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ADVANCES IN THE CHEMISTRY OF CARBENES

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I. INTRODUCTION

Some years ago the journal "Uspekhi Khimii" published a comprehensive review of carbenes by Knuyants *et al.*[1], covering the literature up to and including 1957. In view of the exceptionally rapid development of the chemistry of carbenes and the fundamental interest of this field for a wide variety of investigators, we thought it useful to review the work on carbenes which has been published in the subsequent five years — from 1958 to 1962 inclusive. Some papers published in 1963 have also been covered.

Although the literature dealt with in the present review covers a short period, the data accumulated on carbenes are extensive and often scattered in papers dealing with other problems. It is therefore not impossible that some data on the synthesis or a practical application of carbenes or a particular treatment of a reaction mechanism including the formation of a carbene have been omitted.

II. THE STRUCTURE OF CARBENES

No definite new evidence for the geometrical and electronic structure of carbene has been obtained since the appearance of the review of Knunyants *et al.*[1] Of the work in this field, it is only necessary to mention that of Herzberg[2], who investigated methylene by ultraviolet spectroscopy and showed that it has a triplet ground state, the singlet state having a somewhat higher energy. This is to some extent confirmed by the reactions of free methylene, particularly by its addition to carbon–carbon double bonds. The point is that the carbene being in a triplet state adds to the double bond in several stages, the first involving the formation of a 1,3-biradical in which rotation about the carbon–carbon bond is possible, so that the formation of cyclopropanes is non-stereospecific. However, it is possible to obtain methylene in the singlet state, for example photolytically; such methylene adds to double bonds stereospecifically. If it then passes to its ground (triplet) state, having given up part of its excess energy in a collision, for

example non-stereospecific addition of methylene to carbon–carbon double bonds occurs again[3-6]. In the case of substituted methylenes a wide variety of situations arises, depending on the nature of the substituents linked with the key carbon atom. Thus it has been established that dihalogenocarbenes add to double bonds stereospecifically[7], while diphenylcarbene adds non-stereospecifically[8]; the latter result is also consistent with physical data: it has recently been shown by electron paramagnetic resonance[9] that phenylcarbene, diphenylcarbene, and fluorenylidene obtained by the photolysis of the corresponding diazo-compounds have triplet ground states.

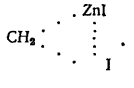
It must be borne in mind that the key carbon atom in carbenes has a lone pair of electrons as well as an unfilled orbital so that, in addition to its electrophilic properties, which until recently have been the only ones to be investigated experimentally, it also has nucleophilic properties, which will be discussed below (pp. 75, 76, 77).

III. PREPARATION AND CHARACTERISTIC PROPERTIES OF INDIVIDUAL CARBENES

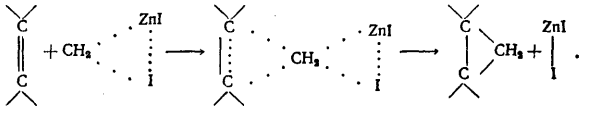
1. Methylene

Although there is no direct proof that free methylene is produced in the reaction between methylene iodide and the zinc–copper couple, the fact that cyclopropanes are obtained in the presence of olefins in the reaction mixture can be explained by the intermediate formation of methylene[10,11]. The reaction of methylene iodide with the zinc–copper couple in dry ether is known to yield iodomethylzinc iodide[12], from which cyclopropanes can be obtained in two ways.

a. Iodomethylzinc iodide may be regarded as a complex of methylene and zinc iodide which breaks down spontaneously into zinc iodide and free methylene, the latter reacting with double bonds:



b. The π-bond of the olefin can replace zinc iodide in iodomethylzinc iodide with the formation of cyclopropane[11]:



Comparatively recently a study of ultraviolet, visible, and infrared spectra has established that the photolysis of diazomethane in nitrogen at 90°K yields a complex mixture of products including ethylene, cyclopropane, and a number of other stable and unstable substances. Possibly, free methylene is also present, but its formation in the reaction mixture has not been rigorously demonstrated. The presence of certain substances in this mixture can be accounted for by reactions of methylene with diazomethane[13].

Keten is formed in the photolysis of diazomethane in a mixture of nitrogen and carbon monoxide. However, even when the concentration of carbon monoxide is eighteen times greater than that of diazomethane, the yield of keten is only 50%. This is probably due to the simultaneous occurrence of two competing reactions: reaction of carbon monoxide with methylene and of diazomethane with methylene. Furthermore, it is known that keten itself breaks down into carbon monoxide and methylene when it is irradiated with ultraviolet light[14,15] and therefore a definite equilibrium exists between carbon monoxide and methylene on the one hand and keten on the other, which reduces the yield of the latter.

2. Dihalogenocarbenes

a. Difluorocarbene. In 1960 Simons and Yarwood[16] showed that the photolysis of *sym*-dichlorotetrafluoroacetone in the vapour phase results in the formation of difluorocarbene and proceeds as follows:

$$CF_2ClCOCF_2Cl + h\nu \rightarrow CF_2ClCOCF_2\cdot + Cl\cdot,$$
$$CF_2ClCOCF_2\cdot \longrightarrow CF_2Cl\cdot + CO + CF_2.$$

The authors draw attention to the low reactivity of difluorocarbene.

Haszeldine and coworkers[17] obtained difluorocarbene by decarboxylation of sodium chlorodifluoroacetate:

$$ClCF_2COO^- \rightarrow Cl^- + CF_2 + CO_2.$$

Difluorocarbene readily reacts with water, fluoride ions, and chlorine[18]:

$$CF_2 + H_2O \xrightarrow{H_2O} \begin{cases} CO + 2\,HF \\ HCOOH + 2\,HF, \end{cases}$$
$$CF_2 + F^- \xrightarrow{H_2O} CHF_3 + OH^-,$$
$$CF_2 + Cl^- \xrightarrow{H_2O} CHClF_2 + OH^-.$$

It can also be obtained by the reaction of potassium isopropoxide with chlorodifluoromethane in isopropanol[18]:

$$(CH_3)_2CHO^- + CHClF_2 \rightleftarrows (CH_3)_2CHOH + CClF_2^-,$$
$$CClF_2^- \rightarrow CF_2 + Cl^-.$$

Hine and Porter[19] obtained difluorocarbene by the action of sodium methoxide on difluoromethylphenylsulphone:

$$CF_2H-S(O)(O)-C_6H_5 \xrightarrow{NaOCH_3} CF_2.$$

Under suitable conditions difluorocarbene dimerises to tetrafluoroethylene with a yield reaching 95%[20]:

$$2CF_2 \rightarrow CF_2=CF_2.$$

b. Dichlorocarbene. The generally known method of preparing dichlorocarbene is by alkaline hydrolysis of chloroform[21]. A modification of this method is the reaction of chloroform with potassium t-butoxide in an inert solvent such as pentane[22]:

$$CHCl_3 + (CH_3)_3CO^- \rightleftarrows (CH_3)_3COH + CCl_3^-,$$
$$CCl_3^- \rightleftarrows CCl_2 + Cl^-.$$

The advantage of t-butoxides compared with other alkoxides is probably to a large extent associated with the weak reactivity of the anions of the sterically hindered tertiary alcohol[23].

The synthesis of dichlorocarbene from carbon tetrahalides and lithium alkyls in ethereal solution appears to be very promising[24]:

$$CCl_3X + RLi \rightarrow CCl_3Li + RX,$$
$$CCl_3Li \rightarrow CCl_2 + LiCl.$$

The effectiveness of this method of synthesising dichlorocarbene is evident from Table 1, which lists the yield of dichloronorcarane obtained by the addition of dichlorocarbene to cyclohexene. The reaction of lithium alkyls with chloroform finds a useful application when the dichlorocarbene formed is trapped by the nucleophilic triphenylphosphine. One then obtains alkylidenephosphorane which can be converted into substituted vinyl chlorides by the Wittig reaction[25]:

$$(C_6H_5)_3P + CCl_2 \rightarrow (C_6H_5)_3P=CCl_2,$$
$$(C_6H_5)_3P=CCl_2 + \rangle C=O \rightarrow \rangle C=CCl_2 + (C_6H_5)_3PO.$$

Recently a new method has been proposed for the preparation of dichlorocarbene, by the reaction of chloroacetate esters with alkoxides in an inert solvent:

$$CCl_3COR + RO^- \rightarrow CCl_3\overset{O^-}{\underset{OR}{C}}-OR \rightarrow CCl_2 + Cl^- + RO-\overset{O}{\overset{\|}{C}}-OR.$$

The effectiveness of this method may be judged from the yield of cyclopropanes formed when olefins are introduced into the reaction system. When t-butyl dichloroacetate is allowed to react with potassium t-butoxide and isobutene, 1,1-dichloro-2,2-dimethylcyclopropane is obtained in only 10% yield[26]; Parham and coworkers[27] were able to increase the yield of cyclopropanes to 72–88% by carrying out the reaction with ethyl trichloroacetate and potassium t-butoxide, sodium ethoxide, or sodium methoxide. Thus the above reaction can give higher yields of cyclopropanes than the reaction in which chloroform is used as a source of dichlorocarbene. The use of readily available sodium methoxide is also an advantage of this method.

Table 2 lists the yields of cyclopropane derivatives obtained by the two methods described above. Wagner[30] proposed a modification of Parham's method[26,27] consisting in thermal decomposition of sodium trichloroacetate in an inert solvent:

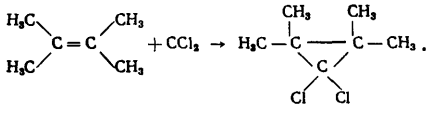
$$CCl_3COONa \xrightarrow{t} CCl_2 + NaCl + CO_2.$$

It has recently been established by polarography that the electrochemical reduction of carbon tetrachloride in solution in acetonitrile proceeds via a stage in which dichlorocarbene is formed[31]:

$$CCl_4 + 2\bar{e} \rightarrow CCl_3^- + Cl^-,$$
$$CCl_3^- \rightleftarrows CCl_2 + Cl^-,$$
$$CCl_2 + 2\bar{e} \rightarrow CCl_2^{2-},$$
$$CCl_2^{2-} + 2CH_3CN \rightarrow CH_2Cl_2 + 2CH_2CN^-.$$

This is also confirmed by the synthesis of 1,1-dichloro-2,2,3,3-tetramethylcyclopropane when the electrolysis of carbon tetrachloride is carried out at -20° in the presence of tetramethylethylene[31]:

$$CCl_4 + 2\bar{e} \rightarrow CCl_3^- + Cl^-,$$
$$CCl_3^- \rightleftarrows CCl_2 + Cl^-,$$



In 1963 it was found[32] that dichlorocarbene can add to the double bond of tetrachloroethylene with the formation of hexachlorocyclopropane. Bearing in mind the fact that tetrachloroethylene is resistant to electrophilic attack, the authors suggest that dichlorocarbene behaves in this reaction either as a nucleophilic or a radical reagent.

Dichlorocarbene has been more thoroughly investigated than any other carbene, and we shall therefore return to its various reactions throughout this review.

c. Dibromocarbene. This compound can be formed as an intermediate either by the alkaline hydrolysis of bromoform[18,33,34] or by treatment of a mixture of the latter in anhydrous alcohol with alkali metal alkoxides[7,18,28]:

$$CHBr_3 + :B \rightleftarrows CBr_3^- + HB,$$
$$CBr_3^- \rightleftarrows CBr_2 + Br^-.$$

Strong bases such as methyllithium and n-butyllithium have also been tested in the synthesis of dibromocarbene. Closs and Closs[39] allowed these bases to react with dibromomethane and Miller and Kim[24] with carbon tetrabromide. It was found that, whereas n-butyllithium and carbon tetrabromide convert olefins into dibromocyclocyclopropanes albeit in very small yields, it was impossible to demonstrate the formation of dibromocarbene in the reaction of methyllithium with dibromomethane.

d. Diiodocarbene. Hine *et al.*[21] recently succeeded in synthesising diiodocarbene by the action of sodium ethoxide on iodoform:

$$CHI_3 + C_2H_5O^- \rightleftarrows CI_3^- + C_2H_5OH,$$
$$CI_3^- \rightleftarrows CI_2 + I^-.$$

The diiodocarbene so formed reacts with the excess of ethoxide ions, yielding acetaldehyde and methylene iodide:

$$CI_2 + C_2H_5O^- \longrightarrow CH_3CHO + CHI_2^-,$$
$$CHI_2^- + C_2H_5OH \longrightarrow CH_2I_2 + C_2H_5O^-.$$

TABLE 1. Yields of dichloronorcarane obtained by the reaction of cyclohexene with carbon tetrahalides and different organolithium compounds.

Carbon tetrahalide	Lithium alkyl	Yield of dichloro-norcarane, %
CCl_4	CH_3Li	8
CCl_4	$n\text{-}CH_3(CH_2)_3Li$	50
CCl_3Br	CH_3Li	67
CCl_3Br	$n\text{-}CH_3(CH_2)_3Li$	91
CCl_3I	CH_3Li	71

TABLE 2. Comparison of the yields (%) of cyclopropane derivatives obtained from olefins by the "ethyl trichloroacetate" and "chloroform" methods.

Reaction products	Initial chloride			
	$CCl_3COOC_2H_5$[27]		$CHCl_3$	
	1,1-dichloro-2,2-dimethyl-cyclopropane	7,7-dichloro-norcarane	1,1-dichloro-2,2-dimethyl-cyclopropane	7,7-dichloro-norcarane
In the presence of:				
Potassium t-butoxide	86	72	65[28]	59[28]
Sodium ethoxide	82	—	—	—
Sodium methoxide	76	88	—	38[29]

e. Chlorofluorocarbene. This compound probably forms as an intermediate in the thermal decomposition (70–100°) of dichlorofluoroacetic acid in aqueous solution:

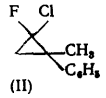
$$Cl_2CFCOO^- \longrightarrow Cl_2CF^- + CO_2,$$
$$Cl_2CF^- \longrightarrow CClF + Cl^-.$$

It later undergoes rapid hydrolysis as follows[36]:

$$CClF \xrightarrow{H_2O} HCl, HF, CO, \text{ and } HCOOH.$$

It has been shown recently that *sym*-tetrachlorodifluoroacetone can serve as a source of chlorofluorocarbene[37]. When the former was allowed to react with cyclohexene in the presence of potassium t-butoxide, 7-chloro-7-fluorobicyclo[4,1,0]heptane (I) was obtained and when 1,1-methylphenylethylene was used instead of cyclohexene, the product was 1-chloro-1-fluoro-2-methyl-2-phenylcyclopropane (II):


(I)


(II)

3. Monohalogenocarbenes

a. Alkoxyhalogenocarbenes. Hine and Tanabe[38] showed that fluoroisopropoxycarbene is formed in the decomposition of chlorodifluoromethane by potassium isopropoxide in isopropanol. Probably, initially difluorocarbene is formed[18] and then reacts with isopropanol, undergoing conversion into fluoroisopropoxycarbene:

$$CHClF_2 + (CH_3)_2CHO^- \rightleftharpoons CClF_2^- + (CH_3)_2CHOH,$$
$$CClF_2^- \longrightarrow CF_2 + Cl^-,$$
$$(CH_3)_2CHOH + CF_2 \longrightarrow (CH_3)_2CH\overset{+}{O}-\overset{-}{C}F_2 \xrightarrow{-HF} \underset{H}{\overset{OCH(CH_3)_2}{C}}\!\!<_{F}.$$

Fluoroisopropoxycarbene is also formed in the reaction of dichlorofluoromethane with a dilute solution of potassium isopropoxide, but in this case the intermediate is chlorofluorocarbene and not difluorocarbene[21].

It seems strange why the above reaction has only a single final product, triisopropyl orthoformate in 71% yield. Under the same conditions chloroform and bromoform yield in addition carbon monoxide, propene, and isopropyl ether. Evidently the difference is due to the fact that the halogen in fluoroisopropoxycarbene is less strongly bound than in chloroisopropoxy- or bromo-carbene. The latter compound loses a halide anion forming the cation (A) which then undergoes the following chain of reactions:

$$(CH_3)_2CHOC^+ \xrightarrow{-CO} \underset{(A)}{(CH_3)_2CH^+} \xrightarrow[-H^+]{(CH_3)_2CHO^-} CH_3CH{=}CH_2 + (CH_3)_2CH{-}O{-}CH(CH_3)_2.$$

b. Chlorocarbene. This compound forms when methyllithium[39], n-butyllithium[35,25], or phenyllithium[25] react with methylene chloride in dry ether:

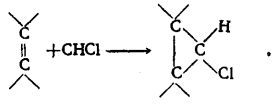
$$CH_2Cl_2 + RLi \longrightarrow LiCHCl_2,$$
$$LiCHCl_2 \longrightarrow CHCl + LiCl.$$

When methylene chloride reacts with n-butyllithium in the presence of triphenylphosphine, the corresponding alkylidenephosphorane forms in 65% yield, which falls to 40% when phenyllithium is used to form chlorocarbene[25]. This reaction is very important, since substituted vinylidene chloride can be obtained from the alkylidene phosphorane and aldehydes or ketones by the Wittig reaction[25]:

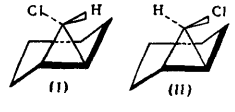
$$(C_6H_5)_3P + CHCl \longrightarrow (C_6H_5)_3P{=}CHCl,$$
$$>C{=}O + (C_6H_5)_3P{=}CHCl \longrightarrow >C{=}CHCl + (C_6H_5)_3PO.$$

Like the majority of carbenes, chlorocarbene is an electrophilic agent which reacts with olefinic double bonds, forming chlorocyclopropanes, whose yield depends on the nucleophilic properties of the olefins[35,40]:

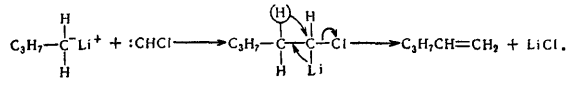
$$CH_2Cl_2 + n\text{-}C_4H_9Li \longrightarrow LiCHCl_2 \longrightarrow CHCl + LiCl,$$



Thus 2,3-dimethylbut-2-ene yields 1-chloro-2,2,3,3-tetramethylcyclopropane in 67% yield and *trans*-but-2-ene yields 1-chloro-2,3-*trans*-dimethylcyclopropane in 40% yield. Cyclohexene gives a 31% yield of a mixture of the two stereoisomeric 7-chlorobicyclo[4,1,0]heptanes (I) and (II) in 1 : 2 ratio, their reduction with sodium in liquid ammonia giving bicyclo[4,1,0]heptane[41]:

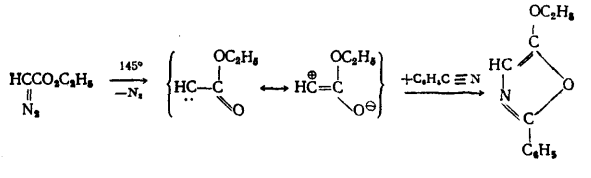

(I) (II)

In the absence of an olefin in the reaction medium, chlorocarbene reacts with n-butyllithium to give 1-chloro-n-pentyllithium which then undergoes α-elimination of lithium chloride, forming pent-1-ene following the rearrangement of the hydride anion[35,41]:



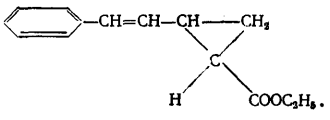
4. Keto- and Thioketo-Carbenes

Since by ketocarbenes we understand any carbenes containing the C=O group in their molecules, we think it appropriate to include in this Section some information about ethoxycarbonylcarbene. It can be obtained by the removal of nitrogen from diazoacetate ester, for example. Thus by the thermolysis of diazoacetate ester in benzonitrile, Huisgen *et al.*[42] obtained in 42% yield 5-ethoxy-2-phenyloxazole which is a product of the 1,3-dipolar cyclo-addition of ethoxycarbonylcarbene to benzonitrile:



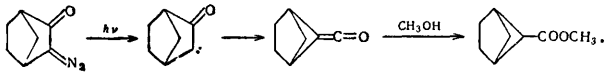
The high yield of the substituted oxazole is probably associated with the inability of ethoxycarbonylcarbene to undergo the Wolff rearrangement. Acetonitrile and phenylacetonitrile[42] also react with ethoxycarbonylcarbene, giving 2-substituted 5-ethoxyoxazole. When the decomposition of diazoacetate ester is catalysed by copper in the presence of tolane, the corresponding derivative of cyclopropene is formed[43]; the replacement of copper by copper sulphate sharply alters the mode of reaction, 2-ethoxy-4,5--diphenylfuran being formed[44,45]. Unfortunately this fact has not as yet been adequately explained (see pp. 81 and 82).

Comparatively recently the addition of ethoxycarbonylcarbene to phenylbutadiene has been described[46]. The reaction results in the formation of the following cyclopropane derivative:

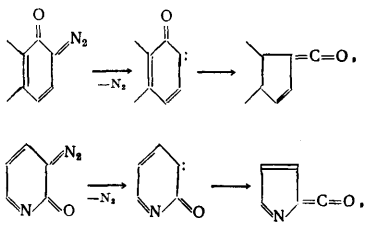


Other reactions of ethoxycarbonylcarbene are described on pages 81, 82, and 85.

Among the latest investigations of other ketocarbenes the work of Wiberg *et al.*[47], for example, is of interest; by irradiating diazonorcamphor in methanol, they obtained methylbicyclo[2,1,1]hexane-5-carboxylate:

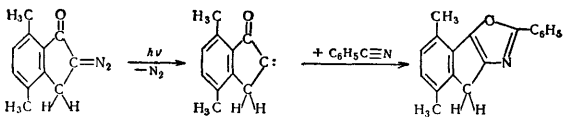


Similar ring contraction as a result of a Wolff rearrangement occurs in the photochemical[48,49] and thermal[50] decomposition of quinone diazides and naphthalene diazo-oxide, in the photochemical decomposition of diazopyridones[51],

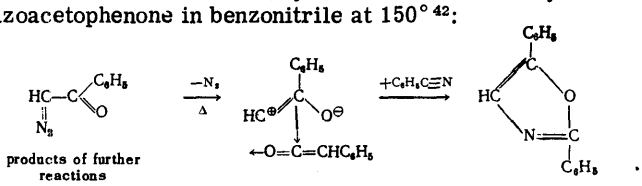


and in the photolysis of 4,7-dimethyl-4-diazoindan-1-one in aqueous tetrahydrofuran[52,53].

In the last case the Wolff rearrangement is somewhat retarded, probably as a result of the large amount of strain in the ring, so that when the reaction is carried out in benzonitrile it is possible to obtain the 1,3-adduct of the dipolar cyclo-addition of the intermediate ketocarbene to benzonitrile (the corresponding condensed oxazole)[54]:

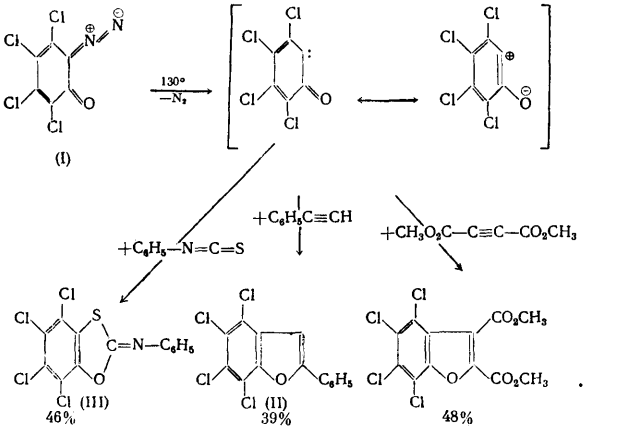


In other cases the formation of ketocarbenes was also confirmed by introducing into the reaction mixture various dipolarophiles which resulted in the formation of the corresponding 1,3-adducts. For example, 2,5-diphenyloxazole was isolated in 0.4% yield after the thermolysis of diazoacetophenone in benzonitrile at 150°[42]:

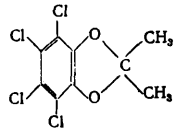


The very low yield of the 1,3-adduct in this case is due to the high rate of the Wolff rearrangement as a result of which a large part of the initially formed benzolycarbene is converted into the corresponding keten. When the carbene is stabilised with metallic copper or certain cuprous and cupric compounds, the product of 1,3-dipolar cyclo--addition can be obtained in higher yields. For example, when the above reaction is carried out in the presence of copper powder, cuprous cyanide, or cupric acetylacetonate, 2,5-diphenyloxazole is obtained in 16–17% yield[42]. By stabilising the ketocarbene with copper, Novak and coworkers[55] were able to obtain acylcyclopropanes in the decomposition of a diazoketone in the presence of olefins. It is interesting that, when the decomposition of diazoacetonephenone is catalysed with copper in the presence of tolane, 2,3,5-triphenylfuran is formed[54]. The formation of the corresponding adducts of acetonitrile and acetone with ethoxycarbonyltrifluoroacetylcarbene has recently been described[56].

Aromatic ketocarbenes are distinguished by a long "life-time" in the absence of substances capable of reacting with them. This is because such carbenes would lose their aromatic character by undergoing a Wolff rearrangement. For example, the carbene formed in the photolysis of 3,4,5,6-tetrachlorobenzene-*o*-diazo-oxide (I) is so resistant to rearrangement than in methanol it gives the monoethyl ether of tetrachlorocatechol in 70% yield[54]. On the other hand, thermolysis of 2,3,4,5-tetrachlorobenzene-*o*--diazo-oxide in phenylacetylene at 130° gives the 1 : 1 adduct of the corresponding ketocarbene and the solvent; the adduct is 4,5,6,7-tetrachloro-2-phenylbenzo(b)furan (II).[42] If the decomposition of the diazo-oxide (I) is carried out in styrene, the 2,3-dihydro-derivative of the above adduct is obtained while in dimethyl fumarate the product is the diester of dihydrobenzo[b]furandicarboxylic acid. The intermediate ketocarbene also readily forms the corresponding adduct (III) with phenylisothiocyanate, whose C=S double bond is an active dipolarophile. The reactions undergone by the ketocarbene formed in the thermolysis or photolysis of 3,4,5,6-tetrachlorobenzene-*o*-diazo-oxide (I) can be represented schematically as follows:

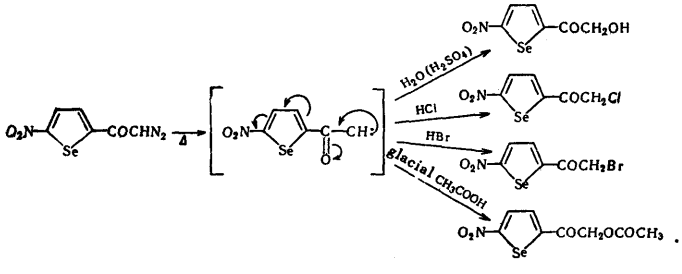


In the photolysis of the diazo-oxide (I) in acetone the carbene adds to the keto-group of acetone forming 1,3-benzodioxole in 30% yield:

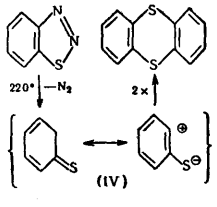


The low dependence of the rate of decomposition of the diazo-oxide (I) on the nature of the dipolarophile used as solvent is a definite indication that the reaction between these components takes place after the removal of the nitrogen molecule from the diazo-oxide (I), i.e. the corresponding aromatic carbene really exists.

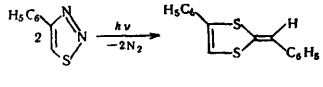
Ketocarbenes are longer-lived than alkylcarbenes, for example, which may be due to the conjugation of the lone pair of electrons of the key carbon atom and the carbonyl double bond[1]. However, the usual ketocarbenes nevertheless fairly readily undergo the Wolff rearrangement (particularly in the presence of colloidal silver), giving the corresponding ketens. The resistance of the ketocarbenes to rearrangement increases with increase in the extent of conjugation in the molecule. Thus it is reasonable that aromatic ketocarbenes are the most stable. Using aromatic ketocarbenes or ketocarbenes with a fairly long conjugation chain, it is possible to obtain high yields of the products of their direct reaction with alcohols, amines, water, hydrogen halides, etc., without resorting to additional stabilisation of the carbene with copper[57]. Thus it proves possible[58] to obtain ketones derived from selenophen, starting with 2-diazoacetyl-5-nitroselenophen:



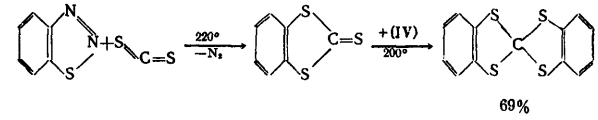
Turning now to thioketocarbenes, we must mention that as early as 1893 Jacobson and Janssen[59] obtained thianthrene by the thermolysis of 1,2,3-benzothiadiazole, which probably involves the intermediate formation of the corresponding thioketocarbene (IV):



The formation of the derivative of dithiafulvene in the photolysis of 4-phenyl-1,2,3-thiadiazole[60] may be explained by the 1,3-addition of phenylthiocarbene to the product of its rearrangement — phenylthioketen:



In contrast to the ketocarbene obtained by the degradation of the diazo-oxide (I), the thiocarbene (IV) exhibits a striking tendency towards dimerisation. Only the most active dipolarophiles with a C=S double bond can give the corresponding adducts with this thioketocarbene. Such dipolarophiles are, in particular, carbon disulphide and phenyl isothiocyanate:

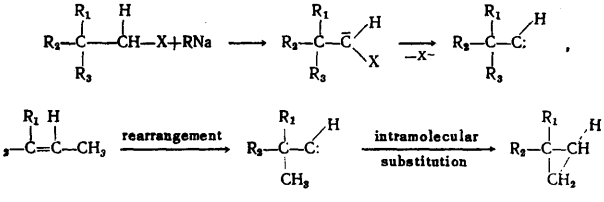


69%

There is as yet little information in the literature about the reactions of the thioketocarbene (IV) obtained in the photolysis of 1,2,3-thiadiazole[61].

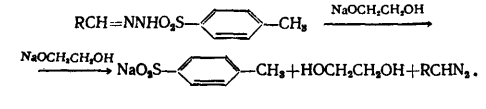
5. Other Carbenes

a. Alkylcarbenes. These compounds are obtained by the dehydrohalogenation of alkyl halides, the reaction being greatly affected by the strength of the base used for the dehydrohalogenation and by steric factors. For example, phenylsodium is more effective for the preparation of alkylcarbenes than sodium methoxide. When a secondary or a tertiary alkyl group is linked to the α-carbon atom of the alkyl halide, the main products of the reaction are olefins and cyclopropanes formed from the carbene by rearrangement or intramolecular substitution (see below) respectively[62,63]:



It is also significant that alkyl iodides are dehydrohalogenated more sluggishly than the corresponding bromides and chlorides.

Bamford and Stevens[66] developed a method for the preparation of diazoalkanes which consists in the reaction of the corresponding tosylhydrazones with sodium in ethyleneglycol:



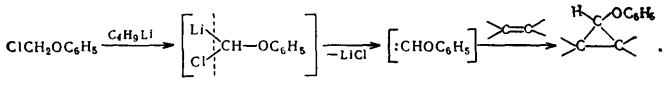
This reaction has been widely used for the preparation of alkylcarbenes. For example, it has been established that

TABLE 3. Extent of dehydrohalogenation of alkyl halides (%) as a function of the base used.

Base	Alkyl halide								
	n-butyl (Ref. 64)			isobutyl (Ref. 64)			neopentyl (Ref. 65)		neohexyl (Ref. 65)
	Cl	Br	I	Cl	Br	I	Cl	Br	Cl
C_6H_5Na	94	94	65	89	62	13	70	25	67
$NaNH_2$	30	15	—	7	1	—	60	—	—
$NaOCH_3$	10	—	—	0	—	—	—	—	—

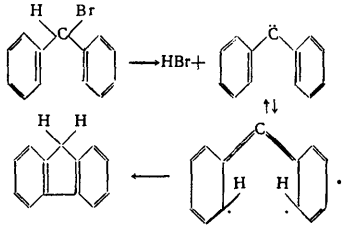
the tosylhydrazones of aromatic[63,67], aliphatic[63,68], and alicyclic[69] aldehydes and ketones react with bases in aprotic solvents, such as diethyl Carbitol, forming diazo-compounds which on thermal decomposition between 160° and 220° generate the corresponding carbenes. Alkylcarbenes obtained from aliphatic tosylhydrazones tend to undergo rearrangement with formation of olefins, and intramolecular substitution resulting in cyclopropanes. The rearrangement takes place to a greater extent in view of the higher yields of olefins.

b. Alkoxy- and phenoxy-carbenes. Schöllkopf and Paust[70] obtained in high yields a number of alkoxycyclopropanes by the reaction of dichloromethyl alkyl ethers with olefins in the presence of methyllithium. They believe that this reaction proceeds with the intermediate formation of the alkoxycarbene. Later these workers and Lerch[71] described a synthesis of phenoxycyclopropanes by the reaction of chloromethyl phenyl ether with olefins in the presence of butyllithium. They believe that the reaction proceeds as follows:

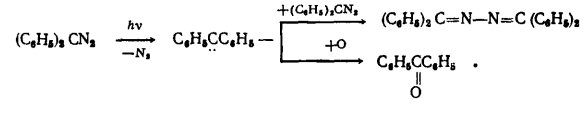


The addition of phenoxycarbene to the double bond takes place stereospecifically, like *cis*-addition.

c. Diphenylcarbenes. By pyrolysing diphenylmethyl bromide, Harrison and Lossing obtained fluorene and hydrogen bromide[72]. Probably diphenylcarbene forms as an intermediate and is then converted into fluorene as a result of migration of hydrogen atoms:

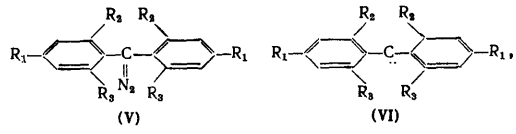


Photolysis of diphenyldiazomethane at low temperatures also result in the formation of diphenylcarbene, the latter rapidly reacting with diphenyldiazomethane and oxygen to give benzophenone azine [bis(diphenylmethylene)hydrazine] and benzophenone[73]:



Diphenylcarbene can also be obtained by the thermal decomposition of diphenyldiazomethane, the nature of the final reaction products depending on the solvent used. When the reaction is carried out with solvent or in benzene, benzophenone azine is formed exclusively. When petroleum ether is used, benzophenone azine, *sym*-tetraphenylethane, and a molecular complex of tetraphenylethane and benzophenone azine are formed. The authors believe that in this case diphenylcarbene reacts with petroleum ether forming diphenylmethyl radicals which on dimerisation give the substituted ethane.

Fairly stable substituted diphenylcarbenes (VI) were obtained by the pyrolytic and photolytic decomposition of the corresponding diazo-compounds (V):[74]



(V) (VI)

Va, VIa; R_1, R_2, R_3=CH_3;

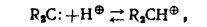
Vb, VIb; R_1, R_2, R_3=Cl;

Vc, VIc; R_1=CH_3, R_2=R_3=OCH_3.

The low reactivity of carbenes of type (VI) is a consequence of steric hindrance. Paskovich's dissertation deals in particular with sterically hindered carbenes[75].

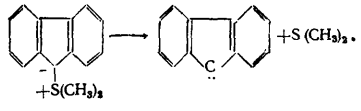
It is interesting that diphenylcarbene exhibits radical properties[76]; for example its addition to olefins is non-stereospecific[8]†.

Recently Kirmse[78] observed nucleophilic behaviour in the case of diphenylcarbene: the latter was converted into the diphenylcarbenium cation after its synthesis by the photolysis of diphenyldiazomethane in alcohol. Thus the equilibrium

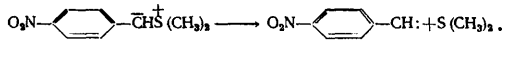


which previously was regarded as purely formal, found practical confirmation. The author notes that diphenylenecarbene obtained from diazofluorene shows much weaker nucleophilic activity.

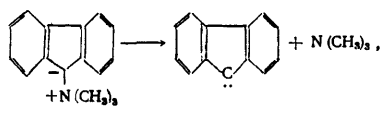
d. Fluorenylidene and cyclopentadienylidene. Johnson and La Count[79] showed that when dimethylsulphonium 9-fluorenylide is decomposed the corresponding carbene, fluorenylidene, is formed as an intermediate:



Swain and Thornton[80] found that other dimethylsulphonium compounds also break down with the formation of the corresponding carbenes. Thus decomposition of *p*-nitrobenzyldimethylsulphonium *p*-toluenesulphonate in the presence of sodium hydroxide at 60° yields *p*-nitrobenzylcarbene, which dimerises to *cis*- and *trans*-*pp'*-dinitrostilbenes:

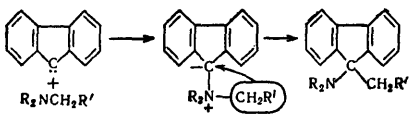


Franzen[81] showed that trimethylammonium 9-fluorenylide also decomposes into fluorenylidene,

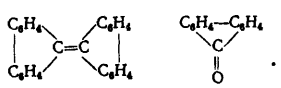


† Somewhat later Skell and Klebe[77] observed radical properties in the case of another carbene — propargylidene (HC≡C–C̈–H).

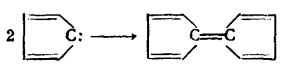
which then reacts, with amines for example[81,82] in the following way:



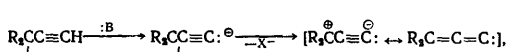
In the absence of suitable reagents fluorenylidene dimerises to difluorenylidene or reacts with oxygen to form fluorenone[13]:



The photochemical decomposition of diazocyclopentadiene yields fulvalene; this is probably due to the formation of a carbene (cyclopentadienylidene) as an intermediate, which subsequently dimerises[13]:

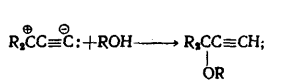


e. Vinylidenecarbenes. Hartzler[83] made a thorough study of the rearrangement of acetylene systems into allene systems in the presence of alkoxide and hydroxide ions and concluded that the formation of vinylidenecarbene is an intermediate stage in this reaction:

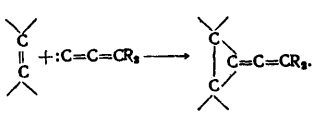


where R = CH_3, C_6H_5, H; and X = Cl, Br, OH, $OCOCH_3$.

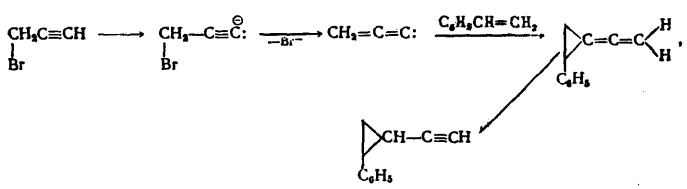
In the presence of alcohol the vinylidenecarbene reacts in the "propargyl form" with the formation of the corresponding propargyl ether[84],



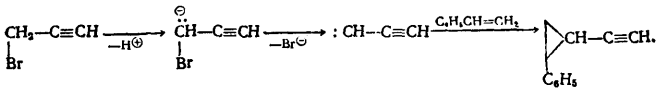
while in the presence of olefins it reacts in the "allenyl form" and is converted into cyclopropanes[83-85]:



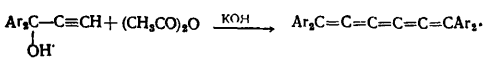
The reaction of propargyl bromide with potassium t-butoxide in styrene yields 1-ethynyl-2-phenylcyclopropane. This compound can form in two ways: either via the vinylidene carbene[83]:



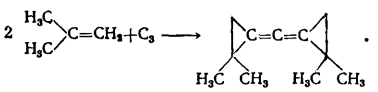
or by α-elimination of hydrogen bromide with subsequent addition of the resulting propargylidene to styrene[83]:

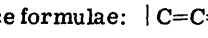


According to Hartzler[83], the formation of tetraarylhexapentaenes in the reaction of diarylethynylmethanols with acetic anhydride and potassium hydroxide in dry ether[86] also proceeds via vinylidenecarbene:



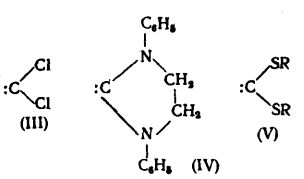
The dicarbene C_3 observed recently in the atmosphere of comets proved to be the main constituent of gaseous carbon[87]. This dicarbene is obtained by evaporating carbon into a vacuum corresponding to 10^{-3}–10^{-5} mmHg. It can enter into a variety of reactions on the walls of the reaction vessel cooled to -196°. For example, the reaction of the dicarbene C_3 with isobutene yielded a compound of a new class — the bisethanoallene series. The structure of the products, whose yield was 40%, was demonstrated by infrared and nuclear magnetic resonance spectroscopy[88,89]:



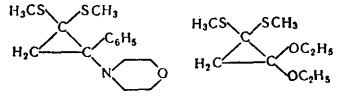
The reaction of the dicarbene with *cis*- and *trans*-but-2-enes is stereospecific to the extent of 90–95%, i.e. 90–95% of the dicarbene molecules are in the singlet state at the instant of the reaction and the remainder in the triplet state. Skell and Wescott[88] suggest that the structure of the C_3 molecule should be represented by a combination of the following two resonance formulae: .

f. 1,3-Diphenylimidazolidin-2-ylidene. By reacting dianilinoethane with orthoformates, Wanzlick and coworkers[90-92] were able to synthesise an olefin which readily dissociated into two molecules of a carbene–1,3-diphenylimidazolidin-2-ylidene. This carbene, which we shall henceforth call stable carbene, is markedly nucleophilic probably because of the strong electron-donor properties of the nitrogen atoms, and does not react with the usual olefins. The authors isolated only the product of the reaction of stable carbene with tetracyanoethylene, in which the electron density at the double bond is known to be greatly reduced[91]. The structure of this product has not as yet been elucidated.

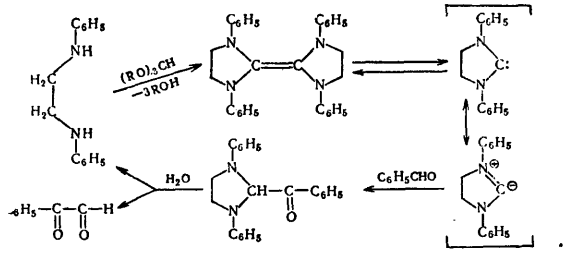
The electrophilic or nucleophilic properties of a carbene depend on the electron-acceptor (or correspondingly the electron-donor) properties of the atoms linked to the key carbon atom. In this connection it is interesting to compare dichlorocarbene (III), stable carbene (IV), and the carbene (V) in which two sulphur atoms are linked to the key carbon atom, since sulphur is intermediate between nitrogen and chlorine in its electron-donor properties.



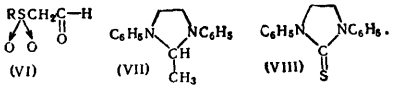
Dichlorocarbene (III), being a typical electrophilic agent, readily reacts with the usual olefins and only to a very slight extent with olefins whose double bond is markedly deactivated, the reaction mechanism being evidently different in the latter case[32]. The stable carbene (IV) is a nucleophilic compound and does not react at all with the usual olefins. Schöllkopf and Wiskott[93] have established that the di(methylcapto)carbene (V) (R = CH_3, for example), does not react with a solution of cyclohexene in the dimethyl ether of ethylene glycol, because the sulphur atoms greatly reduce its electrophilic properties by virtue of their lone pairs of electrons. Nevertheless, in certain cases di(methylmercapto)carbene also shows electrophilic properties. Thus it is capable of adding to double bonds with enhanced electron density, yielding, for example, cyclopropane derivatives on reaction with 1-morpholino-1--phenylethylene or keten diethyl acetal:



Although the chemistry of the nucleophilic carbene has only just begun to be investigated, its possible synthetic applications are already apparent. Its preparation and certain reactions can be shown schematically as follows:

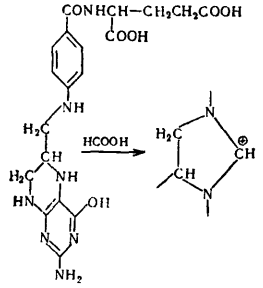


Apart from its use in the synthesis of keto-aldehydes, the stable carbene provides, for example, a possible pathway to the synthesis of the as yet unknown class of β-sulphone-aldehydes (VI).[94] Hydrolysis of the primary product of the reaction of the stable carbene with acetic anhydride yields 2-methyl-1,3-diphenylimidazolidine (VII) and monoacetylated dianilinoethane. The stable carbene reacts with sulphur even at room temperature, giving the corresponding derivative of thiourea (VIII):



While in their reaction with dichlorocarbene diazo--compounds eliminate a molecule of nitrogen[95], with the nucleophilic carbene they yield ketazines. On treatment with carboxylic acid chlorides, the stable carbene gives imidazolidinium salts acylated at the carbon atom in position 2, which are readily hydrolysed.

It is nowadays believed that tetrahydrofolic acid combines with formic acid or formaldehyde and participates in the metabolism of certain substances in living organisms, promoting transformylation, transhydroxymethylation, and certain other reactions[96]. It is interesting that tetrahydrofolic acid itself is structurally related to dianilinoethane, while the product of its reaction with formic acid, the so--called "anhydrocitrovorum factor", is none other than the protonated form of a carbene very similar in structure to the stable carbene[97]:



Hence it is not impossible that reactions involving the participation of carbenes occur also in nature. Quite recently Wanzlick and coworkers[98] have described the synthesis of new compounds of the type of bis(1,3-diphenylimidazolidin--2-ylidene).

IV. SOME ASPECTS OF THE SYNTHETIC APPLICATIONS OF CARBENES

1. Substitution of Carbenes in C–H, C–Halogen, and Other Bonds

a. Intermolecular substitution of carbenes. Franzen and Fikentscher[99] allowed methylene labelled at the carbon atom to react with ethyl ether and showed that this results in the formation of ethyl n-propyl ether by direct substitution of methylene in the C–H bond of the ethyl group. Franzen and Kuntze[100] described similar reactions with other alkyl ethers, tetrahydrofuran, and *N*-methylpyrrolidine.

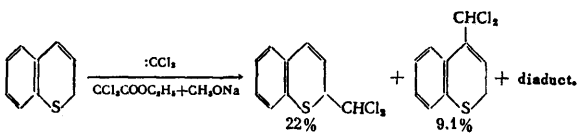
Doering and coworkers[101] showed that methylene obtained by the photochemical decomposition of diazomethane readily interacts with the C–H bonds of saturated hydrocarbons, for example n-pentane, 2,3-dimethylbutane, cyclopentane, etc., the products of the substitution of methylene in various C–H bonds being formed in amounts corresponding to the number of these bonds in the hydrocarbon molecule regardless of the nature of the bond. In view of the absence of selectivity in this reaction, Doering suggested that its activation energy is close to zero[101,102].

However, Frey[103] was able to show that methylene obtained by gas-phase photolysis of diazomethane reacts selectively with $\rangle CH$, $\rangle CH_2$, and $-CH_3$ bonds in hydrocarbons, in the ratios 1.5 : 1.2 : 1.0. Richardson *et al.*[4] carried out liquid-phase photolysis of diazomethane in solution in isomeric octanes and arrived at the same conclusions as Doering. They believe that the difference between the reactivity of methylene in the gas phase and in solution can be readily explained on the basis of Herzberg's spectroscopic data on its structure[3,104]. During photolysis in solution excited singlet methylene forms initially, almost each of its collisions with the solvent molecules resulting in reaction. Since the frequency of collisions is much greater than the frequency of the singlet–triplet transition, non-selective substitution of methylene in carbon–hydrogen bonds occurs. In the gas-phase reaction the frequency of the collisions of methylene with hydrocarbon molecules is approximately the same as that of the singlet–triplet transition and therefore methylene reacts selectively as a typical radical agent.

This interpretation is consistent with a number of experimental data[4,103,105,106]. Doering and Knox[102] showed that the replacement of hydrogen atoms in methylene by electronegative groups greatly increases the selectivity of the reaction of the carbene with C–H bonds. The ratios of the rates of substitution at tertiary, secondary, and primary carbon atoms of the alkane greatly increase in the following sequence of carbenes: $CH_2 < CHCOOC_2H_5 < C(COOC_2H_5)_2$. Doering and Knox suggest that the presence of the alkoxycarbonyl group increases the activation energy for the reaction and favours the reaction at the tertiary carbon atom relative to that at the primary atom.

Recently it proved possible to substitute methylene in the C–H bond of pyridine, with 83% yield of α-picoline[107]. The specificity of the reaction was explained by the initial addition of methylene to the nitrogen atom with subsequent rearrangement.

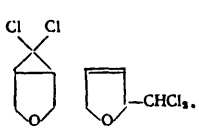
Until 1961 it was regarded as generally accepted[108] that dihalogenocarbenes cannot be substituted in C–H bonds. However, Parham and Koncos[109] showed that this reaction is possible:



They suggest that the benzothiopyranate anion forms initially under the action of sodium methoxide.

Since the formation of tetrachloroethylene from dichlorocarbene and chloroform is never observed in the liquid phase, its formation in the pyrolysis of chloroform probably involves the substitution of dichlorocarbene in the C–H bond of chloroform, the resulting pentachloroethane being converted into tetrachloroethylene after losing the elements of hydrogen chloride[97].

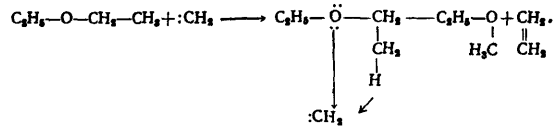
Anderson and Reese[110] showed that the addition of dihalogenocarbenes to carbon–carbon double bonds and their substitution in C–H bonds of olefins may compete with one another. Thus when 2,5-dihydrofuran is treated with a slight excess of dichlorocarbene obtained from ethyl ether, trichloroacetic acid, and sodium methoxide at 0°, a mixture of 6,6-dichloro-3-oxabicyclo[3,1,0]-hexane and 2-dichloromethyl-2,5-dihydrofuran is formed with an overall yield of 62%:



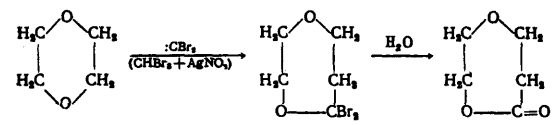
In the case of dibromocarbene a mixture of the corresponding bromo-compounds forms with an overall yield of 28%.

Of the latest work on the substitution of free methylene in C–halogen bonds, the investigation of Bradley and Ledwith[111] must be mentioned. They were able to substitute methylene in C–Cl bonds of primary, secondary, and tertiary alkyl chlorides. The substitution of methylene in C–halogen bonds is described in greater detail in D'yakonov's review[112].

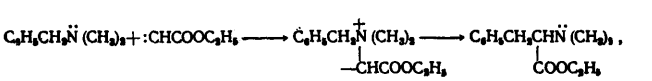
The C–O bond is fairly vulnerable with respect to carbenes. For example, methylene is not only substituted in the C–H bonds of alkyl ether but the latter are actually split with the formation of olefins and the corresponding methyl alkyl ethers. The reaction probably proceeds as follows[99]:

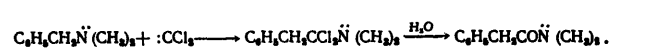


Phenylcarbene and ethoxycarbonylcarbene[99], obtained by the photolysis of the corresponding diazo-compounds, react similarly. The reaction of dibromocarbene with dioxan in aqueous solution is also an example of substitution in the C–O bond[113]:

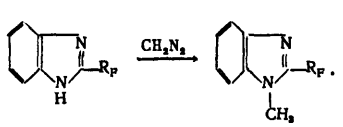


The substitution of carbenes in C–N bonds usually occurs only in those cases where the amino-nitrogen is linked to the benzyl radical, which is distinguished by exceptional cationoid activity[108,110,114]. The reaction probably takes place by a "ylid" mechanism:

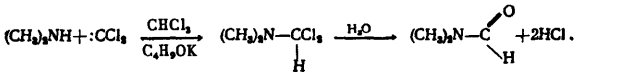




Braz *et al.*[115] showed that methylene is readily substituted in N–H bonds of benzimidazoles with a perfluoroalkyl substituent in the 2-position, which greatly increases the mobility of the hydrogen atom in the imino-group:



Other examples of substitution of carbenes in N–H bonds are known[116,117]:

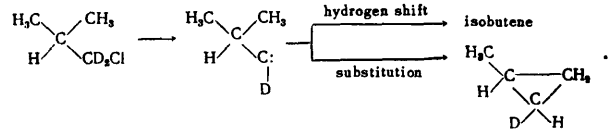


It has recently been shown that this reaction can be used also for the preparation of thioformamides[118].

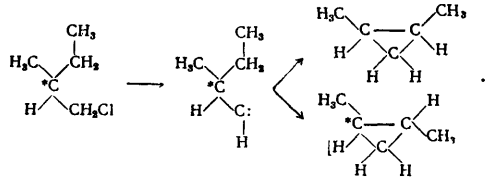
Reutov and Lovtsova[119] suggest that dichlorocarbene can be substituted in the Hg–Cl bond with the formation of trichloromethylorganomercury compounds.

b. Intramolecular substitution of carbenes. In the case of alkylcarbenes the substitution in C–H bonds often takes place intramolecularly. Kirmse and Doering[120] found that the formation of methylcyclopropane and isobutene under the conditions of the Wurtz reaction from isobutylene chloride labelled with deuterium

proceeds via α-elimination of deuterium chloride, i.e. in the intermediate dehydrohalogenation stage carbene is formed and then gives the final product by intramolecular substitution:

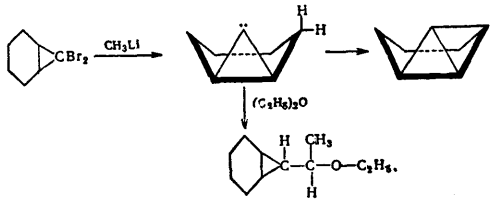


Doering and Kirmse[121] found an elegant application for the above reaction: they used it to establish the *cis*- and *trans*-configurations of the isomeric 1,2-dimethylcyclopropanes. This depends on the fact that the carbene formed from the optically active 2-methylbutyl chloride can react further in several ways: with formation of an olefin, ethylcyclopropane, and two dimethylcyclopropanes. Of the last two, only the *trans*-isomer can be optically active and therefore the presence of optical activity in the case of one of the dimethylcyclopropanes proves that it has the *trans*--configuration:

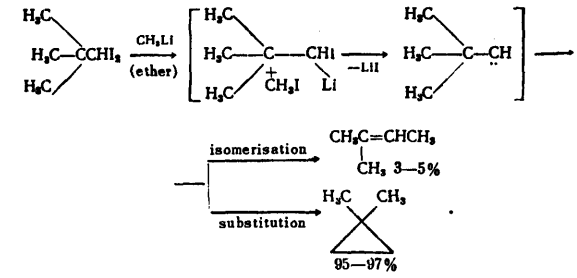


Skell and Krapcho[122] confirmed the mechanism of formation of the cyclopropanes, involving the α-elimination of the elements of hydrogen chloride, using the reaction of dideuteroneopentyl chloride with metallic sodium.

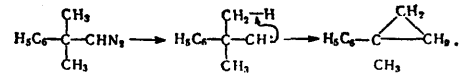
Another example of intramolecular substitution is the reaction of 7,7-dibromonorcarane with methyllithium yielding a carbene which reacts with the ether used as solvent: it is intramolecularly substituted in the C–H bond[123]:



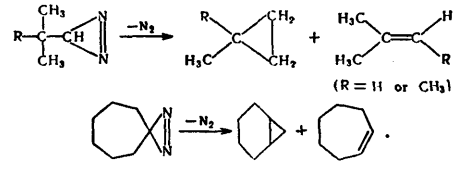
The reaction of the last type was investigated in greater detail by Kirmse and Wedel[124], who showed that, when lithium alkyls or metals (lithium, magnesium) are allowed to act upon *gem*-dihalogeno-compounds, both halogen atoms are eliminated with the formation of a mixture of the corresponding unsaturated compounds and cyclopropane derivatives. For example, the reaction between 1,1-dibromobutane and methyllithium or magnesium yields mainly but-1-ene, methylcyclopropane being formed only in small amounts. The tendency of the intermediate alkylcarbene towards intramolecular substitution in the C–H bond increases with the extent of branching of the alkyl group. Thus the reaction of 1,1-diiodo-2,2-dimethylpropane with methyllithium in ether gives a mixture of products consisting of 95–97% of 1,1-dimethylcyclopropane and 3–5% of 2-methylbut-2-ene.



The rearrangement which Philip and Keating[125] discovered and called "neophilic" rearrangement, is also an example of intramolecular substitution of a carbene in a C–H bond:



Schmitz *et al.*[126] showed that thermal degradation of diazirines yields carbenes which react further to give cyclopropane derivatives, products of intramolecular substitution, together with olefins formed as a result of rearrangement:



In contrast to the examples known until now, the solvent has no effect on the relative yields of the products in this case: whether the solvent contains hydroxy-groups or not, the yields of cyclopropanes and olefins are the same.

2. Addition of Carbenes to Carbon–Carbon and Other Double Bonds

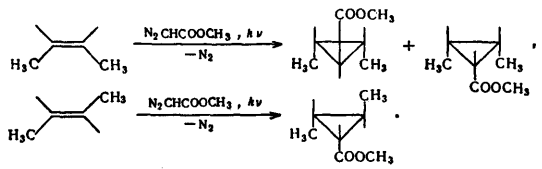
All the carbenes, except the so-called nucleophilic carbene (see p. 76) add to the double bonds of olefins with the formation of cyclopropanes. Although this reaction is often used to prove the existence of carbenes, it is necessary to exercise a certain caution in this respect. Thus in the synthesis of cyclopropanes in the reaction of Simmons and Smith[11,127,128] an organometallic compound and not a carbene is probably formed in the intermediate stage[11,127,128]. However, in most cases there is no doubt about the formation of carbenes as intermediates in the synthesis of cyclopropanes from olefins.

We shall mention first of all the series of carbenes (produced by the reactions shown below) through which an enormous number of substituted cyclopropanes have become readily available[129–133]:

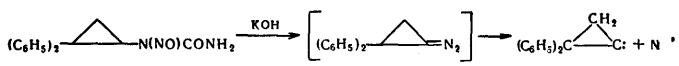
$$CF_2Br_2+RLi \rightarrow RBr+LiBr+ : CF_2,$$
$$ClH_2COR+RLi \rightarrow RH+LiCl+ : CHOR,$$
$$ClH_2CSR+RLi \rightarrow RH+LiCl+ : CHSR.$$

Having at their disposal the method at present available for the preparation of dihalogenocarbenes under neutral. conditions, which consists in the thermal decomposition of the salts of trihalogenoacetic acids, researchers are able to synthesise cyclopropanes from olefins which are sensitive to bases, for example allyl chloride[30,134].

While speaking of the characteristic features of the addition of carbenes to carbon–carbon double bonds, it must be mentioned that, as shown by Doering and Mole[135] and also D'yakonov and coworkers[136,137], alkoxycarbonylcarbenes, for example, add stereospecifically to the double bond in the *cis*-position:



2,2-Diphenylcyclopropylidene described by Jones[138],

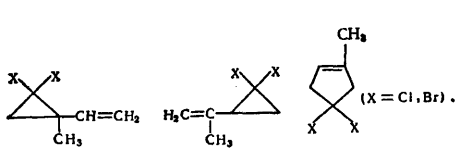


also probably adds stereospecifically to the isomeric but-2-enes[112].

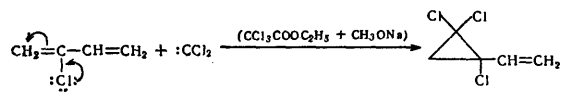
Skell and Etter[139] found that ethoxycarbonylcarbene, formed in the photolysis of diazoacetic ester, is much less stereoselective in the reaction with olefins than the same carbene prepared in a different way — by the decomposition of the diazoacetic ester in the presence of copper. Possibly under the conditions of copper catalysis the complex of the carbene with copper (or copper ions) reacts, and not the free carbene. Complex formation may increase the dimensions of the carbene reacting with the double bond and at the same time reduce its electrophilic activity[139].

Skell and Etter[140] established that the reactivity of ethoxycarbonylcarbene with respect to olefins of different structure varies in the same sense as that of the electrophilic bromonium cation. The rate of reaction in both cases diminishes as the nucleophilic properties of the olefin are weakened. This constitutes further evidence that the additions of carbenes to olefins are electrophilic reactions. In this connection we may mention that the rate of addition of the nucleophilic trichloromethyl anion to the same olefins varies in the opposite sense in the same sequence.

The reaction of dihalogenocarbenes with isoprene has been studied[141,143] and it has been found that the addition takes place mainly in the 1,2-position. Orchin and Herrick[141], who obtained a small amount of the product of 3,4-addition as well as that of the 1,2-addition, suggested that a very small amount of the product of the 1,4-addition is also formed:

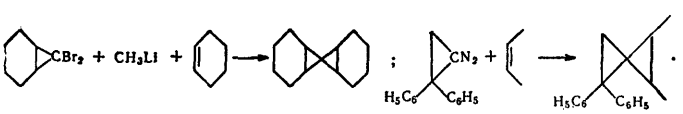


Later D'yakonov and coworkers[144] showed that dichlorocarbene also adds to chloroprene, mainly in the 1,2-position:

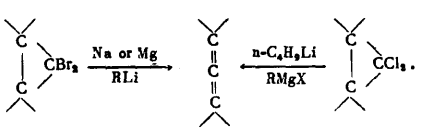


D'yakonov[112] explains this result by suggesting that during the reaction the important feature is not the negative inductive effect of the chlorine atom in the chloroprene molecule but its positive conjugation effect, which makes the 1,2-bond more nucleophilic than the 3,4-bond. It should be noted that the mode of addition to chloroprene of an electrophilic agent such as hydrogen chloride or bromide is consistent with the above explanation; in both cases the proton of the hydrogen halide is directed to the first carbon atom of chloroprene[145]. When dihalogenocarbenes are allowed to react with hexa-1,3,5-triene, mono- and di-adducts are formed. Clearly the more nucleophilic double bonds of the terminal vinyl groups of hexa-1,3,5-triene are involved in the reaction. Vinylcyclopropanes may be of interest as monomers. Thus polymerisation of vinylcyclopropane in the presence of $Al(C_2H_5)_3.TiCl_3$ gave a crystalline polymer[146,147].

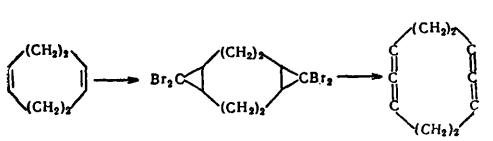
Using the addition of cyclic carbenes (cyclopropylidenes) to olefins[138,148], it is possible to obtain spiran derivatives:



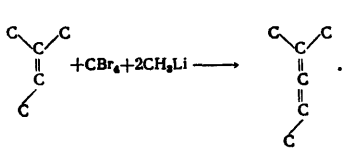
It is interesting that, when the adducts of olefins and dichloro- or dibromo-carbenes are acted upon by various alkaline agents, they lose two halogen atoms and are converted into allenes[10,148-150]:



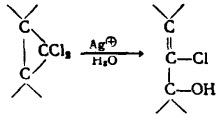
Skatteböl[149] used this reaction to convert cycloocta-1,5-diene into cyclodeca-1,2,6,7-tetraene:



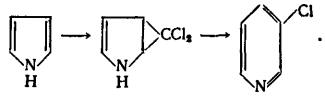
Since lithiumalkyls are among the reagents which convert dihalogenocyclopropanes into allenes and since, on the other hand, the reaction of lithiumalkyls with carbon tetrahalides can give dihalogenocarbenes, there is a possibility of converting olefins into allenes in one step, which Skatteböl[149] in fact achieved:



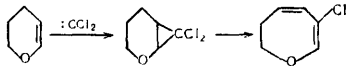
Dihalogenodicyclopropanes can be converted into allyl compounds as well, for example by treatment with an aqueous solution of silver nitrate[151]:



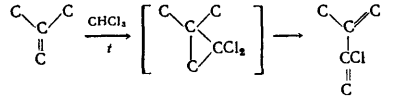
The rearrangement into allyl compounds takes place also with adducts of cyclopentene[152] and bicyclo[2,2,1]-heptadiene[153], the latter forming bicyclo[3,2,1]octadiene. The removal of a molecule of hydrogen halide together with the opening of the cyclopropane ring takes place particularly readily if an aromatic compound or a compound with conjugated multiple bonds is the product of the reaction[154]:



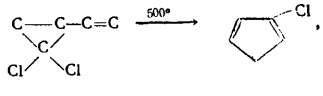
Chlorobenzene and β-chloronaphthalene are obtained in the same way from cyclopentadiene[159] and indene[156]. Monochlorocarbene, formed from methylene chloride and a lithium alkyl, gives pyridine on reaction with pyrrole[157]. Other dichlorocyclopropanes require more severe conditions for reactions of this kind. For example, the adduct of dichlorocarbene and dihydropyran is converted into chlorodihydrooxepin in boiling quinoline[158]:



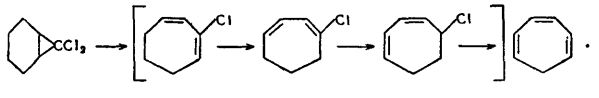
Pyrolysis of suitable adducts also gives dienes. Since chloroform, for example, is pyrolysed to dichlorocarbene[159], it is possible to obtain chlorobutadiene by the pyrolysis of chloroform in the presence of isobutene[160]:



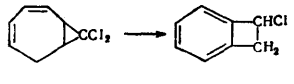
In a number of cases the pyrolysis of the adduct of an olefin and dichlorocarbene does not give the expected chlorodiene; for example, the adduct of butadiene is converted into chlorocyclopentadiene on pyrolysis[161]:



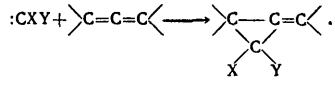
while 7,7-dichloronorcarane yields cycloheptatriene[29,162]:



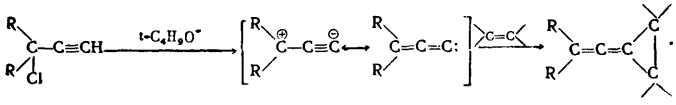
The pyrolysis of the adduct of cycloheptatriene results in the formation of chlorobenzocyclobutene[155] and not chlorocyclooctatetraene:



Comparatively recently alkylidenecyclopropanes were obtained by the addition of carbenes to allenes[163-165]:



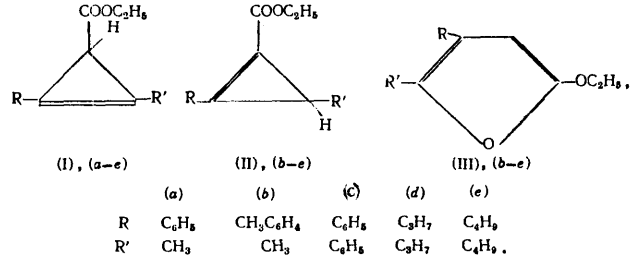
Hartzler established that αγ-elimination of the elements of hydrogen halide from a 3-halogenoalk-1-yne results in an intermediate compound of the carbene type which adds to olefins with the formation of alkenylidenecyclopropanes[83,85,166]:



As regards the addition of carbenes to double bonds other than carbon-carbon, for example the carbonyl group, we may mention the hypothesis of Knunyants *et al.*[1] concerning the possibility of the participation of carbenes in the Darzen reaction. The formation of epoxy-derivatives of alkenes from keto-derivatives of diazomethane probably occurs without the intermediate formation of the carbene[167]. The 1,3-dipolar cyclo-addition of suitable carbenes to the carbonyl groups of ketones has already been mentioned on page 73. Fields and Sandri[168] observed the addition of dichlorocarbene to the C=N double bond of *N*-benzylideneaniline.

3. Carbene Synthesis of Cyclopropene Derivatives

By allowing ethoxycarbonylcarbene to react with various acetylenic hydrocarbons, D'yakonov and coworkers[44,169,170] showed that, depending on the experimental conditions, the reaction can yield either two isomeric compounds or only one of them. Initially it was assumed that both isomers are esters of cyclopropenecarboxylic acids, (I) and (II), differing in the position of endocyclic double bonds. (I) forms in the high-temperature reaction without catalyst or in the presence of very small amounts of copper sulphate [in the latter case there is an admixture of (I)], and (II) forms in the low-temperature reaction in the presence of large amounts of copper sulphate[44,169,170]:

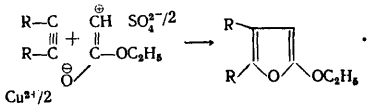


	(a)	(b)	(c)	(d)	(e)
R	C_6H_5	$CH_3C_6H_4$	C_6H_5	C_3H_7	C_4H_9
R′	CH_3	CH_3	C_6H_5	C_3H_7	C_4H_9.

Later it was found that (I) also forms in the presence of copper as a catalyst.

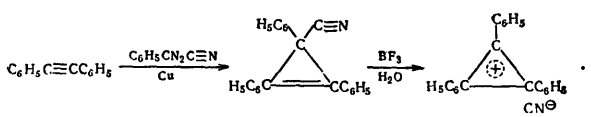
Breslow and Chipman[45] suggested that the properties of the compound hitherto assumed to be (IIc) are more consistent with 5-ethoxy-2,3-diphenylfuran (IIIc). Similarly they suggested that the formulae (II*d*) and (II*e*) should be changed to (III*d*) and (III*e*) respectively. D'yakonov and coworkers made an additional investigation of the above compounds whose results[169] proved to be in complete agreement with the remarks of Breslow and Chipman.

The American workers explained the formation of 5-ethoxyfurans by 1,3-addition of ethoxycarbonylcarbenes to the triple bond, possibly as a complex with copper sulphate. There is also a possibility that the presence in the reaction medium of cupric and sulphate ions bearing opposite charges stabilises the 1,3-dipolar form of ethoxycarbonylcarbene, since in the absence of copper sulphate or the presence of metallic compounds which Breslow used[43], 1,1-adducts are formed:

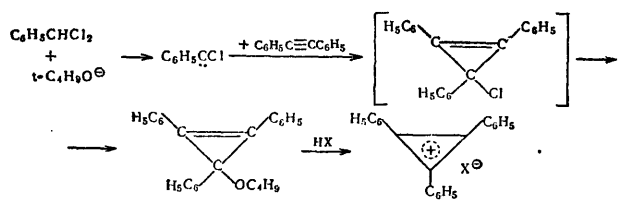


D'yakonov and coworkers succeeded in obtaining derivatives of dicyclobutane from the corresponding cyclopropene derivatives (Id) and (Ie) and the diazoacetate ester in the presence of copper[171].

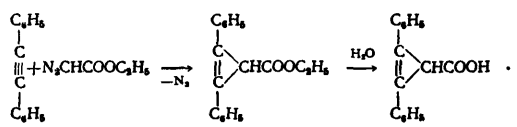
The cyclopropene derivative prepared by Breslow[172,173] from phenylcyanocarbene and tolane was used to form a new aromatic system — the *sym*-triphenylcyclopropenyl cation:



Breslow and coworkers[174,175] also obtained the same cation by the reaction of benzylidene chloride with potassium t-butoxide in the presence of diphenylacetylene, with subsequent acid treatment of the resulting cyclopropenyl ether:

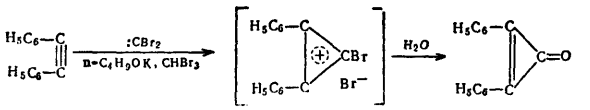


Breslow also carried out reactions between tolane and the diazomalonic ester and between tolane and the diazoacetic ester[176], with formation in the latter case of 1,2-diphenylcycloprop-1(2)-ene-3-carboxylic acid, identical with that synthesised by D'yakonov from the ester (Ic) (see p. 81):



Doering and Mole[135] carried out a photochemical reaction between diazomethane and but-2-yne which resulted in the formation of 1,2-dimethylcyclopro-1(2)-ene. Frey[177] attempted to obtain cyclopropene by the addition of methylene, produced by the photolysis of diazomethane, to acetylene in the gas phase, but only allene, methylacetylene, and a large amount of polymeric products were actually formed. When this reaction is carried out with acetylene labelled with deuterium, the final products are 1,3-dideuteropropyne and 1,1-dideuteropropadiene which suggest the formation of dideuterocyclopropene as an intermediate.

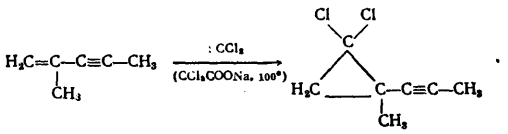
The addition of a dihalogenocarbene to a triple bond was first achieved by Vol'pin *et al.*[178,179] in the reaction between dibromocarbene and tolane:



Somewhat earlier Breslow *et al.*[180] obtained diphenylcyclopropenone from phenylchlorocarbene and the acetal of phenylketen. The authors explained the unusual properties of this ketone in terms of the concept of the cyclopropenyl cation as an aromatic species.

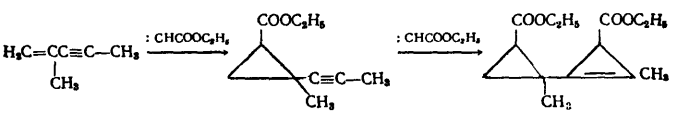
Dipropylcyclopropenone, which Breslow and Peterson[181] obtained from oct-4-yne and dichlorocarbene, proved to be even more stable.

D'yakonov and coworkers[182] showed that enyne hydrocarbons also react with carbenes:



It is reasonable that the electrophilic dichlorocarbene should add to the double bond since the latter is more nucleophilic than the triple bond. This corresponding diadduct could not be obtained. The authors explained this both by the weakening of the nucleophilic properties of the triple bond and the low reactivity of dichlorocarbene. Later Vo-quang and Cadiot[183], who studied the reactions of dichloro- and dibromo-carbenes with other enynes, confirmed that the reaction stops at the stage in which the dihalogenocarbene adds to the double bond of the enyne hydrocarbon.

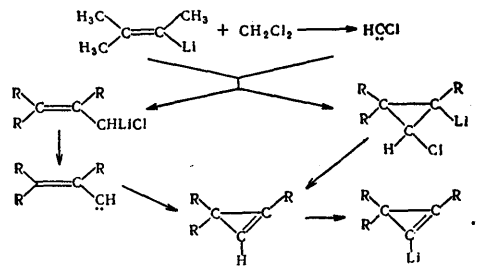
D'yakonov and Danilkina[184] studied the action of ethoxycarbonylcarbene, obtained by the decomposition of diazoacetic ester in the presence of copper or its sulphate, on 2-methylpent-1-en-3-yne. In this reaction the diadduct was obtained in addition to the monoadduct, and it was shown in a separate experiment[112] that the reaction proceeds in two stages as follows:



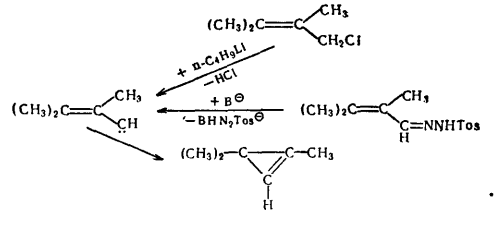
In this reaction ethoxycarbonylcarbene is more reactive and more selective than dichlorocarbene, which is consistent with the comparative characteristics of these reagents established by Skell and coworkers[140,185].

There exist two other possible ways of synthesising cyclopropenes from carbenes: (a) by the reaction between methylene chloride and lithium alkenyls[186] and (b) by intramolecular carbene–olefin addition using vinylcarbene. Let us consider the first of these reactions. In this case the monochlorocarbene formed initially can react with lithium alkenyls in two ways: (1) the carbene can add to the double bond of the lithium alkenyl with $\alpha\beta$-elimination of lithium chloride, and (2) the carbene can be substituted in the C–Li bond with subsequent $\alpha\alpha$-elimination of lithium chloride, resulting in vinylcarbene, which is then converted into cyclopropene by intramolecular addition. Since the

vinyl hydrogen in cyclopropenes is acidic[187], the product of the reaction is the lithium salt of the cyclopropene derivative. Under the given experimental conditions it can react further:

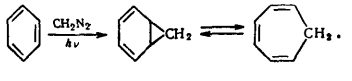


Like bromovinylcarbene, the above vinylcarbene can also be obtained by metal-substitution of mono- and di--halogeno derivatives of the allyl type[188] or from a tosylhydrazone[189] and then converted into cyclopropene:



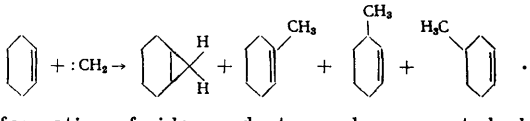
4. Ring Enlargement

The photochemical reaction of benzene with methylene resulting in the enlargement of the ring of the former has been known for a comparatively long time[190]; a mixture of cycloheptatriene and norcaradiene is formed. On heating, norcaradiene can be almost completely converted into cycloheptatriene. Nevertheless the problem of the relation between these two valence-tautomeric structures still cannot be regarded as resolved[191]:



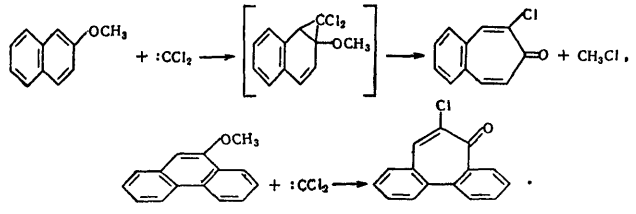
It is interesting that cycloheptatriene can be obtained by the reaction between benzene and diazomethane not only under the action of radiation but also in the presence of catalysts (cuprous chloride and bromide). According to Müller and Fricke[192], in the latter case benzene is subjected to electrophilic attack by the complex $\overset{+}{C}H_2CuBr_2$, formed from diazomethane and cuprous bromide.

A fairly large number of reactions of carbenes involving the enlargement of other rings are known. However, by no means all of them proceed equally smoothly. Kopecky and coworkers[6] established that the reaction between free methylene and cyclohexene yields a small amount of methylcyclohexene in addition to bicyclo[4,1,0]heptane (norcarane):

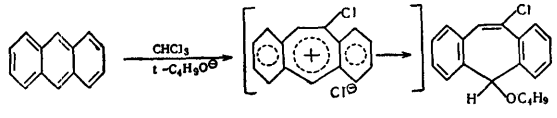


The formation of side-products can be prevented when methylene is produced by photolysis of diazomethane in solution using benzophenone as sensitiser, or by thermal–catalytic decomposition of diazomethane using powdered copper or iron dipivaloylmethide as catalysts.

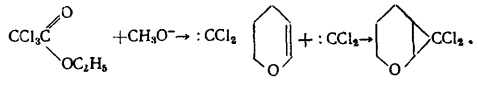
Generally speaking, aromatic double bonds combine with carbenes less readily than olefins. For example, dichlorocarbene does not react with benzene[193]. However, if the aromatic ring contains an electron-donor group, the addition is substantially facilitated. For example, the addition of dichlorocarbene, produced from ethyl trichloroacetate and sodium methoxide, to 1- and 2-methoxynaphthalenes and to 9-methoxyphenanthrene[194] results in the formation of the corresponding chlorotropones:



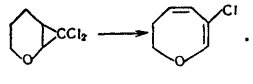
The hydrolysis of chlorotropone yields tropolone. Anthracene, in which certain positions have an enhanced electron density, reacts with dichlorocarbene and undergoes ring enlargement[195]:



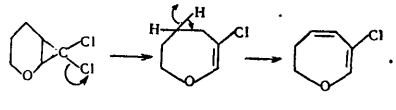
Dichlorocarbene, produced from ethyl trichloroacetate, was also used for the enlargement of certain heterocyclic rings. Thus when ethyl trichloroacetate is added to a mixture of dihydropyran and sodium methoxide in pentane, 7,7-dichloro-2-oxanorcarane is formed[158]:



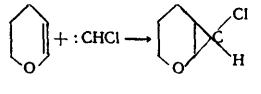
When it is heated with quinoline at 140–150° and a reduced pressure, 6-chloro-2,3-dihydrooxepin is obtained[158]:



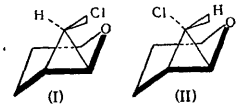
The conversion of 7,7-dichloro-2-oxanorcarane into 6-chloro-2,3-dihydrooxepin proceeds via the allyl carbonium ion, which then loses a proton:



Schweizer and Parham[158] found that chlorocarbene is also suitable for the enlargement of heterocyclic and aromatic rings. For example, when dihydropyran reacts with this carbene, a racemic mixture of the *endo*- and *exo*-forms of 7-chloro-2-oxanorcarane is obtained in 1 : 1.5 ratio:

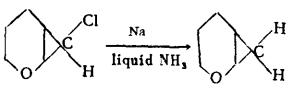


The above workers ascribed the structure (I) to the predominating isomer and structure (II) to the minor isomer, on the grounds that the formation of structure (II) in the activated complex is difficult due to the shielding of the ring by the large chlorine atom of chlorocarbene, whereas the influence of the small hydrogen atom is less marked and isomer (I) forms more rapidly.

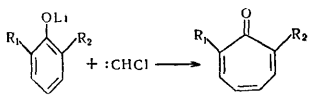


(I) (II)

Consequently isomer (I) is *exo*-7-chloro-2-oxanorcarane while isomer (II) is the *endo*-compound. Isomer (II) distils at atmospheric pressure, while the *exo*-compound decomposes even at 120° and when it is distilled with quinoline at a reduced pressure ring enlargement occurs and 2,3-dihydrooxepin is formed. The ease of conversion of isomer (I) into 2,3-dihydrooxepin is due to the influence of the *trans*-oxygen atom at the instant of the removal of the chlorine atom. Both isomers are readily reduced to 2-oxanorcarane, and in high yield, by sodium in liquid ammonia:

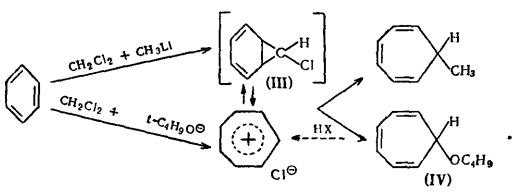


Chlorocarbene, obtained from methylene chloride and methyllithium, yields tropones on reaction with lithium phenoxides [39]:

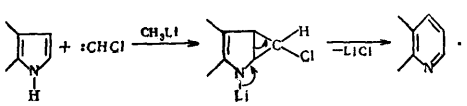


where R_1, R_2 = H (a), R_1 = H, R_2 = CH_3 (b), and R_1 = R_2 = = $(CH_3)_3C$ (c). The above synthesis of tropones is an example of the influence of electron-donor substituents on the reactivity of the benzene ring because chlorocarbene obtained in the above way reacts to only a slight extent with the benzene ring itself, the reaction involving, according to Closs and Closs [196], the initial formation of the hypothetical compound (III) which is subsequently converted into the tautomeric tropylium chloride; the latter then reacts with methyllithium to give 7-methylcyclohepta-1,3,5--triene.

When the reaction is carried out in the presence of a weak base, potassium t-butoxide [193], the ether (IV) is formed and subsequently yields the tropylium ion on interaction with acid:

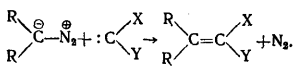


Addition of chlorocarbene to pyrrole and indole also results in the formation of ring-enlargement products, pyridine in 32% yield and quinoline in 13% yield respectively [157]:

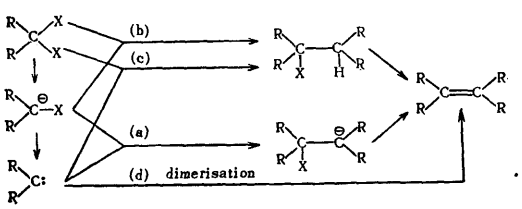


5. Carbene Syntheses of Olefins

As already pointed out (see p. 71), the phosphorus atom in triphenylphosphine, which has a free electron pair and is capable of passing to the pentavalent state, readily reacts with carbenes, yielding relatively stable alkylidenephosphoranes. The latter were obtained from dichloro-, difluoro-, and monochloro-carbenes [22,25,197,198]. When such alkylidenephosphoranes are introduced into the Wittig reaction, olefins which are otherwise difficult to obtain can be prepared. Such olefins can also be synthesised by another procedure also involving carbenes. When diazo--compounds are allowed to react with different carbenes, the latter attack the carbon atom of the diazo-compound marked with the minus sign, yielding olefins [95,199]:



A number of reactions are also known in which compounds of the type R_1R_2CHX yield the olefins $R_1R_2C{=}CR_1R_2$ under the action of base. Since it is possible to visualise the participation in this reaction of three different types of species, the molecule R_1R_2CHX, the anion $R_1R_2XC^-$, and the carbene R_1R_2C, the olefin may form by several different pathways:



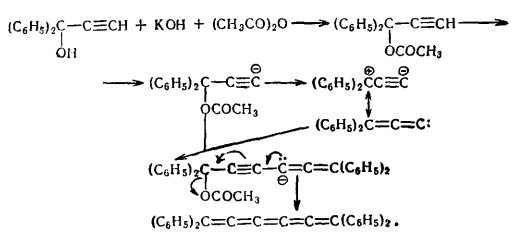
In view of the electrophilic properties of most carbenes, pathway (a), i.e. the interaction of the anion and carbene, is very probable. According to literature data, the following reactions proceed by this mechanism [80,200,201]:

$$p\text{-}NO_2C_6H_4\overset{\oplus}{C}H_2S(CH_3)_2 \rightarrow p\text{-}NO_2C_6H_4CH{=}CHC_6H_4\text{-}p\text{-}NO_2$$

(this reaction has already been mentioned on p. 75) and

$$(CH_3S)_3CH \rightarrow (CH_3S)_2C{=}C(SCH_3)_2.$$

As already pointed out in passing on p. 76, tetraphenylhexapentaene is also synthesised by this pathway:



Nucleophilic substitution of the anion in the molecule in pathway (b) should in the first place give ethane derivatives [202], which in fact have been isolated in a few cases but they could have been formed also by the substitution of the carbene in the C–H bond of the molecule by pathway (c).[1]

In recent years dimerisation of carbenes by pathway (d) has been put forward to account for the formation of olefins[203]:

$$p\text{-}NO_2C_6H_4CH_2Cl \rightarrow p\text{-}NO_2C_6H_4CH{=}CHC_6H_4\text{-}p\text{-}NO_2.$$

---o0o---

Carbenoids, the electronic analogues of carbenes, are fairly similar to the latter in chemical and certain physical properties. Although the key atoms in these compounds are not of carbon but of other elements, their most characteristic property, like that of carbenes, is the capacity to form two new covalent bonds in reactions. Fairly extensive data are at present available on the carbenoids, but their discussion is outside the scope of the present review.

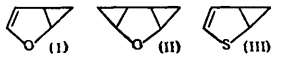
ADDED IN PROOF

After our article had been sent to press, a number of interesting papers having direct relevance to the present review appeared, and we therefore felt bound to give at least a brief description of them. Thus we must mention a very thorough French review[204] as well as other review articles[205-207]. Of the experimental investigations, the work of Nefedov *et al.*[208], who proposed a new general method for the synthesis of carbenes, merits considerable attention. This method can be schematically represented as follows:

$$RR'CXX' \xrightarrow[\text{tetrahydrofuran}]{Li} RR'CLiX' \xrightarrow{-LiX'} RR'C:$$

where X and X′ are halogens and R and R′ are hydrogen, halogens, and aryl, alkyl, or alkylidene groups.

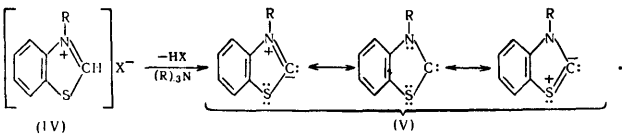
Among the latest spectroscopic studies of carbenes, that of Trozzolo *et al.*[209], who investigated *p*-phenylenebis-(phenylmethylene), is interesting. Another interesting paper is that of Russell and Hendry[210], who studied the effect of solvents on the reactions of methylene. The reaction of methylene radicals with acetylene in the gas phase has been investigated by Terao *et al.*[211] Müller *et al.*[212] discovered a reaction in which five-membered aromatic compounds are converted into their homologues by means of diazomethane. Using this reaction, compounds (I), (II), and (III) were obtained from furan and thiophen:



A number of papers have dealt also with the reactions of dihalogenocarbenes. Thus Skattebŏl[213] has continued the study of the reaction mentioned on p. 80. Certain olefins are known to be very inert towards dihalogenocarbenes prepared by the usual methods. For the preparation of *gem*-dihalogenocyclopropane from such olefins, Seyferth *et al.*[214] proposed a procedure involving the use of organomercury compounds: $C_6H_5HgCCl_2Br$, $C_6H_5HgCClBr_2$, and $C_6H_5HgCBr_3$. Landgrebe and Mathis[215] studied several examples of the substitution of dichlorocarbene in the carbon–mercury bond and also the thermal decomposition of compounds obtained in this way. The work of Ohno[216] dealing with the reaction of enamines with dichlorocarbenes is also interesting.

A paper has been published on the reaction of dichlorocarbene with benzofuran and benzothiophen[217]. Krapcho and Huyffer[218] described the thermal decarboxylation of sodium trichloroacetate in the presence of activated carbon and halogeno-compounds.

Kirmse[219,220] recently published two papers on alkylchlorocarbenes. Other communications deal with alkyl-, aryl-, and alkylidene-carbenes[221-224], allylcarbenes[225], and also with the rearrangements of carbenes obtained by the decomposition of 2,2,2-triaryldiazoethanes[226]. Several papers describe the reactions of ethoxycarbonylcarbene[227-229]. We may also mention that Schöllkopf and Küppers[230] obtained a number of phenylselenocyclopropanes starting with phenylselenocarbene and various olefins. In a quite recent paper Wanzlick and Kleiner[231] state that their attempts to find carbenes with "quasi-aromatic resonance stabilisation" have been successful. When *N*-alkylbenzothiazolium halides (IV) are treated with tertiary amines, the former lose the elements of hydrogen halide yielding substances which can be represented by the resonance hybrids (V):



The carbene (V) dimerises and also participates in a number of other chemical reactions.

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PERCHLORIC ACID AND ITS COMPOUNDS IN ORGANIC SYNTHESIS

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I. INTRODUCTION

In recent years acid catalysts, among which perchloric acid and its compounds occupy an important place, have been attracting increasing attention. During the past 10–15 years more than 300 papers and patents have appeared, dealing with the use of $HClO_4$ and its compounds in organic chemistry.

Perchloric acid is the strongest mineral acid but at ordinary temperatures its oxidising power is less than that of the other oxygen acids of chlorine, bromine, and iodine[1]. In many organic solvents perchloric acid is readily solvated and this changes the polarity of the bond between the hydrogen atom and the ClO_4 residue. In polar organic solvents (acetic acid[2-4], nitromethane[5], nitrobenzene[6], etc.) perchloric acid is ionised to a greater degree than other acids. Comparison of the ionisation constants of mineral acids in anhydrous acetic acid confirms that perchloric acid ($K = 1.6 \times 10^{-4}$) is tens or hundreds of times stronger than hydrobromic ($K = 4 \times 10^{-5}$), sulphuric ($K = 6 \times 10^{-7}$), hydrochloric ($K = 1.4 \times 10^{-7}$), nitric ($K = 4.2 \times 10^{-8}$), and trichloracetic ($K = 2.3 \times 10^{-10}$) acids.

For many years the wide use of perchloric acid in organic synthesis has been hindered by greatly exaggerated ideas about the danger of explosions. However, although work with the anhydrous acid is in fact not without danger, the use of an aqueous solution (30, 60, and 72%) involves practically no risk. Solutions of the anhydrous acid in acetic acid or acetic anhydride containing less than 55% of $HClO_4$ by volume, which are frequently used, are also quite safe[8].

Much experimental data on the use of perchloric acid and its compounds in various fields of organic chemistry has accumulated. This work requires to be correlated and systematised since the published reviews dealing with only parts of the problem are already out of date[8-10].

II. PERCHLORATES OF ORGANIC COMPOUNDS

The study of organic perchlorates started in the 19th century when crystalline perchlorates of alkaloids were obtained[11]. Later it was found that perchloric acid readily forms perchlorates with ethers, ketones, weakly basic compounds containing nitrogen, and pyridine; this property is used successfully in the purification and identification of many basic organic compounds[12-15]. Organic perchlorates are usually obtained by treating solutions of organic compounds in polar or non-polar solvents (water, alcohols, ether, nitromethane, etc.) with perchloric acid in the cold[16-18].

In their structure the esters of perchloric acid are superficially similar to salts, the metal being replaced by a hydrocarbon radical. The bond between the perchlorate ion and the hydrocarbon radical is covalent or nearly ionic, depending on the degree of polarisation. Nearly all these compounds are unstable and only some of them can be obtained in the pure state. Among the various methods of