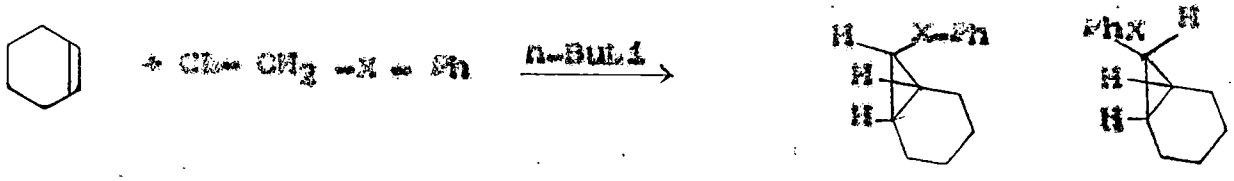
X,X' = halogens; Y,Z = alkyl or aryl.

The new method of Kawabata[29(d)] enjoys most of the advantages of Simmons & Smith reactions. The reaction is not water or air sensitive and minimal two-fold excess of CH_2I_2 is required[30]. There

is no insertion product found, yields generally, additions to stilbene and 2-methyl styrene isomer pairs are stereospecific. Cyclopropanation of 3-methoxy cyclohexene occurs via cis to the methoxyl (72%) demonstrating oxygen based stereochemical control of the familiar form of Simmons-Smith reaction (organo-copper intermediate) with strong steric requirements. Monoalkylated octene-1 is more rapidly cyclopropanated than dialkylated cyclohexene and styrene is more reactive than either 1-methyl styrene or 1, 1-diphenyl ethylene.

A high enantioselective synthesis for cyclopropane derivatives were carried out by Inouge et al[33], Cram[34], Prelog[34] and other coworkers. They observed reversal of stereoselectivity in partial synthesis of cyclopropane derivatives with the help of solvent effects.

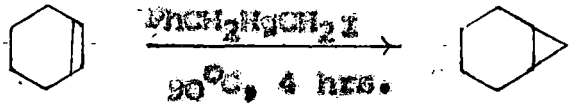
Scholkoff et al[35-37], however, applied the base conducted carbene reaction to formulate cycloprogyl-phenyl ether, phenyl mercapto-cyclopropane and phenyl selene-cyclopropane from their corresponding carbene with active olefin substrate.

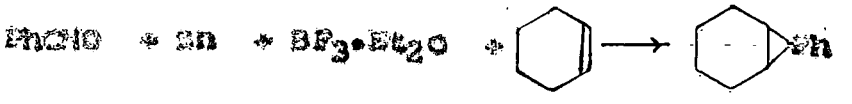


where X = O, S and Se.

Various methods for preparation of diazocompounds like Bamford-Stevens reactions and modifications[38] have used as a prelude to carbene and use of metals, their salts and their complexes like copper[39], palladium[40], rhodium[41] have served useful purposes. Optimation have also been effected with phase transfer catalyst (Nakossa reaction) using crown ethers, quarternary nitrogen salts and other catalysts. Other carbene sources are :

(i) haloform/base; (ii) dihalomethane alkyl-lithium;
(iii) ethyl trichloroacetate / base (Parham's method);
(iv) phenyl trihalomercurials (Seyferth's method).





Some of the newer methods employ dicarbonyl-cyclopentadienyl iron methyl dimethyl sulphonium tetrafluoroborate $[CpFe(CO)_2CH_2S^+(Me)_2BF_4^-]$ [42,43].

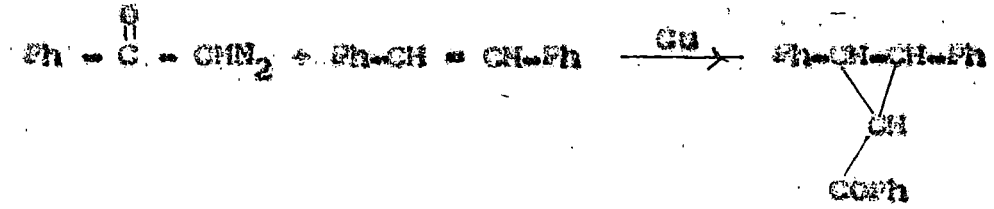
1.2 Ketocarbene and Ketocarbenoid reactions catalysed by metals, metal salts and metal complexes.

Photochemical, catalytic or thermal conditions are employed for generation of ketocarbenes from α-diazo ketone. Of these, catalytic

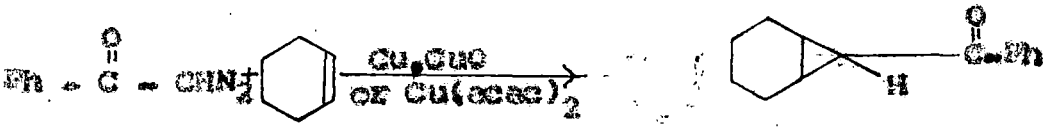
(homogeneous or heterogeneous) conditions are most commonly used in synthetic organic chemistry.

One of the earliest reviews on preparative significance of diazoketones was published by Bistert[44] and Huisgen[45]. Here the preparative aspect of diazoketone is not particularly dealt with in detail but a study of the influence of metals, metal salts and metal complexes in decomposing diazocompounds in the field of diazoketones referred to.

Intermolecular cycloaddition by benzoyl carbene[49] and p-phenyl benzoyl carbene[50] were found to react with olefins even in the absence of catalytic process but the yields of cyclopropane derivatives were considerably improved by the presence of copper powder, copper salts and copper chelates.



cis-or trans

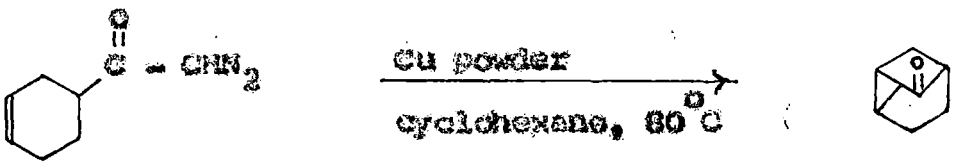


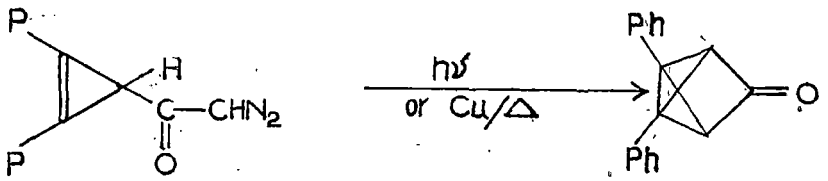
exo or endo product

The nature of active catalyst species in copper and copper salt decomposition of diazo compounds has been the subject of much

discussion[46,47]. Acetyl carbene generated by copper catalysed decomposition of diazoacetone added easily to olefins such as styrene, cyclohexene and cyclopentene[48].

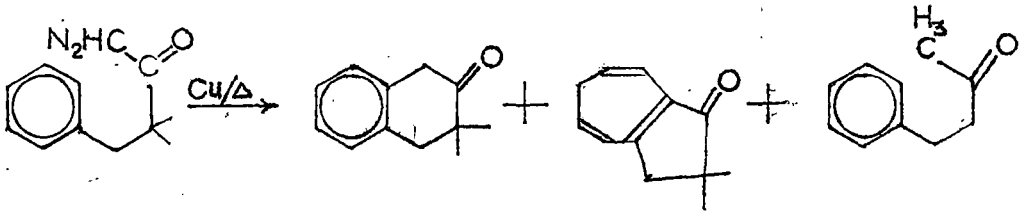
The intramolecular cycloaddition reactions of diazoketones were also effected with copper powder catalyst in thermal[51-56] as well as photolytic processes[57-60].



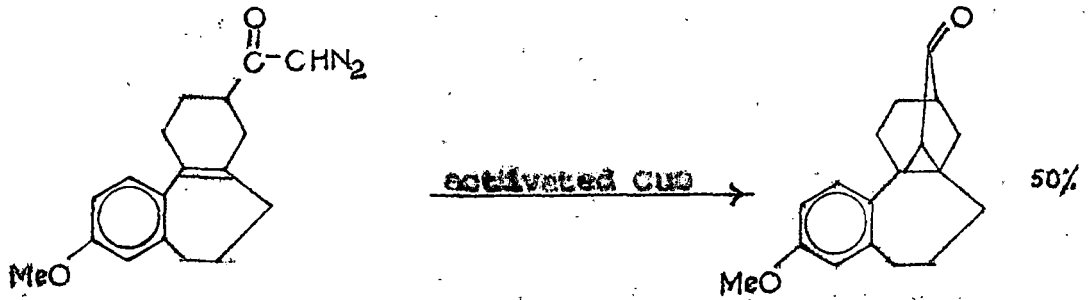


Doering et al[51,55] also adopted intramolecular cycloaddition reaction from ketocarbenoid path ($CuSO_4$) to prepare barbaralone, a precursor for the synthesis of terpenoid bullavalene. Mori and Matsuri[62] achieved a 59% yield of cyclopropane derivatives by the copper/copper sulphate catalysed decomposition of δ-unsaturated diazo-ketones and similar reactions were performed by House and Blankley[63].

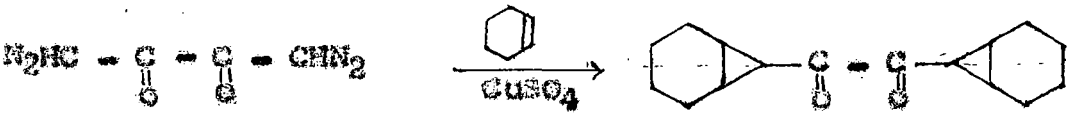
In addition, reaction of ketocarbene to aromatic systems have generally failed (even in copper catalysed method). But it has recently been demonstrated that both intermolecular[64] and intramolecular[65] reactions are possible.



Until recently all the reported catalytic decompositions were carried out under heterogeneous and homogenous conditions with a variety of copper salt catalysts[66]. An efficient heterogeneous "activated copper oxide" catalyst was extensively used by Ghatak et al[67] and Beams and Nander et al[60,69] for intramolecular α-ketocarbenoid reactions for the formation of bicylic and tricylic cyclopropyl ketone derivatives.

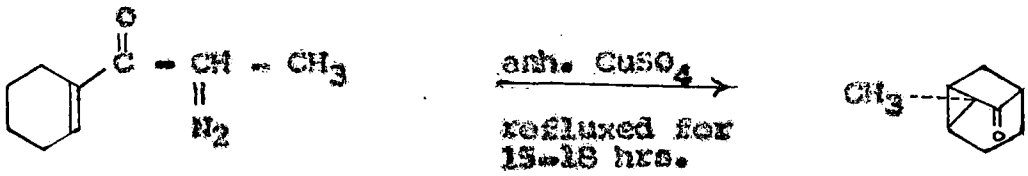


Intermolecular cycloadditions have also been employed by A. Bien et al[70] in presence of anh. copper sulphate catalyst[71,72] in synthesizing cyclopropane derivatives. They have also used other catalysts viz. Cu_2Cl_2 /CuCl/$CuSO_4$/$Cu(PPh)_2$/$Ni(CP)_2$/$Ni(CO)_4$/$AgNO_3$ etc. and found $CuSO_4$ to be the best catalyst. Irradiation with or without sensitiser (Michler's Ketone) were also carried out.



low yield

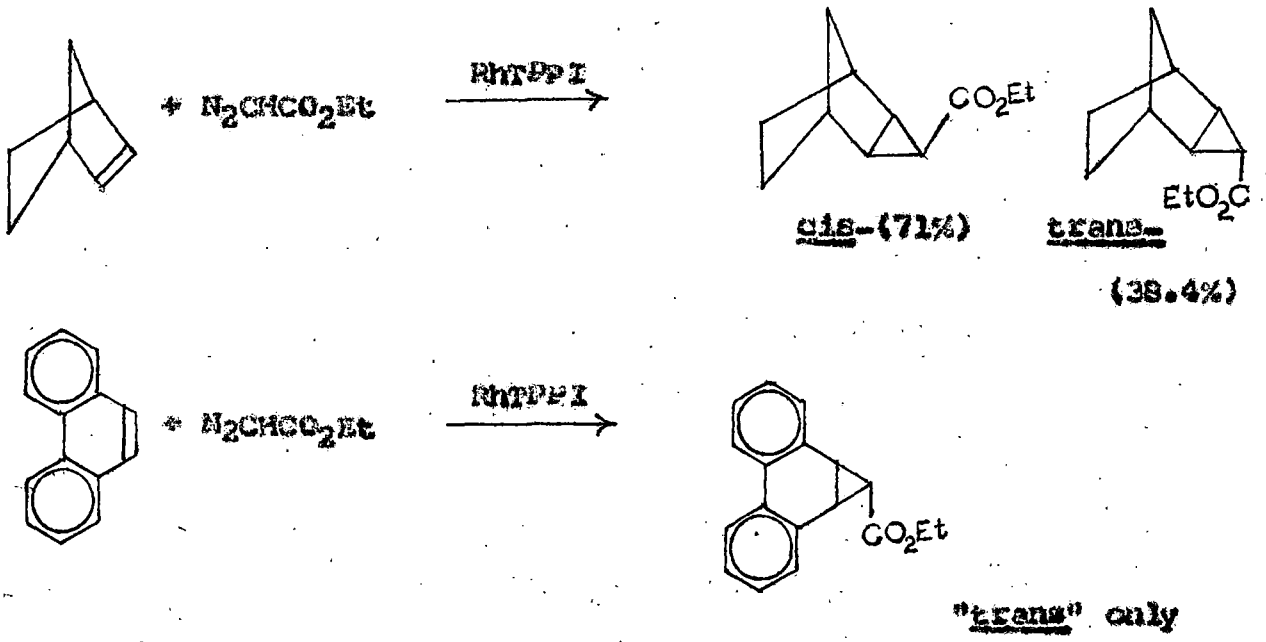
But the intramolecular cycloaddition of the following diazo compound was observed by Charles J.V. Scanio and Donald L. Lickel[73] in presence of anh. copper sulphate in good yield.



House et al[74], however, showed that the thermal decomposition of α-diazoacetophenone and α-diazomethyl cyclohexyl ketone in cyclohexene under refluxing condition had given higher yield (55-57%) of norcarane derivatives in presence of heterogeneous catalysts like anh.copper oxide and cuprous iodide rather than soluble homogenous alkyl or aryl phosphite copper (I)[75-77] iodide, $(nBu_2S)_2CuI$, $(MeO)_3PCuI$, $(PhO)_3PCuI$, $(nBu)_2SCuI$. But CuO and Cu_2I_2 are found to be better catalyst.

Recently a few efficient and selective catalysts such as copper (I) trifluoromethyl sulphonate (CuTF)[78] and copper complex of pyridine[79,80] have been introduced for intermolecular cyclopropanation reaction of olefins with diazocompounds.

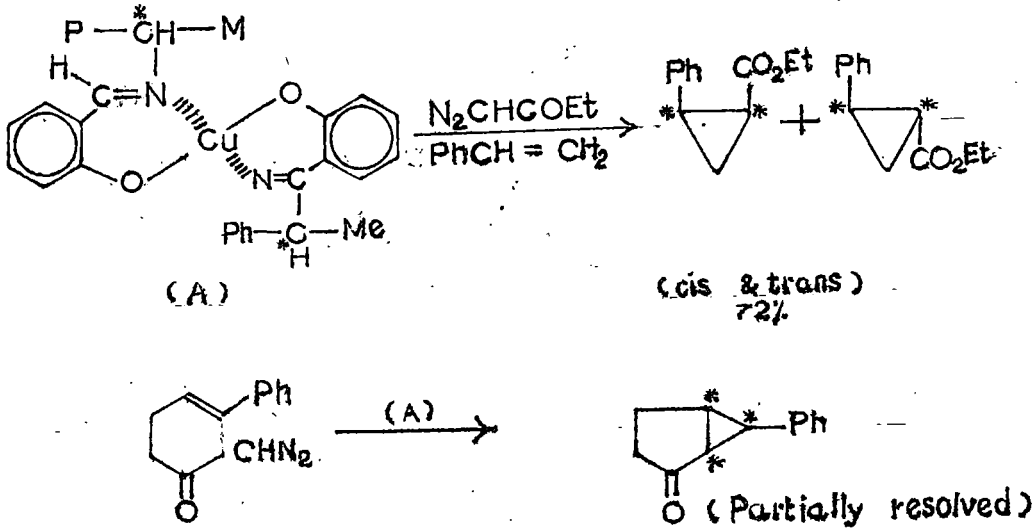
The influence of various catalysts such as Rhodium^{II} (II) carboxylate, Rhodium^{II} Pivalate, Rhodium^{III} tetraphenyl propyrine Iodide (RhTPPI)[82] and Palladium^{II} carboxylates and -allylic Palladium^{II} chloride complex[83] on the regioselectivity of cyclopropanation to various types of olefins was studied in details (Scheme-I).



Scheme - I

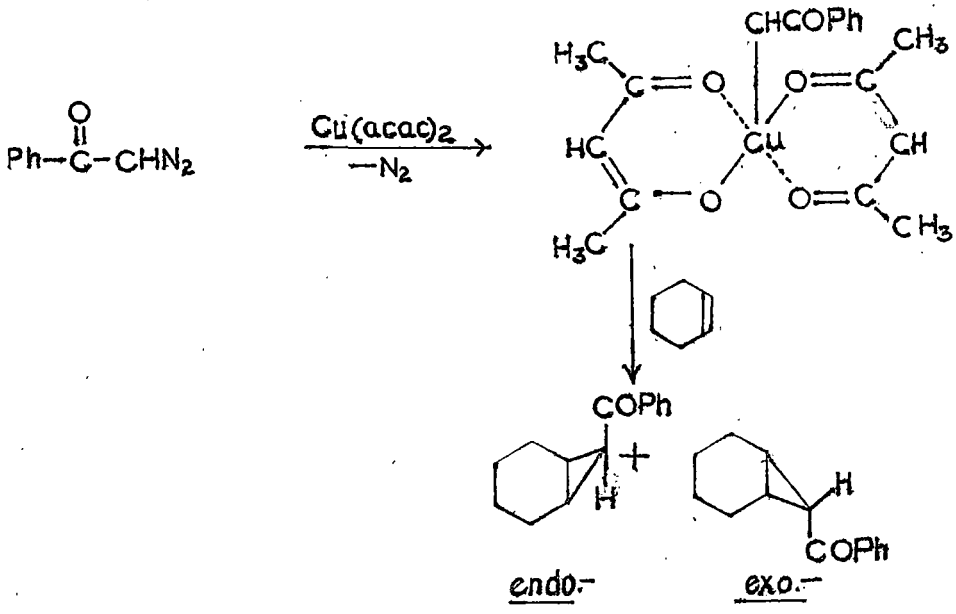
Another interesting and significant achievement is the highly enantio-selective cyclopropane derivatives obtained by carbenoid reactions between olefins and diazoalkane in the presence of bis [(-) camphore Quinone dioximate] Cobalt^{II} in excellent yields[84].

H. Nozaki et al[85], however, modified a new type of copper chelate complex bis [N-(R)-α-phenyl ethyl salicylaldeminito] Copper^{II} catalyst in synthesizing optical isomers of cyclopropane derivatives in 70-80% yield by carbenoid reaction of olefins with diazo compound (Scheme - XI).



Scheme II

A most effective copper chelate complex bis(acetylacetonato) Copper[II] used by Takebayashi et al[86] in the decomposition mode of ∝-diazo-acetophenone in alcohols, phenols and olefins and demonstrated that the carbene complex gave cyclopropane derivatives with olefins in excellent yields.



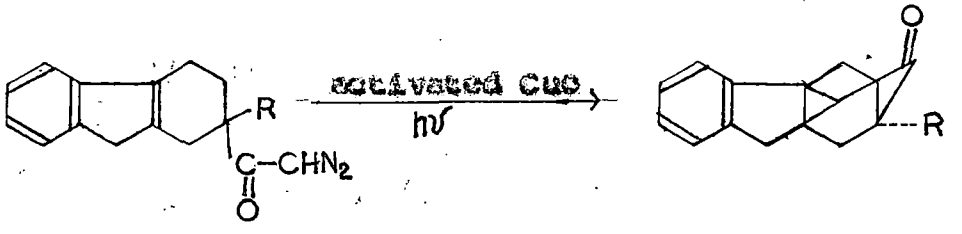
They also found catalytic efficiencies of different metal complex of acetylacetonate in decomposition of ethoxy acetophenone and concluded that $Cu(acac)_2$ and $Ni(acac)_2$ were the most effective catalysts. But in comparison to $Ni(acac)_2$, $Cu(acac)_2$ catalyst was the more effective catalyst at low temperature even in very low concentration $[Cu(acac)_2 - 1.9 \times 10^{-6}$ mol $]$.

1.3 Carbenoid reactions under catalyst and irradiation:

Diazoacetophenone has been decomposed under a variety of conditions[139,140]. The sensitized and direct photochemical decomposition both appear to produce the triplet ketocarbene which adds to cis- and trans-2-butene in a non-stereospecific manner. The ketocarbenoid is relatively unreactive and exhibits radical properties as characterised by the large amount of bicyclohexenyl and acetophenone (70%) and the low amount of 7-norcaryl phenyl ketone (10-12% yield) produced in the direct and sensitized photolysis of diazoacetophenone in cyclohexene. The phtochemical decomposition of diazoketone is intriguing because of the possibility that the triplet ketomethylene could be produced upon direct irradiation. The result is predicted as a consequence of the high rates of intersystem crossing by carbonyl compounds in general. In the above reaction the high yields of bicyclohexenyl and acetophenone is suggested by the fact that the ketomethylene is highly reactive in hydrogen abstraction.

Ketocarbenoid additions in presence of light and catalysts is not studied extensively but it is reported that decomposition of the diazoketones in presence of catalyst without irradiation required

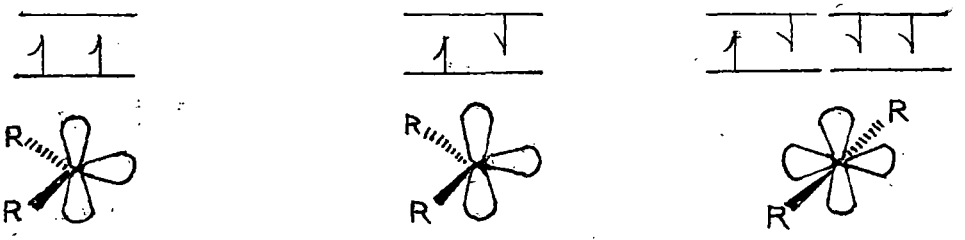
considerably longer reaction times and the yields are improved[141]. Ghatak and Chakraborti[142] have used CuO catalyst and irradiation method for the cyclopropanation.



Latter, Chakraborti et al[143] have reported that bis(acetylacetonato)Ni^{II} act as a highly efficient homogeneous catalyst for intramolecular α-ketocarbenoid addition to double bond of γ,δ-unsaturated diazomethyl ketones leading to cyclopropyl ketones under irradiation with tungsten lamp. Earlier less effective Ni catalysts, Nickelocene had been developed by Warner et al[144] for cyclopropanations.

1.4 Structures of carbenes:

Carbenes[87,95] are neutral bivalent carbon intermediates in which a carbon atom has two covalent bonds (sp^2 and sp) to other groups and two non-bonding orbitals containing two electrons between them. Depending upon the possible arrangement of the two non bonding electrons between the two orbitals of different energy, spin states of carbene may be designated as lowest singlet, triplet and excited singlet as shown below.



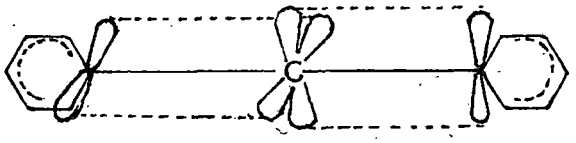
Lowest singlet I | Triplet II | Excited singlet. III

Energy difference of the orbitals often range between 8.1 and 13.1 K cal/mol[88].

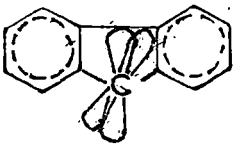
A carbene in the lowest singlet and triplet states are sp^2-hybrid and therefore, resemble respectively a carbonium ion and a free radical in their structure. On the otherhand, the carbene in the other excited singlet and triplet states is linear sp-hybrid[89].

Spectroscopic evidence: Various experimental observation and analysis of simple carbens viz. methylene[90] should give detailed information concerning both ground and excited states of the molecule. An absorption of a group of lines at 4050^{o}A in the spectra of comets to methylene gave a great interest of fruitful evidence in early discussion of methylene although it was latter ascertained that the lines are due to C_3 rather than CH_2. Herzberg and Shoosmith[91] recorded the electron spectrum of methylene produced in the gas phase by flash photolysis of CH_2N_2, $CHDN_2$ and C_2DN_2. Electron spin resonance spectra of methylene trapped in a xenon matrix at 4.2 K have been one of the most recent achievements in this field[92,93]. The results demonstrated that the formation of a linear or near linear species with a C-H bond length of 1.03^{o}A, which absorbed ultra-violet radiation at about 1414^{o}A and a bent species, bond

angle 102-103°, C-H bond length 1.12°Å, which absorbed U-V radiation in the 5500-9500°Å region. The absorption of short wavelength of linear CH_2 was enhanced at the expense of that of the long wave length of bent CH_2 whenever the same experiment were carried out in the presence of large excess of nitrogen. This experiment inferred that methylene, diphenyl carbene, phenyl carbene and fluorenylidene exist as triplet ground state. Wasserman and coworkers[93], however, observed two carbene states with D = 0.6636 cm^{-1}, E = 0.002 cm^{-1} and D = 0.6844 cm^{-1}, E = 0.00347 cm^{-1} respectively. The value of D is proportionated to the average $1/r^3$ where r is the distance between two spins interaction and closeness of the two spins. The value of E represents qualitatively the value of the extent of the deviation of the spin-spin interaction from cylindrical symmetry. Wasserman and coworkers concluded that singlet methylene with an angle of 136° is in good agreement with most theoretical calculations. The angles of 150-156° (nearly linear) for phenyl and diphenyl carbenes has also been estimated. The two unpaired electrons of diphenyl carbene are localized on the divalent carbon atom[94], is a consequence of higher D-value of that carbene (D = 0.4055 cm^{-1}, and E = 0.0194 cm^{-1}). Surprisingly, the extent to which the unpaired electrons are constrained to stay at central carbon atom is nearly the same in diphenyl carbene and in fluorenylidene despite of their different geometries[95].



Diphenyl methylene
IV

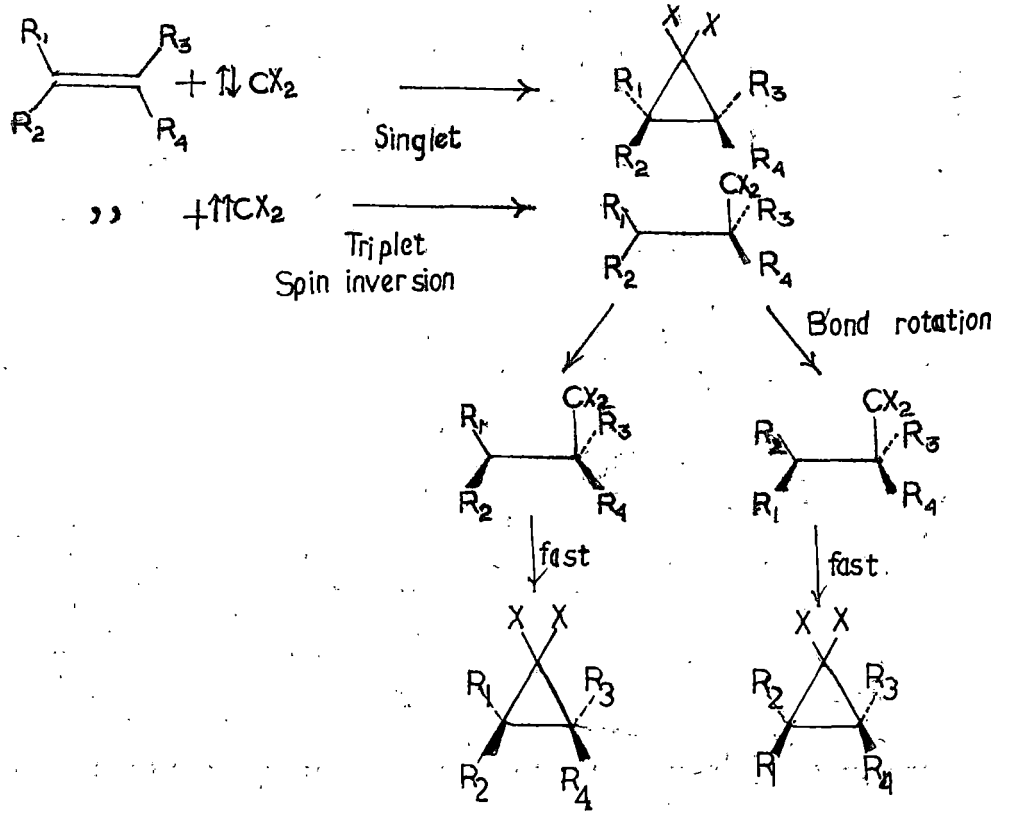


fluorenylidene
V

Several carbenes have been assigned to a triplet ground state by e.p.r experiments[96-101]. Closs and coworkers[102] reported the long wavelength absorption band of diphenyl carbene oriented in a single crystals of 1,1-diphenyl ethylene. Moritani and coworkers[103] found two new absorption bands in photolysed solutions of diphenyl diazomethane by correlating e.s.r. studies, fluorescence, fluorescence excitation and absorption spectroscopy. Gibbons and Trozolo[104] reported the luminescence, excitation and absorption spectra of diphenyl carbene assigning a triplet ground state.

1.5 Mechanism of cycloaddition reactions of carbenes:

Skoll and other coworkers[105-107] rationalized the mechanism for cycloaddition reaction of methylene to ethylenic double bond by pointing out that a singlet carbene could add to an olefin in a concerted manner as the new bond formation takes place without chaning the spin of any of the electrons involved. On the other hand, triplet carbens participate in cycloaddition reactions through a triplet diradical intermediate[105]. Before the ring closure by this diradical, there must be an inversion of spin of one of the electrons. If the free rotation about the C-C bonds of the diradical is faster than the spin inversion, then the stereochemistry[107,108] of the original olefin will not be retained in the cyclopropanes.



Woodward and Hoffmann[109] have successively applied the principle of conservation of orbital symmetry to cycloaddition reactions. Hoffmann concludes that the bent singlet methylene approaches the ethylene initially though an unsymmetrical transition state (VI); the ethylene and methylene can then correlate with the ground state of cyclopropane and the cycloaddition is a "Symmetry allowed" process. For methylene in the triplet state or the excited singlet state (III), a different geometry is predicted for the transition state, and the correlation is now, not with the ground state of cyclopropane, but with a triplet state of an excited configuration of the trimethylene diradical, "·$CH_2CH_2CH_2$·" having no barrier to rotation. This however leads to the same results as the Skell theory for the addition of the lowest singlet and the triplet to olefins although it is not

primarily the spin state that determines the course of the addition, but the spatial distribution[110,111] of the wave function. This idea proves that carbenes, in the lowest singlet state, add stereospecifically to olefins, and carbenes in the triplet state do not.

Of course a theoretical analysis[112-115] of cycloaddition reaction of the same also suggests a π-approach (VI) on which the vacant p-orbital of the carbene begins to overlap with the π-electrons of the double bond. As reactant move along the reaction coordinate towards product geometry, the "π-approach" goes over "σ-approach" (VII)[119]. It being an electrophilic addition reaction[116-118], electron density would transfer from the π-bond of olefins to the carbene's p-orbital.

(VI) "π-approach" (VII) "σ-approach"

More recent calculations suggest that "π-approach" VI(a) is energetically favourable to "π-approach" VI(b) in the addition of singlet methylene. Addition of difluoro carbene is calculated to follow a similar phenomenone[119] with less charge transfer from olefin to carbene in the transition state. Related calculation[120-122] for cycloaddition of methylene and difluorocarbene to isobutene again

supports that VI(a) is preferred to VI(b) but only by a small energy difference.

VI(a) VI(b)

The following reaction may also be considered

$$C_6H_5CHX_2 \xrightarrow[18\text{-crown-6}]{KOBu^t} C_6H_5\ddot{C}X \xleftarrow{h\nu} C_6H_5 \quad H \quad C \quad X \quad H$$

The mechanistic interpretation of the reaction by which phenylcarbenes interconvert is available[123a,123b].

Any carbene addition must be best described as a simultaneous transfer or delocalisation of the electrons of carbene sp^2-orbital into the LUMO of the π-system and the electrons in the HOMO of the π-system into vacant p-orbital of the carbene. A low lying LUMO with a large coefficient would favour such a process in which the carbene and the π-system act simultaneously as nucleophiles and electrophiles. 4-Pyridyl-phenylcarbene attacks pyridine ring exclusively while 3-pyridyl-phenylcarbene give at least 93% attack on the benzene ring. Ventrup[123c] describes these reactions as involving simultaneous electrophilic attack by the empty p-orbital

of the carbene on the ortho position of a ring as the carbenes π-electrons interact with the LUMO of the more electrophilic ring. Thus ring expansion is favoured by a low energy LUMO with a high lying HOMO with electron density at the ortho-position. In 3-pyridyl phenylcarbene, the carbene is at a low electrophilicity and the HOMO electron densities at the positions ortho to the carbene (2-and 4-pyridine) are low. Thus both nucleophilic and electrophilic interactions with the pyridene ring are poor. Reaction occurs with the phenyl ring overwhelmingly. In contrast, in 2-and 4-pyridyl phenyl carbenes the carbene is attached to relatively electrophilic positions and attack now occurs in the pyridine ring. If one transforms to 2-pyridyl-2-naphthylcarbene thus lowering the LUMO energy of the "benzene" part and creating a favourable position for attack on the carbene p-orbital, (the α-position of naphthalene) addition to napthalene is favoured by a factor of two.

Concerted 1,4-additions of singlet carbenes are rare, as are their stepwise counterparts. Qualitatively, the key interaction in the conjugate addition of, for example, CH_2 to s-cis butadiene in between the carbene p-orbital (LUMO) and the π_2(HOMO) orbital of the diene. The π-orbital of the diene is symmetry forbidden from interacting with p-orbital and in fact because the carbene has to come quite close to the diene to make p- π_2 overlap significant, repulsion between its filled σ-orbital and π_1 offsets much of the favourable p- π_2 interaction. No such difficulty attends the 1,2-addition of CH_2 to butadiene; both π_1 and π_2 can effectively donate

to the vacant carbene p-orbital. These qualitative considerations are reinforced by molecular orbital (MO) calculations[124]. Early example of 1,4-additions is best formulated as 1,2-addition followed by rearrangement. Numerous examples of 1,4-dihalocarbene additions norbornadiene and its derivatives have now been discovered[125].

Addition of a carbene to an alkene is usually formulated in terms of electrophilic attack of its vacant p-orbital (LUMO) on the filled π-orbital (HOMO) of the alkene[118,119]. One must also consider donation of the carbenes lone pair, contained in its sp^2- (HOMO) orbital, to the alkenes π^*- (LUMO) orbital. This nucleophilic action of the carbene is normally minor and overshadowed by the dominant electrophilic behavior, but as noted earlier, it is discernible during certain aromatic carbene-carbene rearrangements[123c] and clearly visible in the addition reaction of cycloheptatrienylidene and 1,2-diphenyl-cyclopropylidene[126].

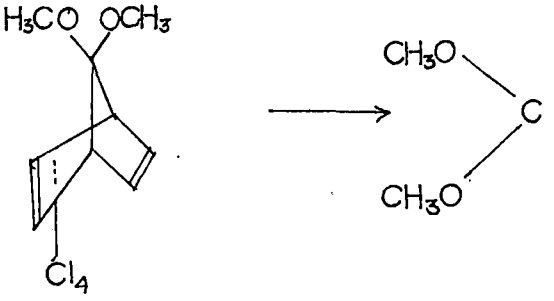
At present the most widely applicable quantitative characterisation of carbenic selectivity[127] relies on linear free energy relationships between the olefinic selectivities of various carbenes[105,116,101].

Carbene selectivity index $m_{CX}Y$ determined:

$$\underline{m}\, C_{X,Y} = -1.10 \sum_{X,Y} \sigma_R^+ + 0.53 \sum_{X,Y} \sigma_I^+ - 0.31$$

Singlet - carbene add stereospecifically to cis-trans butene. Electrophilic selectivity is greatest ($\underline{m}\, C_{XY}$ is largest) when strong resonance interactions of X and Y with the carbenic centre necessitate correspondingly strong π-electron donation by the olefin; electron releasing alkyl substituents moderate the resulting accumulation of

positive charge on the olefinic centres, whereas inductively withdrawing carbenic substituents mitigate accumulation of negative charge on the carbenic centre[128].



The above can cyclopropenate diethyl fumerate, diethyl maleate, styrene, 1,1-diphenylethylene, ethyl cinnamate[129], as well as acetylene dicarboxylate phenylacetylene, diphenylketene, benzoyl chloride, aryl isothiocyanate (nucleophilic attack)[130]. Similar to cycloheptatrienylidene, 1,2-diphenylcyclopropenylidene, the 2-oxa-3, 3-diphenylsilacycloheptanylidene there is extreme attenuation of carbenic electrophilicity[132].

Thermal decomposition of diazomethane must yield both singlet and triplet methylene[133]. However, no triplet methylene can be detected in the thermal decomposition of diazomethane. Presumably, triplet methylene is activated to the much more reactive singlet in a process that must depend critically on the magnitude of the singlet triplet separation in methylene. Thus Duncan and Trimble favour a lower value.

Unsaturated carbene substrates has been of much interest. In vinylidene and vinylidene[134] carbene singlet-triplet energy is about 46-51 Kcal/mol. Calculations[135] on the effects of substitution on the singlet states of alkylidene carbenes and have found that electropositive groups are stabilising and electronegative groups are destabilisin g. It is conceivable[136] that in carboalkoxy a higher lying singlet state might be thermally populated and rates of the singlet reactions considerably faster than those of the corresponding triplet. The triplet ground state was observed by EPR in frozen solutions or deposited matrices. The ground state plot of signal intensity versus 1/T was linear over the range 10-40K i.e. the Curie law was followed.

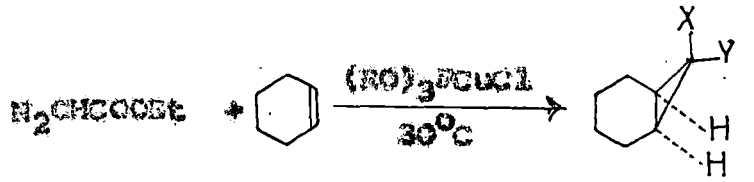
ab initio calculations[137] reveal a distinctly bent triplet ground state for dicyanocarbene which lies about 14 Kcal/mol. below the singlet.

GVB calculations[138] have given description of both singlet and triplet vinylcarbenes. The presence of an electron in a σ-orbital in the triplet leads to a carbene- like triplet lying some 12K cal/mol. below the carbene-like lowest singlet and 14 Kcal/mol. below 1,3-diradical like singlet state.

1.6 Mechanistic Pathways for carbenoid reactions

Metal or metal salt catalyzed reactions of diazo compounds have been known for many years. Particular attention having been paid to catalytic decomposition by copper derivatives[145].

Different workers have proposed that metal-carbene complex is an intermediate in these reactions. Such a scheme was proposed by W.R. Moser[76(b)]. He proposed the scheme on the basis of his experiment and the future concepts of metal-carbene complex as an intermediate in such reactions[51(a),76(b)].



(1) (2)

20 m mol 500 m mol

3 = exo, X = -H, Y = -COOEt

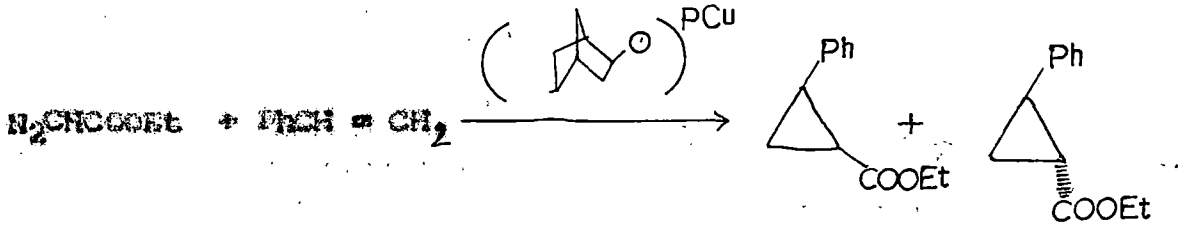
4 = endo, X = -COOEt, Y = -H

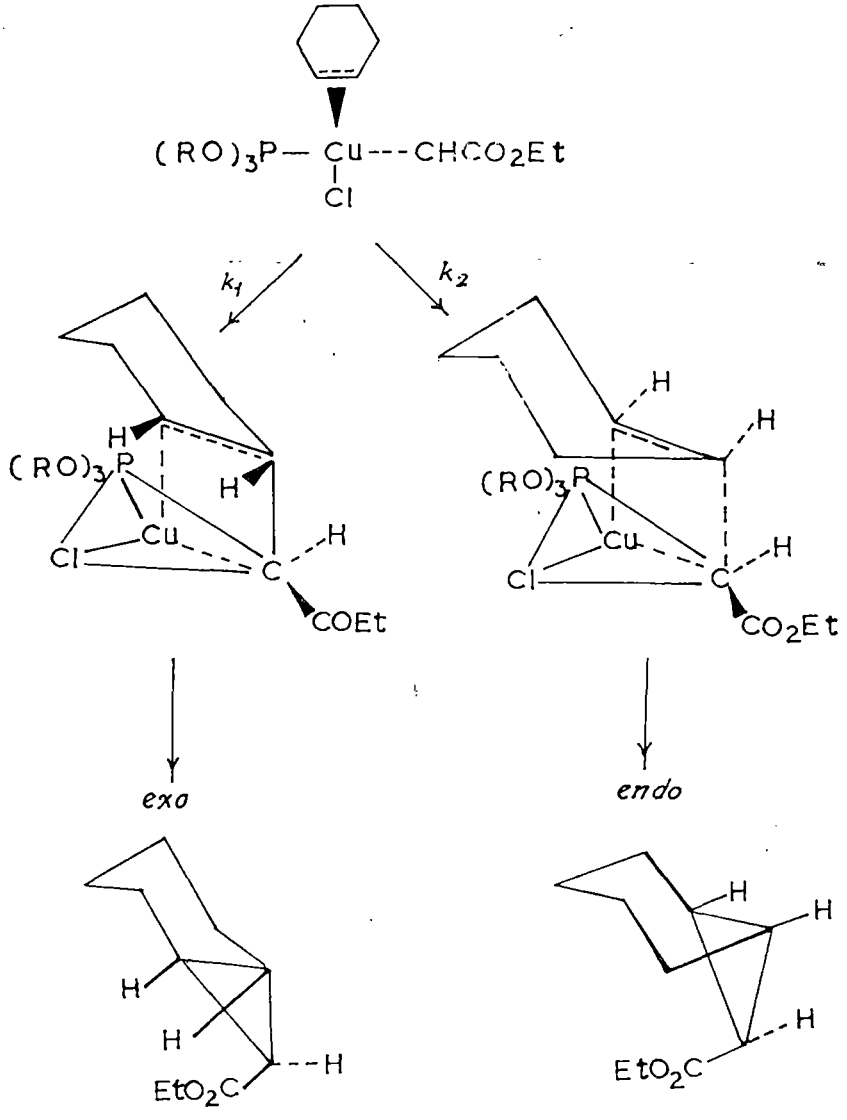
This reaction with copper metal catalyst was first carried out by Ikell and Etter[51(c)]. Moser[76(b)] has repeated the experiment and tabulated the following observations.

	endo-4	exo-3	Insertion
Photolytic (25°C)	1.00	1.89	2.36
Thermal (Reflux, very slow)	1.00	7.14	0.25
Copper metal (Reflux, fast)	1.00	9.66	0.05

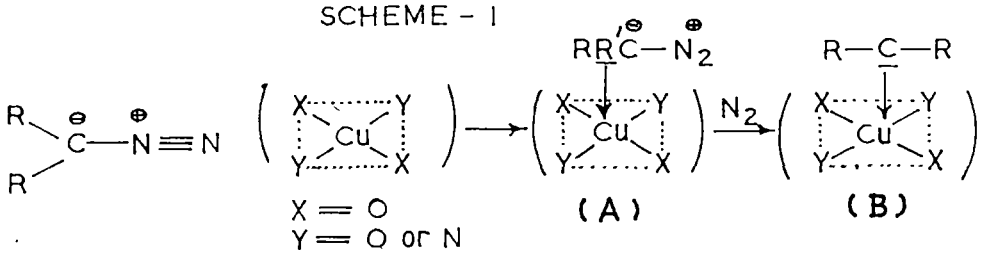
He stated that these data were insufficient to assume carbene metal-complexed intermediate in the reaction. Therefore, Moser carried out an asymmetric, synthesis to state that the soluble carbene-metal complex with a specific stereochemistry as the final excited complex in copper catalyzed addition of ethyldiazoacetate to olefins. Better evidence for such intermediates has now been obtained by a study of the results of changing electronic and steric effects of substituents on the metal catalysts. He further showed that the mechanism of the electronic effect of the ligand on homogeneous metal catalysis is still not clear. Substituents change in ligands attached to a catalyst commonly causes drastic changes in the product distribution. So more light is cast on the phenomenon and ultimately a rational mechanism was derived by him (<u>Scheme - I</u>).

Additionally, use of the optically active (-) tribornyl phosphite copper chloride gave two optically active cyclopropanes[83].





SCHEME - I

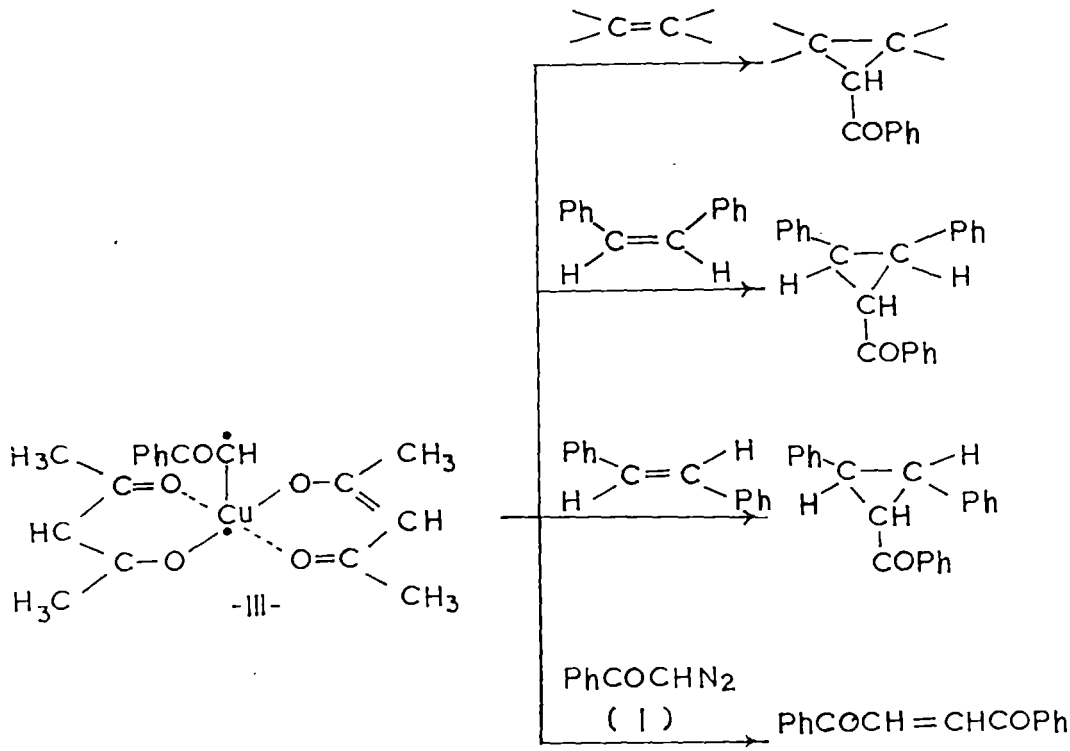


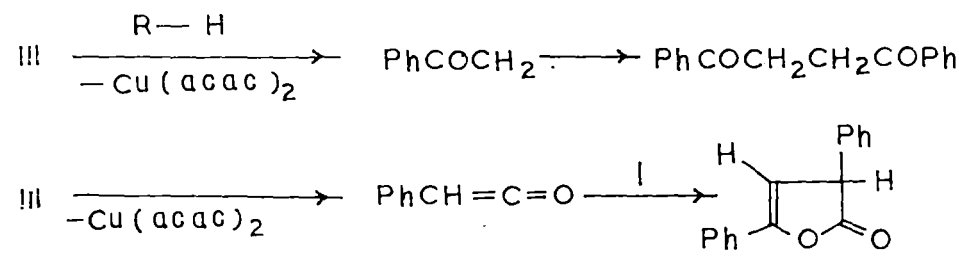
SCHEME - II

From the results, including an Arhenius treatment of the reaction studied at various temperatures it was concluded (i) that the final transition state (exo or endo in Scheme - I) leading to products involve olefins, metal and the carbony methylene, (ii) that the transition state is asymmetric and (iii) that any intermediate leading to it decomposes unimolecularly to products. A mechanism incorporating these factors has been proposed in (Scheme - I) .

H. Nozaki et al[80] have computed some aspects of reactions of diazocompounds in presence of soluble copper chelates and proposed a mechanism (Scheme - II) in which the open copper chelate would undergo electrophilic attack on carbon atom of diazoalkanes yielding a complex. The subsequent elimination of nitrogen molecule would furnish a carbene copper complex or an inverse ylide, in which the carbene moiety is coordinated to the copper atom as the fifth ligand. The possible back donation from the metal atom to the vacant p_π-orbital of the carbenic carbon may contribute to stabilise the complex. It should be noted that we can not rule out an alternative possibility that the initially formed complex (A) directly reacts with substrates. Assuming that the term "copper carbenoid" involves both species (A) and (B). It may be safe to conclude that a chiral carbenoid is responsible for the accomplishment of asymmetric induction method. From dilution studies it is confirmed that copper carbenoid does not dissociate into free carbene during the reaction to substrates.

M. Takebayashi et al[146] have studied various reactions of α-diazoacetophenone in presence of Bis(acetylacetonato) complexes


C=C
C—C
CH
COPh
Ph
C=C
Ph
H
H
Ph
C—C
Ph
H
H
CH
COPh
H3C
PhCOCH
CH3
C=O
O—C
Cu
HC
CH
C—O
O=C
H3C
CH3
-III-
Ph
C=C
H
H
Ph
Ph
C—C
H
H
CH
Ph
COPh
PhCOCHN2
(I)
PhCOCH=CHCOPh


III
R— H
—Cu(acac)2
PhCOCH2·
PhCOCH2CH2COPh
III
—Cu(acac)2
PhCH=C=O
I
H
Ph
H
Ph
O
O
O2
Ph
Ph
H
H
Ph
O
O
O
P

SCHEME III

of Copper^{II} and Nickel^{II} and showed that the intermediate of such reactions is ketocarbene-metal complex chelate (Scheme-XII).

It is assumed that reactivity of this carbenoid is not so large to give addition product with diphenylacetylene and benzene. When the concentration of the substrate reacting with (XII) is small, a part of carbenoid (III) release benzoyl carbene, which leads to phenylketene by concerted phenyl migration. But the release of benzoylcarbene must be slow otherwise the product ( ) would have performed in appreciable amount. But the authors remained silent about the pictorial concept of the transition state.

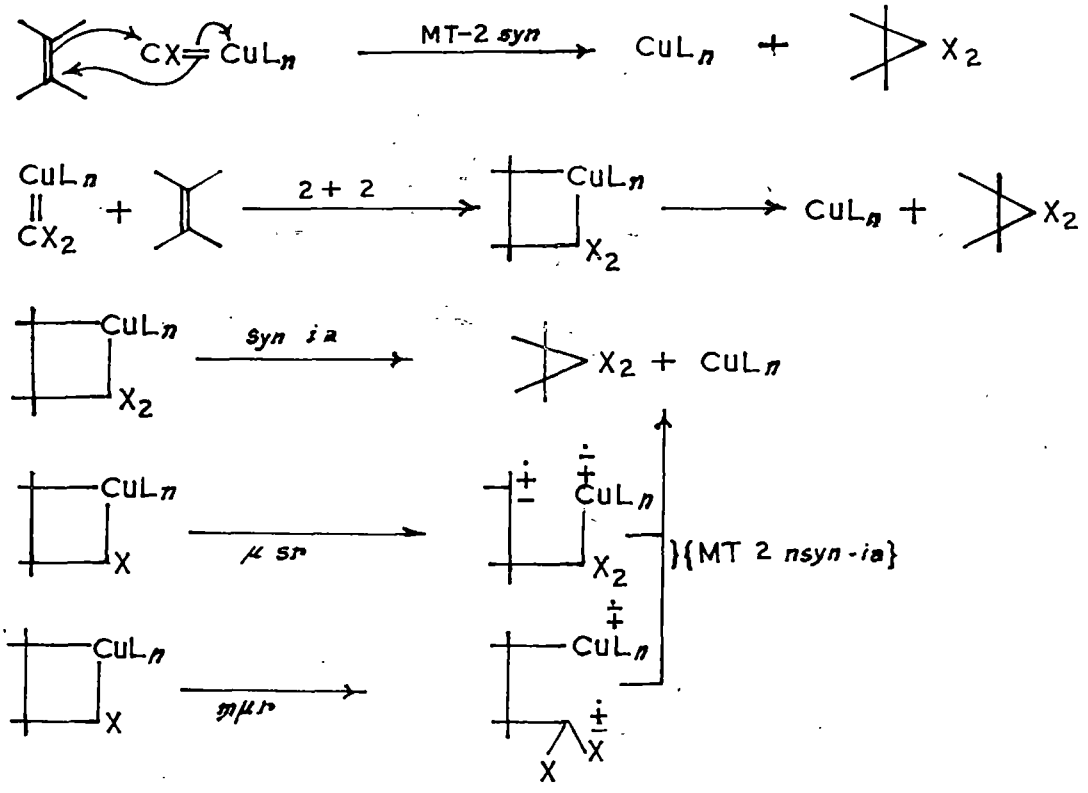
D.S. Wulfman[147] tried to rationalize the carbene transfer process and offered basic guidelines for generating data for these purposes. He stated that there are two basic ways M μ (carbene = M, metal = μ) or RM (RM = diazoalkane) can transfer M or RM to S (S = substrate) to furnish a product RMS (diazoalkane substrate complex) or MS (carbene-substrate adduct).

(a) dissociation to furnish M or RM which then reacts with S to give the product is a MT-1 process (MT-1 = carbene transfer unimolecular) or

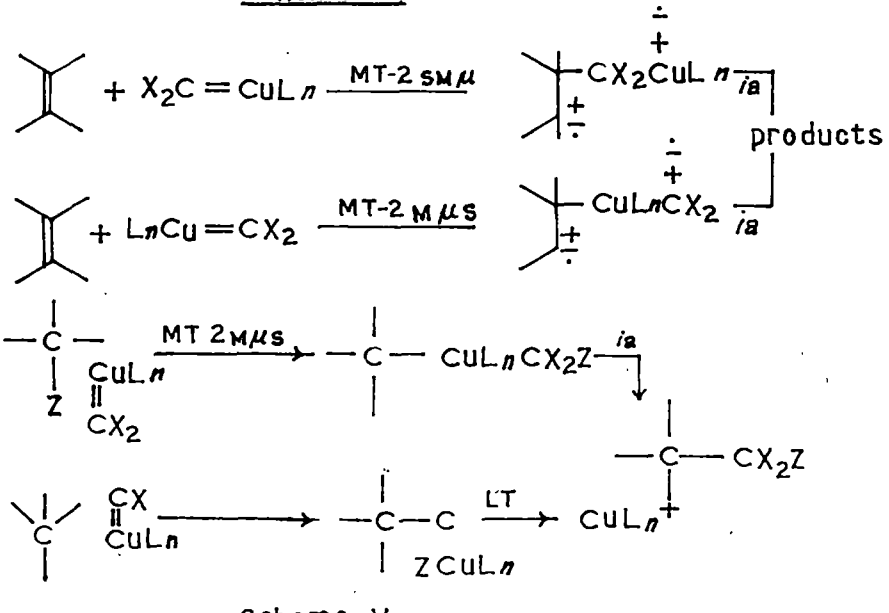
(b) bimolecular process MT-2.

The MT-1 or MT-2 process may however involve a substrate activated by the catalyst metal (μ). These processes are designated as MTS (carbene transfer with substrate enhancement).

MT-1 and MTE-1 process: A well defined example of MT-1 process exists in the work of Seyferth with compounds of the type $HgCX_2$ where warming liberates CX_2 and HgX. A MTE-1 process might



Scheme IV



Scheme V

possibly arise from the introduction of a catalyst to an olefin - $MgCX_3$ mixtures where the catalyst increases the π-electron density of the double bond in some fashion.

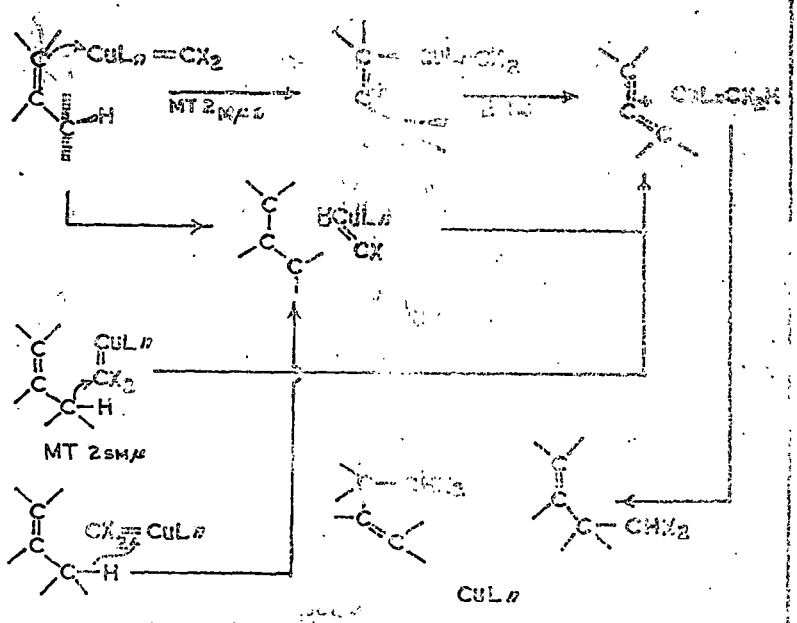
MT-2 process : MT-2 process may be of either synchronous type (MT-2 sync.) or non-synchronous type (MT sync.). The intermediate can lose the metal ligand system by synchronous and non-synchronous process (Scheme - IV).

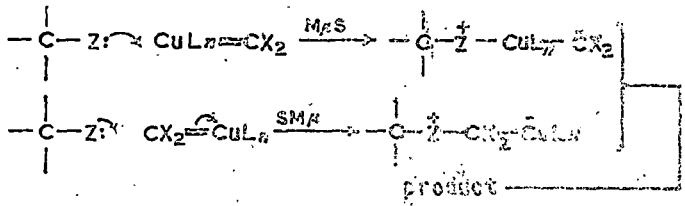
The possibilities for MT-2 sync. fall into two basic categories MT-2 sync. ΔM^M s and MT-2 sync. ΔM^M (Scheme-V).

The ligand transfer (LT) process from metal to carbene for C-H insertion process is known for bis-carboalkoxy carbene (Scheme-VI).

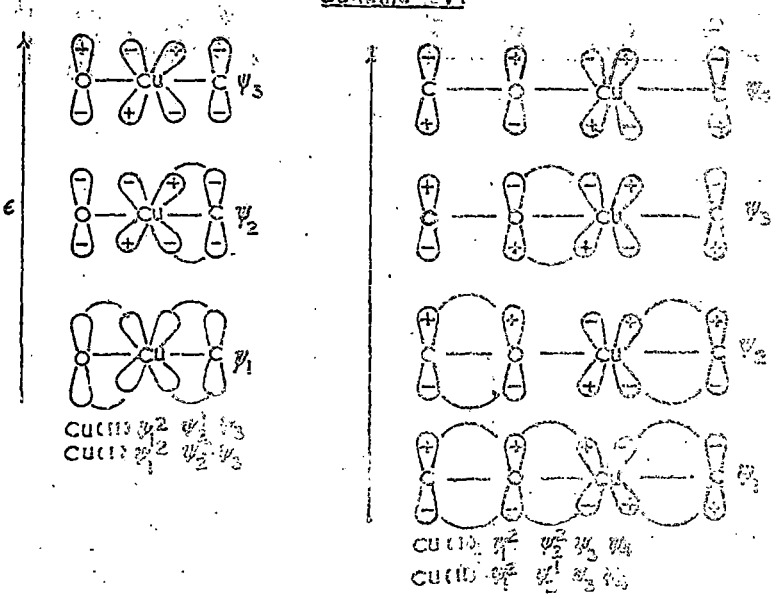
MTE-2 reactions : The real possibility exists that some substrates will be activated by complexation to the catalyst. These need not lead to enhancement towards all MT product formations but may instead lead to a favouring of one process over another.

In order to analyse the mechanism of carbene transfer in MT-2 type of reactions they raised reversal witty question and stressed the conformational effects and concluded that copper - carbenoid must be penta or hexa coordinated to afford the ligands and substrates. Very simple Huckel picture of bonding in copper carbenoids is shown in (Scheme-VII). The first system corresponds to a back bonding arrangement where the oxygen non-bonding orbitals are employed. The second assumes the P-orbital on carbon is available. The highest occupied orbital might be degenerate. But because of the spin states of transition metal complexes are not evaluated. The terminology like 'singloid' and 'triploid' assignments should be





Scheme VI



Scheme VII

reserved for those carbenoid reactions which exhibit near perfect product mimicry of the related carbene species. It is observed that copper-diazomalonate systems mimic singlet process of cyclopropanation and triplet for some allylic C-H insertions. It is also suspected that presence of the additional conjugative ability of the carbene substituents facilitates the formation of the 'stable Cu(II) complexes which are indeed 'doublet' (only a single unpaired electron) whereas in the absence of such substrates Cu(I) is more stable and this leads to 'singlet' carbenoids. As no stable copper carbenoid is known the shape and geometry of the transition state is to be judged from intuitions only.

Experimentally it is verified by Wulfman et al[148] that there must be at least three paths to cyclopropane formation. Two of these involve a single common intermediate which is formed before product partitioning between allylic C-H insertion and cyclopropanation and involves a single molecule of catalyst. A third process involving two molecules of catalyst must be occurring at high catalyst concentrations. Thus they have described that the allylic C-H insertion and cyclopropanation process could best be resolved by employing two formal bimolecular carbene transfer process (MT-2), a formal termolecular process (MTE-2) and possibly a unimolecular process (MT-I).

The author has also elucidated the mechanism carbene-dimer formation process in some carbenoid reactions[149].

From the above survey and the works of some other authors[56,77,81(a)] it is clear that intermolecular cyclopropanation reactions, using a variety of metal catalysts, proceeds via two

competitive pathways viz. MS and RMMS as the first intermediates. The influence of various catalysts on the regioselectivity of cyclopropanation to dienes and trienes was studied in detail by Anciaux et al[61(a),150] and it is revealed that rhodium catalysts are extensively efficient for cyclopropanations of any kind of alkene, the electron rich double bond being regioselectively cyclopropanated. In contrast, palladium catalysts cyclopropenate the less substituted double bond regioselectively whereas the copper catalysts exhibit borderline cases. Based on these results, two fundamental mechanistic pathways have been forwarded e.g.

(i) carbenoid mechanism

$$M + RM \longrightarrow [RMM] \xrightarrow{-N_2} MM \xrightarrow{+S} \text{product} + M$$

(ii) coordination mechanism

$$M + S \rightleftharpoons SM$$

$$S + RM \rightleftharpoons [RMMS] \xrightarrow{-N_2} MMS \rightarrow \text{product} + M$$

M = metal, RM = diazoalkene, M = carbene.

U.R. Ghatak et al[67] have reviewed beautifully the application of the intramolecular alkylation of α-diazomethyl ketones through metal-catalysed addition and insertion reactions, and acid-catalysed olefinic and aryl participations, towards the synthesis of a variety of complex polycyclic natural products.