Russian Chemical Reviews **62** (5) 447–472 (1993)
© 1993 Russian Academy of Sciences and Turpion Ltd

UDC 547.467.2

Carbene reactions of diazoesters with σ-bonds as an effective method for the alkoxycarbonylmethylenation of organic compounds

E A Shapiro, A B Dyatkin, O M Nefedov

Contents

I.	Introduction	447
II.	Carbon–hydrogen bonds	448
III.	Heteroatom–hydrogen bonds	453
IV.	Carbon–carbon bonds	457
V.	Carbon–heteroatom bonds	457
VI.	Heteroatom–heteroatom bonds	466

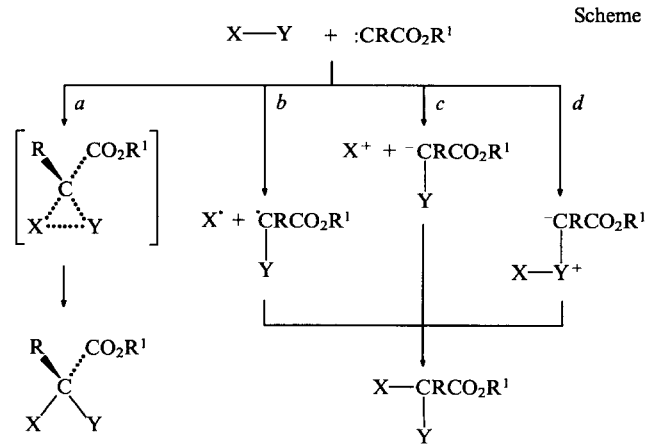
Abstract. Data on the carbene reactions of diazoesters with carbon–hydrogen, heteroatom–hydrogen, carbon–carbon, carbon–heteroatom, and heteroatom–heteroatom σ-bonds in organic molecules, demonstrating the synthetic possibilities of such reactions as an effective and universal method of the alkoxycarbonylmethylenation of organic compounds, are considered systematically. The bibliography includes 179 references.

I. Introduction

The reactions involving the carbene decomposition of the esters of diazoacetic and other carboxylic diazoacids (diazoesters) are widely used in organic synthesis for the preparation of the esters of cyclopropanecarboxylic and cyclopropenecarboxylic acids from unsaturated compounds.[1–8] The reactions of diazoesters with saturated compounds, leading in the general case to the insertion of the $CRCO_2R^1$ fragment in the X–Y σ-bonds as a result of the dissociation of these bonds and formation of new C–X and C–Y bonds, are much less well known. This reaction can be achieved either as a concerted process via a three-centre transition state with retention of the configuration of the asymmetric atom (pathway *a*) or as the opposite stepwise process involving racemisation, of the type of abstraction–recombination with participation of radical species (pathway *b*), dipolar intermediates (pathway *c*), or ylide structures (pathway *d*) (Scheme 1).

Clearly the operation of a particular pathway is mainly determined by the structure of the substrate and also by the mode of generation of the carbene. The synthetic importance of reactions of this type is due to the possibility of the introduction of functional groups at carbon atoms of saturated compounds. However, until recently, their use in organic synthesis was restricted because of the lack of convenient methods for the generation of alkoxycarbonylcarbenes (ACC) capable of entering into selective reactions with σ-bonds. The photolytic and thermal dediazotisation of diazoesters leads to the formation of extremely active carbenes, which react nonselectively with an acceptor to form a large number of products. Catalytic dediazotisation on treatment with traditional catalysts based on copper compounds leads to more selective carbenes but ensures the necessary preparative selectivity of the reactions of diazoesters with saturated compounds only in individual instances.

Scheme 1



Only the latest advances in the catalysis of the carbene decomposition of diazoesters and in first place the use of rhodium(II) compounds as catalysts of this process[9] led to the possibility of the wide scale employment of the insertion reactions for the alkoxycarbonylmethylenation of a wide variety of saturated compounds. Since the discovery of rhodium catalysis, extensive experimental data have accumulated, which, however, have not been treated systematically, although individual examples of reactions of this type have been included in virtually all the reviews devoted to the chemistry of diazoesters.[2–8, 10]

In the present review, an attempt is made for the first time to consider systematically the literature data on the reactions of diazoesters with saturated compounds. The review is not exhaustive and its aim is to provide only a general idea about the synthetic possibilities of reactions of this type. For convenience, the entire data have been grouped in terms of the types of bonds involved in the reaction: carbon–hydrogen, heteroatom–hydrogen, carbon–carbon, carbon–heteroatom, and heteroatom–heteroatom. Within the groups, the classification is based on the type of compounds incorporating these bonds and the kind of heteroatom.

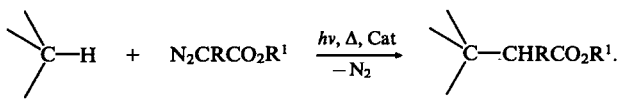
E A Shapiro, A B Dyatkin, O M Nefedov N D Zelinskii Institute of Organic Chemistry, Russian Academy of Sciences, Leninskii prosp. 47, 117913 Moscow. Fax (7-095) 135 52 28

Received 14th January 1993
Uspekhi Khimii **62** (5) 485–509 (1993); translated by A K Grzybowski

II. Carbon–hydrogen bonds

1. Aliphatic C–H bonds

Reactions involving the insertion of ACC in the C–H bonds of alkanes, alkenes, and alkynes are known. They can be represented by the following equation in a general form:

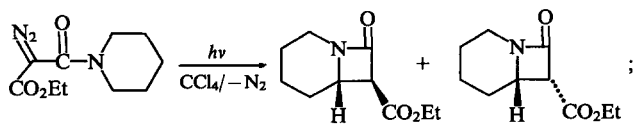


The reaction with alkanes is of limited synthetic applicability because the low selectivity of the highly reactive ACC in relation to primary, secondary, and tertiary C–H bonds and the ease of the dimerisation of carbenes usually lead to mixtures of products, although their overall yields reach 90% when rhodium(II) carboxylates are used as catalysts.[11] The rules governing the catalytic action of the above catalysts as a function of the structure of the substrate, diazoester, and the counterion and the catalyst concentration have been examined.[12,13] The formation of the products of insertion in the C–H bonds of alkanes in high yields (~90%) has been noted in the dediazotisation of diazoesters with an unsaturated alcoholic component, for example, prenyl diazoacetate in hexane in the presence of $CuCl_2$.

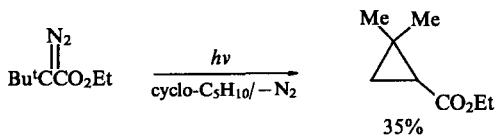
The intermolecular C–H insertion reaction has found a practical application in the modification of ethylenepropylene rubber, which is achieved by treating the latter with ethyl diazoacetate (EDA) at 210 °C (degree of functionalisation 5% – 10%).[14]

The intramolecular C–H insertion reactions are of much greater synthetic importance. These reactions proceed with preparative yields even under the conditions of the photolysis or pyrolysis of diazoesters (Scheme 2).[15–17]

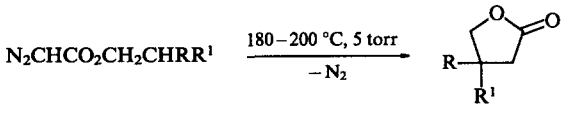
Scheme 2



overall yield 80%; 1 : 2 ratio



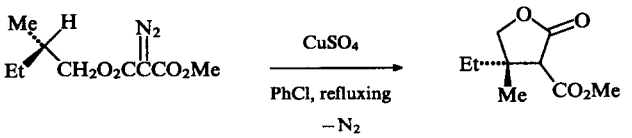
35%



20%

Preparative yields can be achieved also using copper compounds as catalysts of the dediazotisation of the diazoesters (Scheme 3).[18]

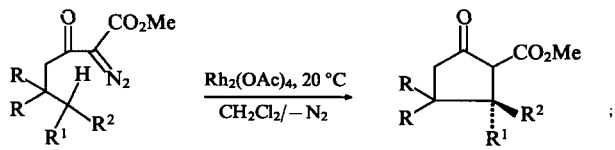
Scheme 3



48%

The use of rhodium(II) carboxylates makes it possible to carry out the reactions under milder conditions, which promotes an increase in the yields of products and the process selectivity (Scheme 4).[19,20]

Scheme 4



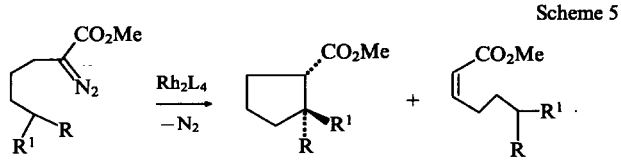
55% – 77%

R = Me, Pr^i, C_8H_{17}, $H_2C{=}CH$, $Me_2C{=}CHCH_2$,
$R^1 = R^2 = H$, Me.

The reactivity of the C–H bonds in this reaction diminishes in the sequence $C_{tert}–H > C_{sec}–H > C_n–H$ and all the bonds are more reactive than the C–H bonds of the benzyl and allyl types.[21,22]

When the molecule contains long unbranched hydrocarbon chains, the bond subjected to attack by the carbene centre is exclusively a C–H bond at the ε-carbon atom with formation of cyclopentane derivatives.[23] The insertion reaction is then complicated by the competing processes involving the elimination of a β-hydrogen atom with formation of acrylic acid derivatives, the relative contributions of these pathways depending on the ligand at the rhodium atom (Scheme 5).

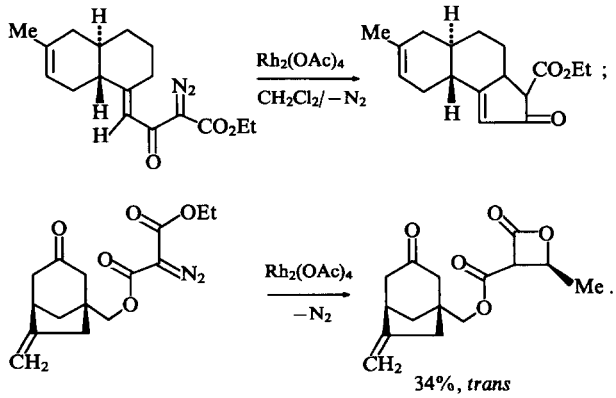
Scheme 5



L	R = H, R^1 = C_7H_{15}		R = Me, R^1 = C_6H_4Me-4	
	overall yield (%)	1 : 2 ratio	overall yield (%)	1 : 2 ratio
OCOBu^t	97	85:15	89	55:45
$OCOCF_3$	93	52:48	99	26:74

The steric factor can exert an even greater influence on the course of the process than the electronic factor, as a result of which the carbene may cyclise with participation of not the tertiary but the secondary carbon atom (Scheme 6).[24,25]

Scheme 6

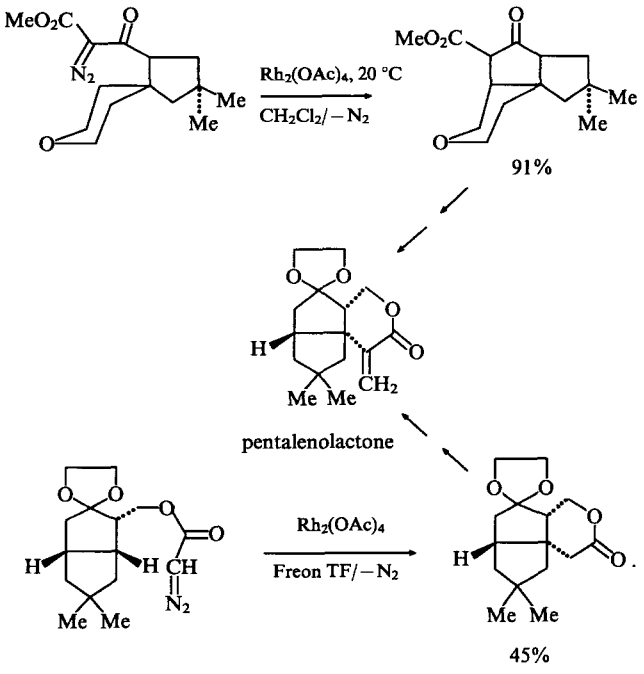


34%, *trans*

These examples demonstrate in addition the ability of rhodium compounds, in contrast to the copper catalysts, to effect the C–H insertion reactions even in the presence of a double bond.

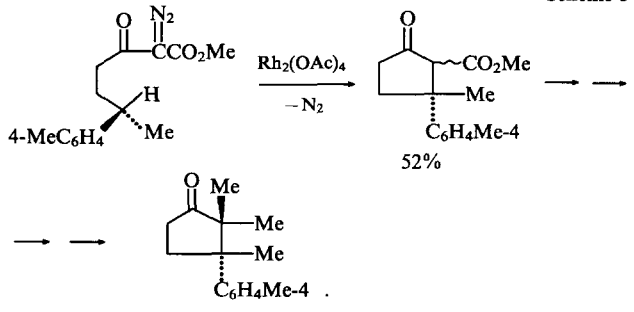
The marked sensitivity of the intramolecular insertion reactions to steric factors must be taken into account in choosing a strategy for the synthesis of the target products. Thus the two schemes proposed by Taber and Schuchardt[26] and Cane and Thomas[27] for the synthesis of pentalenolactone are based on the preferential attack by the carbene on the sterically most accessible bonds, although in the second case this leads to the formation of a six-membered and not a five-membered ring (Scheme 7).

Scheme 7



The intramolecular insertion reaction with participation of rhodium complexes of carbenes, generated by the dediazotisation of β-oxodiazoacetates, is distinguished by a high degree of stereoselectivity and proceeds with retention of the configuration of the attacked carbon atom, which enabled, for example, Taber et al.,[22] to use this reaction for the synthesis of α-cuparenone (Scheme 8).

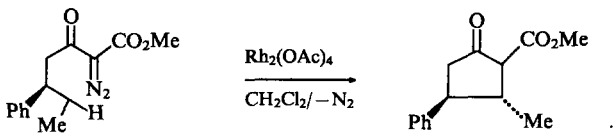
Scheme 8



α-cuparenone

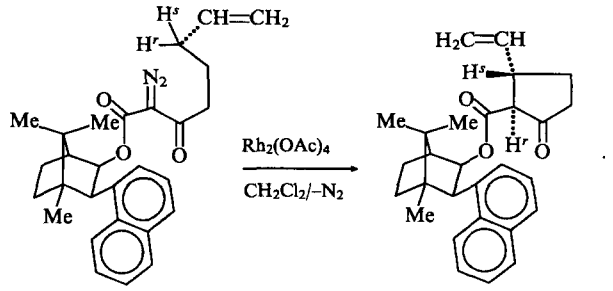
The same group of workers established that the substituents in α-acetyldiazoacetates increase the *trans*-selectivity of the intramolecular C–H insertion (Scheme 9)[28] and the enantioselectivity of the cyclisation to form the rhodium complex of a carbene from the chiral oxodiazoester precursor **3** (Scheme 10).[29] The bulky α-naphthyl substituent in the above diazoester effectively shields one of the sides of the acyl substituent and favours the insertion of the carbene centre in the C–H^r bond. The hydrolysis and decarboxylation of the esters thus obtained permit the enantioselective synthesis of cyclopentanones with an enantioselective excess (e.e.) up to 98%.

Scheme 9



66%, *trans*

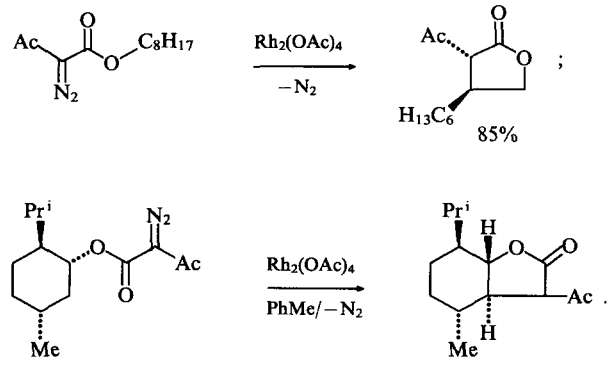
Scheme 10



3 e.e. 98%

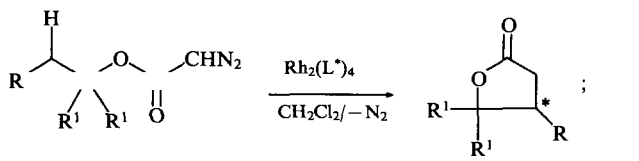
The C–H insertion reactions involving the alcoholic part of α-diazoacetates on treatment with rhodium(II) acetate and acetamide proceeds with a selectivity which is just as high. Thus it is possible to obtain γ-lactones with high regio- and diastereoselectivities and a virtually complete conversion of the diazoester (Scheme 11).[30]

Scheme 11



Data have been published recently on the asymmetric synthesis of lactones with a high enantioselectivity (enantiomeric excess up to 85%) via intramolecular C–H insertion reactions of carbenes generated from certain alkoxyethyl diazoacetates on treatment with chiral rhodium(II) carboxamides, in particular tetrakis(5-methoxycarbonylpyrrolidin-2-one)dirhodium(II) [Rh_2(MEPY)$_4$].[31] The configuration of the resulting lactone is then determined by that of the catalyst ligand and the substituent R (Scheme 12).

Scheme 12



R = MeO, EtO, $PhCH_2O$, Ph; 42%–56%

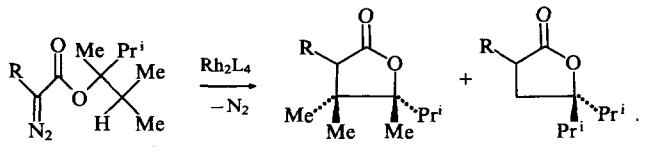
R^1 = H, Me; L* = (*R*)- or (*S*)-MEPY. e.e. 77%–85%

By 'grafting' this catalyst to the polyethylene, it is possible to achieve the enantioselective synthesis of lactones in a heterogeneous version, which simplifies significantly processes involving the recovery of the expensive rhodium catalysts.[32]

Unfortunately, the effectiveness of this catalyst is inferior to that of the homogeneous catalyst and is reduced sharply after its repeated use.

It is noteworthy that the intramolecular C–H insertion reactions with participation of the alcoholic components of diazoesters are extremely sensitive to the structure of the diazoester and the catalyst counterion. Thus, under the influence of rhodium(II) perfluorobutyrate, alkyl diazoacetates (ADA) and alkyl α-acyldiazoacetates cyclise with the preferential formation of the products of insertion in the C–H bonds formed by the primary carbon atom, the process selectivity being somewhat higher in the case of ADA (Table 1). On the other hand, under the influence of rhodium(II) acetate, the insertion takes place mainly, and in the presence of rhodium(II) acetamide, exclusively in tertiary C–H bonds.[30]

Table 1. The regioselectivity of the intramolecular C–H insertion reactions with participation of the alcoholic component of diazoacetates.



4 5

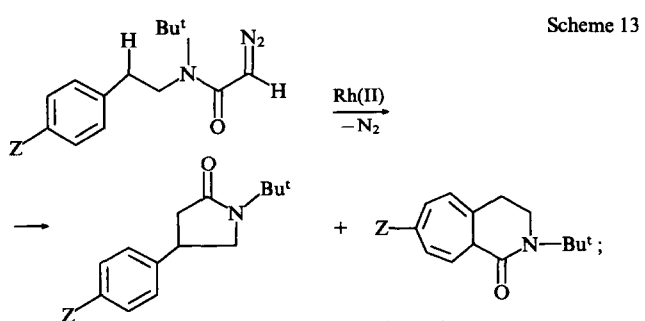
L	R = H		R = Ac	
	overall yield (%)	**4**:**5** ratio	overall yield (%)	**4**:**5** ratio
pfb	56	32:68	45	45:55
OAc	81	53:47	97	90:10
acam	96	>99:1	89	>99:1

Note. pfb = perfluorobutyrate and acam = acetamide.

The influence of the ligand on the selectivity of the rhodium(II)-catalysed C–H insertion processes has been demonstrated in relation to the intramolecular reactions of diazoamides. Thus in the case of substituted *N*-(*tert*-butyl)-*N*-ethyldiazoamides, the attack by the carbene centre can be directed to all the C–H bonds of the ethyl and *tert*-butyl fragments. However, depending on the counterion, it is possible to achieve the required specific cyclisation of the carbene with an appreciable enantioselectivity (Table 2).[33]

The dediazotisation of diazoamides containing an aromatic fragment proceeds either via insertion in the C–H bond at the δ-carbon atom or with participation of the multiple bonds of the aromatic substituent, depending on the ligand (Scheme 13).[34]

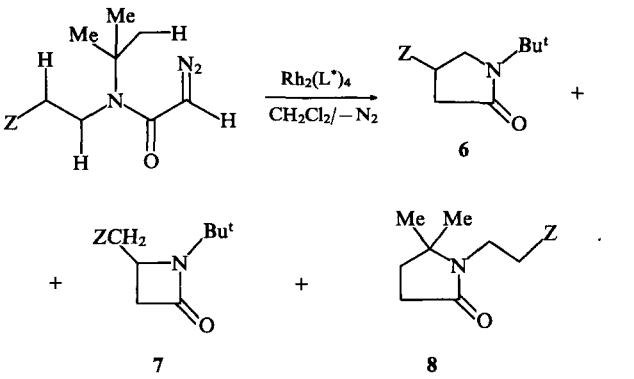
Scheme 13



Z = H, MeO, O_2N

$Rh_2(pfb)_4$, 80% (95:5);
$Rh_2(caprylamide)_4$, 65% (3:97);
$Rh_2(acam)_4$ 90% (0:100).

Table 2. The selectivity of the intramolecular C–H insertion reactions of diazoamides.



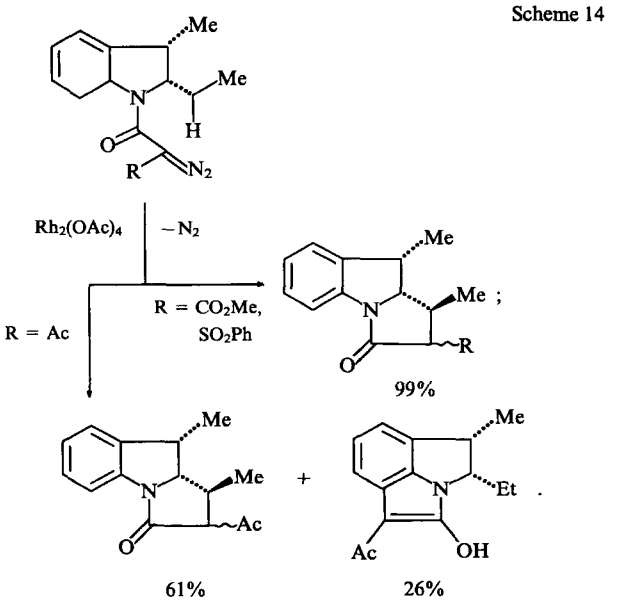
6 7 8

Z	L	Overall yield (%)	**6**:**7**:**8** molar ratios	Enantiomeric excess (%) **6**	**7**
Et	4-(*S*)-MEOX	82	91:9:0	71	80
OEt	4-(*S*)-MEOX	97	100:0:0	78	–
CO_2Et	5-(*R*)-MEPY	64	0:9:91	–	44
CO_2Et	4-(*S*)-BNOX	60	0:100:0	–	20

Note. 4-(*S*)-MEOX = 2-oxazolidine-4-(*S*)-carboxylate and 4-(*S*)-BNOX = 4-(*S*)-benzyloxazolidinone.

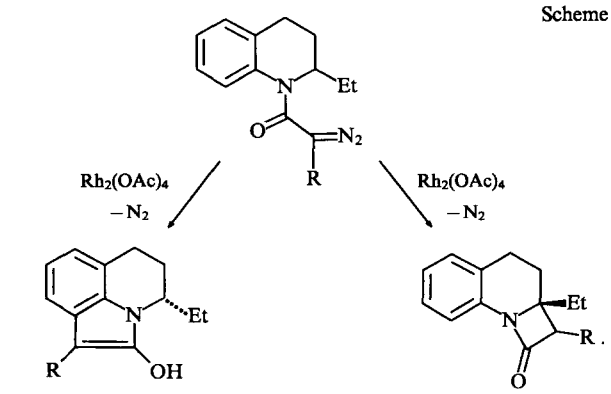
The substituents at the carbon atom of the diazo-group also affect significantly the regioselectivity of the dediazotisation of aromatic aryl-substituted diazoamides. Diazoamides with electron-accepting substituents, for example, Ac, CO_2R, or SO_2Ph, are dediazotised on treatment with $Rh_2(OAc)_4$ usually with the preferential formation of the products of insertion in aliphatic C–H bonds (Scheme 14), although the cyclisation of certain α-acyldiazoamides is accompanied by the formation of products of insertion in aromatic C–H bonds (Scheme 15).[35]

Scheme 14



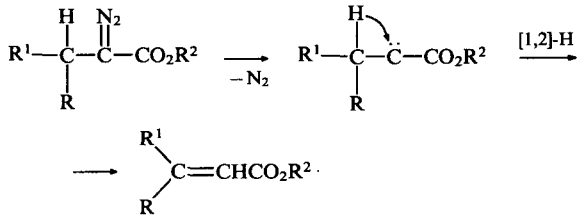
61% 26%

Scheme 15



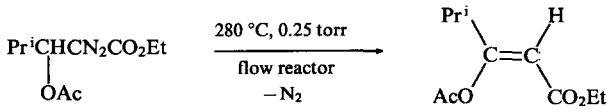
R = CO_2Me 88% R = Ac 61%

An interesting instance of intramolecular reactions of diazoesters with participation of C–H bonds is the [1,2]-hydride shift of the hydrogen atom to a neighbouring carbene centre with formation of acrylic acid derivatives.



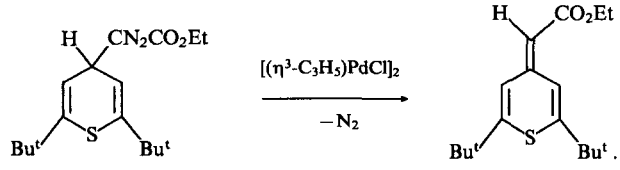
In the absence of active carbene acceptors, this rearrangement is the main pathway in the dediazotisation of diazoacetic acid esters on heating (Scheme 16)[36] and on treatment with catalysts based on transition metals (Schemes 17 and 18)[37,38] and Lewis acids (Scheme 19).[39]

Scheme 16



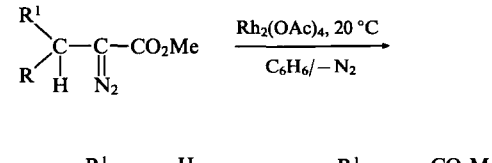
27%

Scheme 17



98%

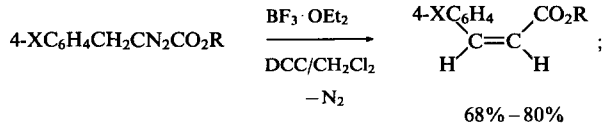
Scheme 18



R	R^1	Fraction of (Z)-isomer (%)	Overall yield (%)
Pr^i	H	~100	99
Ph	H	~100	~100
$PhCH_2O$	H	~100	90
Me	Et	57	95
$H_2C=CH$	H	~100	39[a]

[a] Another product is methylbicyclo[1.1.0]butanecarboxylate (yield 51%).

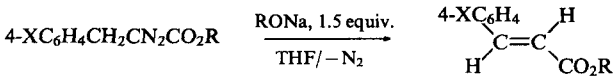
Scheme 19



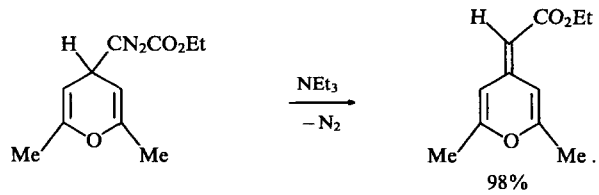
DCC = dicyclohexylcarbodiimide;
X = H, NO_2, MeO; R = Me, Et.

The yields of the acrylic acid derivatives thus obtained reach 98%, the (Z)-isomer predominating. Furthermore, in the case of the H-shift of the hydrogen atom in the methylene fragment, the reaction leads to the (Z)-isomer only. Similar reactions of diazoesters can be initiated also by bases.[39,40] However, in this case the reaction leads to the (E)-isomer (Scheme 20).

Scheme 20



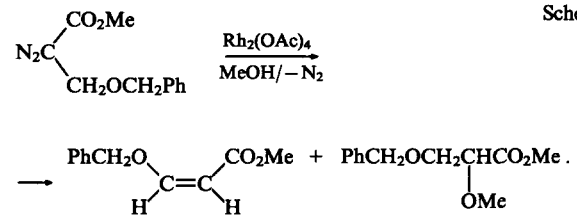
X = H, NO_2, MeO; R = Me, Et E, 59%–72%



98%

The migration of a hydrogen atom in the rhodium(II)-catalysed dediazotisation of certain diazoesters with an active methylene group proceeds to an appreciable extent even in the presence of methanol (Scheme 21),[37] which is an active carbene acceptor under these conditions (Section III).

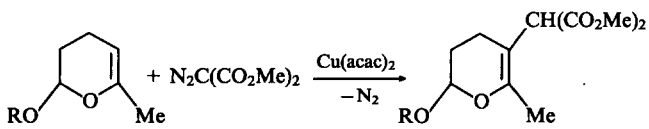
Scheme 21



80% (1:1)

A few examples of reactions involving the insertion of carbenes in the vinyl C–H bonds of alkenes are known. Thus, although the ACC generated by the photolysis or pyrolysis of alkyl diazoacetates afford predominantly cyclopropane adducts on reaction with olefins, the products of insertion in the vinyl C–H bonds are also formed in a small amount (3%–5%).[41] On the other hand, the catalytic dediazotisation of alkyl diazoacetates makes it possible to obtain the corresponding C–H insertion products with a high selectivity. In particular, the formation of vinyl insertion products has been observed in the reaction of dimethyl diazomalonate (MDM) with vinyl ethers in the presence of copper catalysts (Scheme 22).[42]

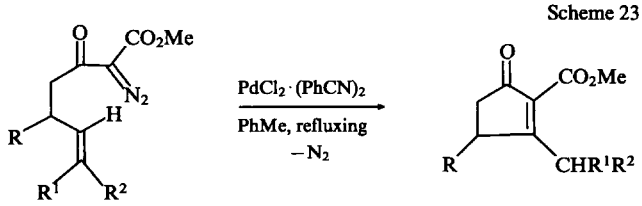
Scheme 22



76%–80%

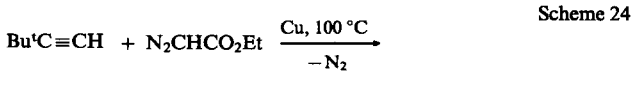
The intramolecular reaction of 2-diazo-3-oxohept-6-enoates on treatment with palladium(II), leading to methyl 3-alkylcyclopent-2-enecarboxylates in 34%–73% yields (Scheme 23), belongs formally to this type of reactions.[43]

Scheme 23



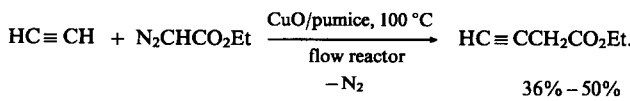
The reaction with ethyl diazoacetate under these conditions leads to the cyclopropane adduct only.[44] Instances of the insertion of ACC in a C–H bond at an *sp*-hybridised carbon atom in alkynes are also known. As in the case of alkenes, here the direct insertion of carbenes in these bonds with formation of the esters of alk-3-ynoic acids is scarcely possible, because the photolysis of alkyl diazoacetates in the presence of terminal alkynes leads only to products of C–H insertion in alkyl substituents together with cyclopropenes. The formal products of insertion in an acetylenic C–H bond in terminal acetylenes, observed[45] in the catalytic dediazotisation of alkyl diazoacetates, are most probably formed from the 1-pyrazoles produced initially (Scheme 24).[46]

Scheme 24



The only example of a preparative reaction of this type is the copyrolysis of acetylene with ethyl diazoacetate over a copper catalyst in a flow reactor, which leads to a butynoic acid ester in a yield up to 50% (Scheme 25).[47]

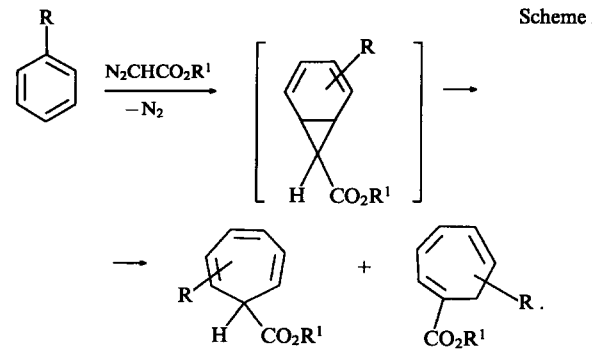
Scheme 25



2. C–H bonds in aromatic compounds of the benzenoid series

The carbenes generated by the dediazotisation of diazoesters add to the multiple bonds of aromatic compounds in the absence of more active acceptors (Scheme 26). However, bicyclo[4.1.0]-heptadienes are usually not identified in the reaction products because they readily isomerise to 1-*H*-cyclohepta-2,4,6-triene-carboxylates and the thermodynamically more stable 7-*H*-cyclo-hepta-1,3,5-trienecarboxylates.

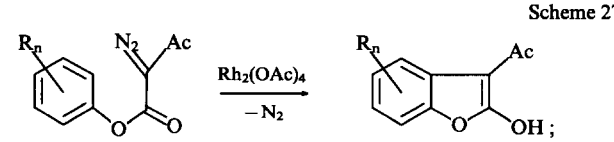
Scheme 26



Much attention has been devoted in recent years to the study of the intramolecular cyclisation reactions of ACC containing aromatic substituents. However, these reactions result in the formation not of cycloheptatriene derivatives but of the products of the formal insertion of the carbene in aromatic C–H bonds. Although it has still not been ultimately established whether this entails the concerted insertion of the carbene in a C–H bond or the isomerisation of the cyclopropane adduct formed initially, this reaction constitutes a convenient method of synthesis of polycyclic systems.

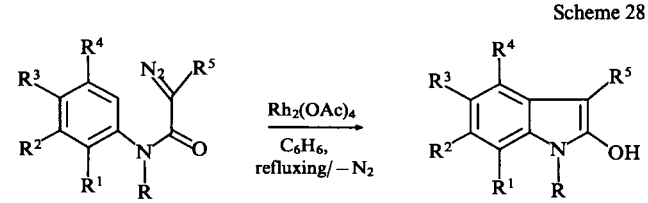
For example, the dediazotisation of phenyl α-acetyldiazo-acetates (Scheme 27)[48] or *N*-phenyldiazoamides (Schemes 28 and 29),[35,49,50] initiated by rhodium(II), is accompanied by the intramolecular cyclisation of the corresponding metal carbene complexes with formation of substituted enols of benzo[*b*]-furanone or oxindoles respectively in satisfactory yields.

Scheme 27



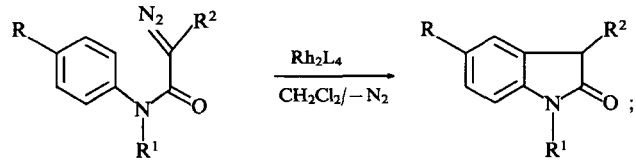
R = H, 2-Me, 2-Br, 3,4-OCH_2O; 92%–98%.

Scheme 28



R = Alk, CH_2Ph, R^5 = H, Ac;
R^1–R^4 = Alk or R^2+R^3 = CH=CHCH=CH. 77%–97%

Scheme 29

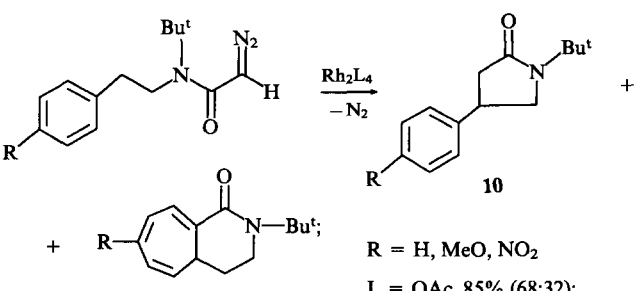


L = OAc, $OCOCF_3$, pfb, acam;

R = R^2 = H, R^1 = Me (86%),
R = MeO, R^1 = Bu, R^2 = SO_2Ph (98%).

At the same time, the cyclisation of *N*-(2-arylethyl)diazoamides on treatment with rhodium(II) compounds proceeds via two other competing pathways: with participation of the multiple bonds of the aromatic ring to form δ-lactams **9** containing a cycloheptatriene fragment and also with participation of α-C–H bonds of the alkyl chain to form γ-lactams **10** (Scheme 30).[51] The selectivity of this reaction depends decisively on the catalyst counterion. Thus the use of $Rh_2(OAc)_4$ leads to a mixture of the products indicated. The δ-lactams are formed exclusively in the presence of rhodium(II) perfluorobutyrate, while the γ-lactams are formed in the presence of rhodium(II) caprylamide.

Scheme 30

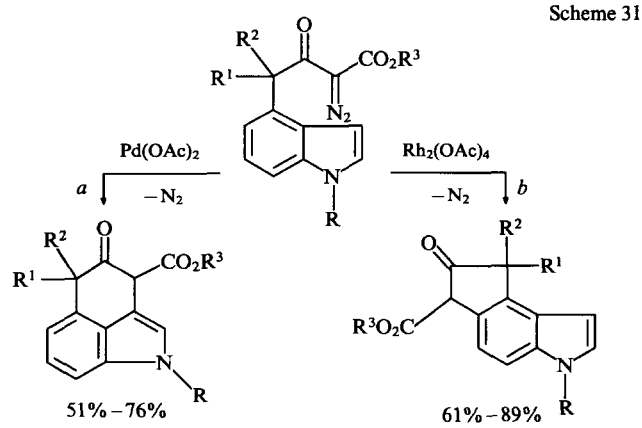


R = H, MeO, NO_2

L = OAc, 85% (68:32);
pfb, 80% (95:5);
caprylamide, 65% (3:97).

Another example of the influence of the nature of the dediazotisation catalyst on the chemoselectivity of the intramolecular cyclisation reactions of aromatic diazoesters is the cyclisation of α-(indolylacetyl)diazoacetates. In the presence of $Pd(OAc)_2$, the reaction proceeds with participation of the heterocyclic fragment (Scheme 31, pathway *a*), while on treatment with $Rh_2(OAc)_4$ it involves the benzene ring (pathway *b*).[52]

Scheme 31

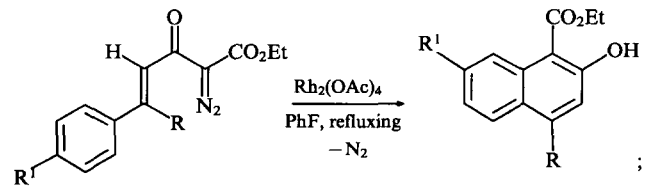


R = H, Ts, CH_2Ph;
R^1, R^2 = H, Alk; R^3 = Me, Et.

This course of the process is apparently determined by the different mechanisms of the catalytic action of palladium and rhodium compounds in the carbene reactions with participation of diazoesters, although in the case of palladium compounds the authors postulate the involvement not of carbene but of carbonium ion intermediates.

The intramolecular C–H insertion in the aromatic ring is preferable in certain cases even in the presence of a multiple bond in the molecule, as has been observed in the case of ethyl α-(arylvinylcarbonyl)diazoacetates, in which the double bond is deactivated by conjugation with the carbonyl group.[53] The reaction affords derivatives of β-naphthols in high yields (Scheme 32).

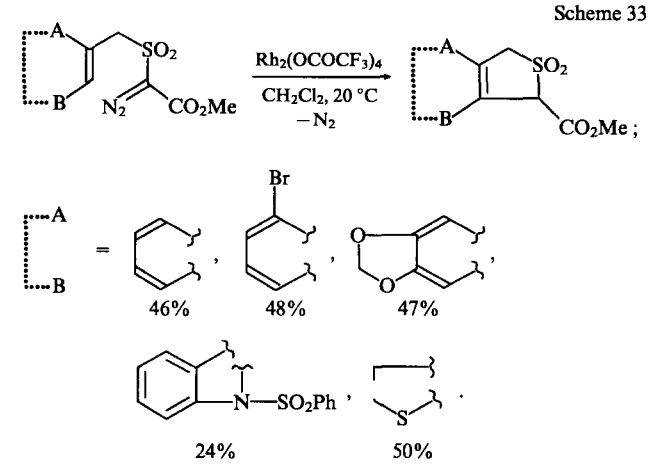
Scheme 32



R = Ph, R^1 = H (90%);
R = C_6H_4Me-4, R^1 = Me (76%);
R = C_6H_4Cl-4, R^1 = Cl (97%).

On treatment with rhodium(II) compounds, intramolecular cyclisation takes place also in the case of α-[aryl (or heteroaryl)-methanesulfonyl] diazoacetates, which leads to the corresponding benzo[*c*]thiophene 1,1-dioxides in moderate yields (24%–48%) (Scheme 33).[54]

Scheme 33

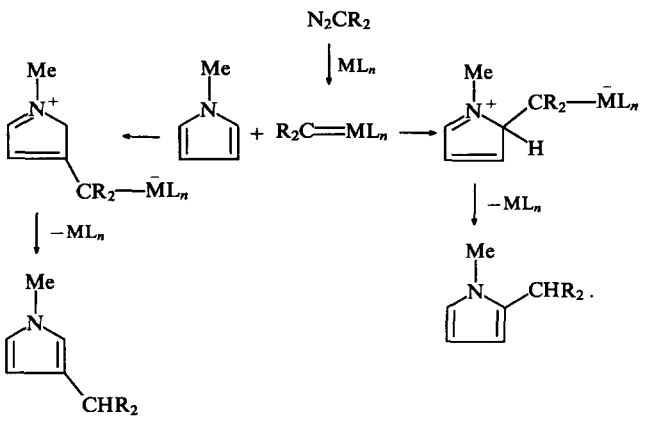


3. C–H bonds in heteroaromatic compounds

The nature of the multiple bonds in heteroaromatic compounds, which occupy an intermediate position between aromatic bonds of the benzenoid type and conjugated bonds of diene systems, as well as the presence of a nucleophilic heteroatom are responsible for the wide variety of reactions of compounds of this class with carbenes or their transition metal complexes. However, selective reactions of diazoesters with heteroaromatic compounds, accompanied by the formation of products of insertion in C–H bonds, are known.

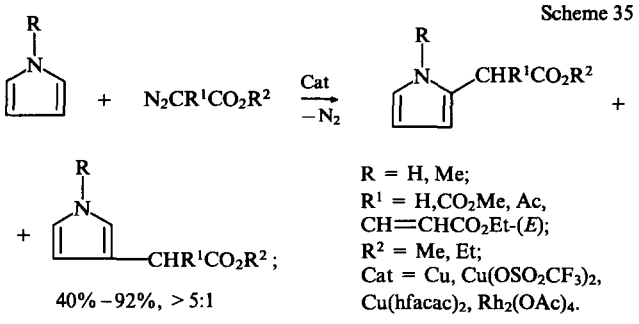
The commonest C–H insertion reactions occur in the pyrrole series, which can be explained by the greater aromatic character of the pyrrole ring.[55] As a result, the insertion products are formed as electrophilic substitution by the metal-carbene in the heteroaromatic ring via a metastable σ-complex (Scheme 34).

Scheme 34



The reactions of diazoesters with pyrrole itself and *N*-alkylpyrroles lead only to the products of formal insertion in the C–H bonds of the pyrrole ring, among which products of insertion in the α-C–H bonds predominate; the formation of N–H insertion products was not observed at all under these conditions (Scheme 35).[56–58]

Scheme 35

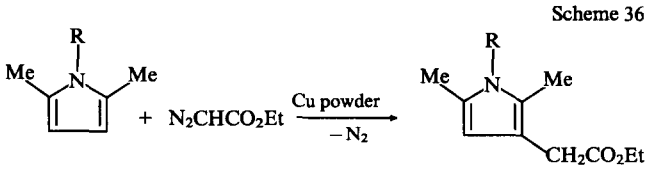


The regioselectivity of this reaction depends on the catalyst, the diazo-compound and the substituent at the nitrogen atom. The highest yields (up to 92%) and the highest reaction selectivity (>90%) in relation to the product of insertion in α-C–H bonds have been achieved in reactions involving dimethyl diazomalonate and homogeneous catalysts based on copper(II) compounds or $Rh_2(OAc)_4$. The reactions of ethyl diazoacetate and other diazoesters with pyrroles proceed in general with lower yields of the insertion products and a lower selectivity; rhodium compounds rapidly lose their activity in the dediazotisation of ethyl diazoacetate under these conditions and afford complex mixtures of products with traces of C–H insertion products.

The influence of *N*-alkyl substituents reduces to an increase in the fraction of the β-isomer with increase in the steric effect of this substituent in the series H < Me < Pr^i < Bu^t with the exclusive formation of the β-isomer in the case of the *tert*-butyl group.

Substituents in other positions in the pyrrole ring do not influence the regioselectivity of the reaction regardless of their nature, with the exception of the case where they occupy the 2- and 5-positions in the ring. The reaction of ethyl diazoacetates with such pyrroles leads to the product of insertion in the β-C–H bonds (Scheme 36).[59]

Scheme 36

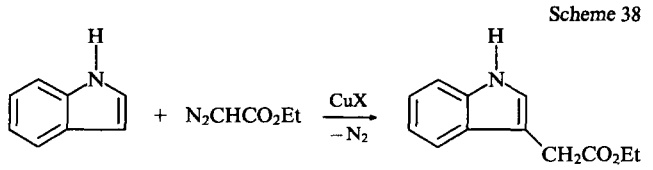


59%

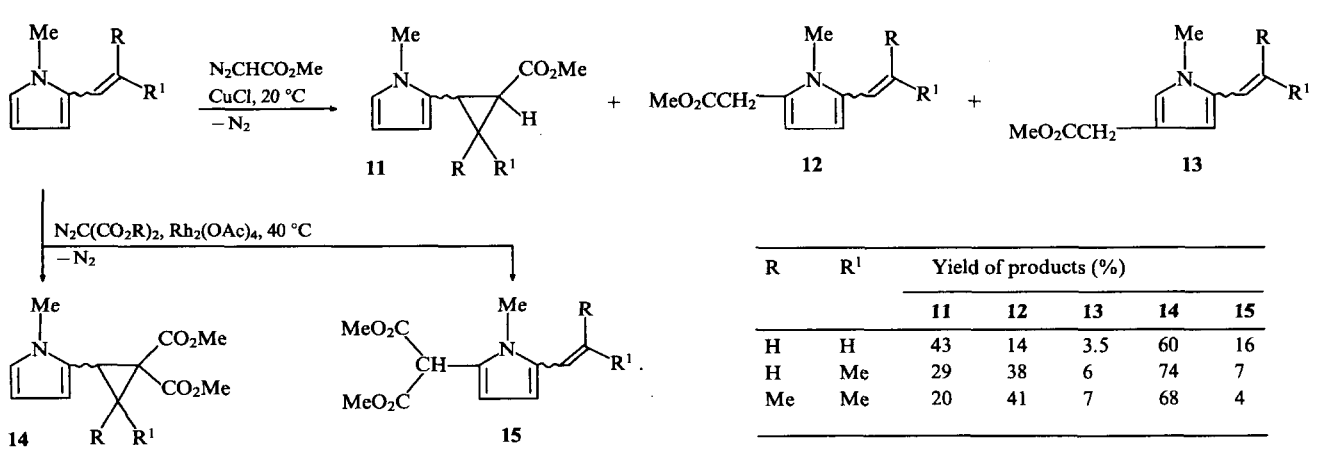
The possibility of competition between the reactions involving the attack by the carbene on the pyrrole ring and the alkenyl group arises in reactions with participation of 2-alkenyl-1-methylpyrroles, as a result of which cyclopropane adducts involving the exocyclic double bond are formed together with the C–H insertion products (Scheme 37).[60] The relative contributions of these reaction pathways are determined by the structure of the diazoesters and to a lesser extent of the substituent at the double bond. In reactions with participation of dimethyl diazomalonate, the alkylation of the pyrrole ring in the α-position predominates in all cases, while in the reaction involving methyl diazoacetate this process becomes the main one only in the presence of substituents at the double bond.

Certain other heteroaromatic nitrogen-containing compounds also behave similarly to pyrroles in reactions with diazoesters. Thus the esters of the corresponding heteroarylacetic acids are the main products of the reactions of ethyl diazoacetate with indoles[61] (Scheme 38) and furazans[62] (Scheme 39). The β-isomer predominates in the products of the reaction with indole under these conditions.

Scheme 38

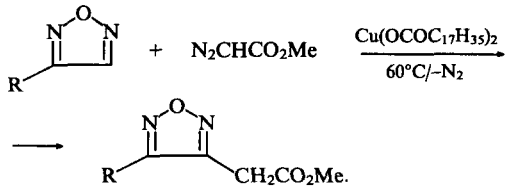


Scheme 37



R	R^1	Yield of products (%)				
		11	**12**	**13**	**14**	**15**
H	H	43	14	3.5	60	16
H	Me	29	38	6	74	7
Me	Me	20	41	7	68	4

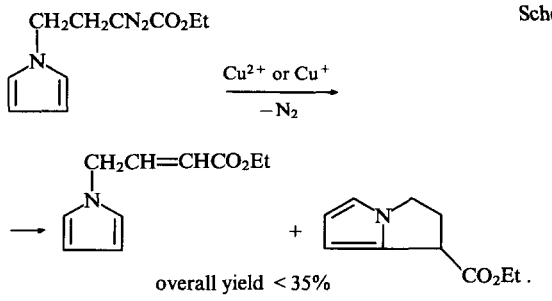
Scheme 39



9%–12% R = H, Ph, 2-thienyl.

Several examples of the intramolecular C–H insertion with participation of the pyrrole ring are known. Thus the carbenes generated by the dediazotisation of α-(2-pyrrolylethyl)diazoacetate (Scheme 40)[63] or α-(3-indolesulphonyl)diazoacetate[64] are converted into the corresponding polyheterocycles albeit with low yields (see Scheme 33).

Scheme 40



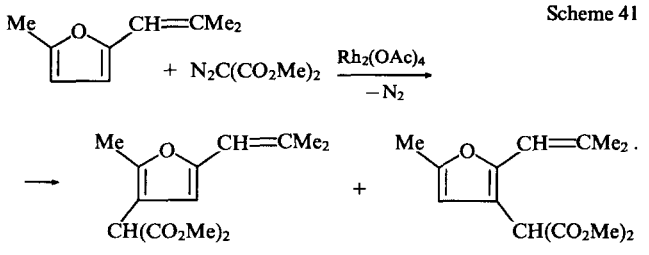
overall yield < 35%

On the other hand, the complexes of carbenes formed from 2-diazo-4-(4-indolyl)-3-oxobutanoates cyclise with participation of the indole ring in yields up to 76% (Scheme 31, pathway *a*).

In the series of thiophene and furan derivatives, only isolated instances of C–H insertion reactions are known. The reason for this is the low aromaticity of thiophene and furan compared with pyrrole and the presence of lone pairs at the O and S atoms, as a result of which the main primary reaction products are the corresponding S and O ylides. The subsequent reactions of these ylides lead in certain cases to C–H insertion products.

Thus the C–H insertion products, namely 3-furylmalonates, are formed in the reaction of 5-methyl-2-(2-methylprop-1-enyl)-furan with dimethyl diazomalonate (Scheme 41).[65]

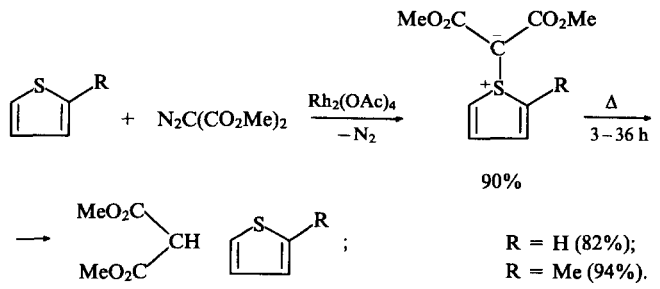
Scheme 41



80% (1:1)

Several examples of the formation of C–H insertion products in the reactions of dimethyl diazomalonate with thiophene are known. Thus the reaction of diazomalonates with thiophenes, catalysed by $Rh_2(OAc)_4$ at 20 °C, leads to the corresponding stable ylides in yields up to 90%. The thermal rearrangement of the ylides affords acceptable yields of 2-thienylmalonates, which are convenient synthons for the preparation of semisynthetic antibiotics of the β-lactam type, for example, cephalothin (Scheme 42).[66,67]

Scheme 42



90%

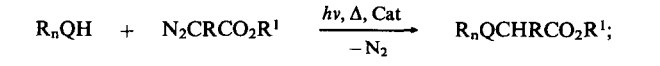
R = H (82%); R = Me (94%).

Other examples of the C–H insertion in reactions with thiophenes are examined in Section V devoted to reactions involving C–S bonds.

III. Heteroatom–hydrogen bonds

On irradiation, heating, or under the influence of catalysts, diazoesters react with compounds containing a heteroatom–hydrogen bond with formation of products of the insertion of the corresponding carbenes — esters of acetic acid derivatives.

Reactions involving insertion in the N–H, O–H, S–H, Si–H, Ge–H, and P–H bonds, which as a rule proceed selectively and with high yields of the insertion products, are now known.

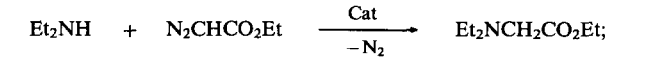


Q = N, O, S, Si, Ge.

1. N–H bonds

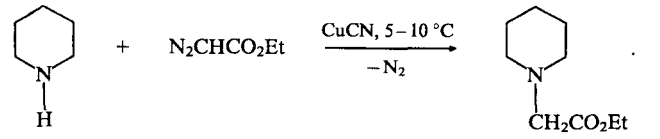
Regardless of the method of dediazotisation, both aliphatic (Schemes 43 and 44)[68] and aromatic primary and secondary amines (Schemes 45 and 46)[69,70] react with alkyl diazoacetates, affording high yields of *N*-alkylated glycine esters.

Scheme 43



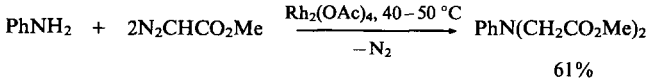
Cat = CuCN (72%), CuCl (33%).

Scheme 44



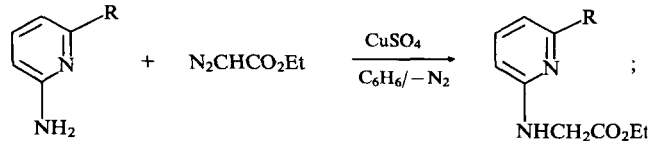
72%

Scheme 45



61%

Scheme 46

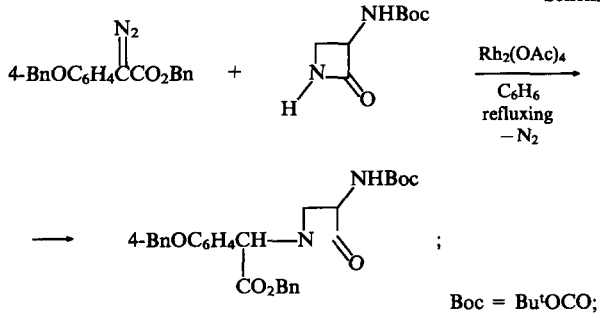


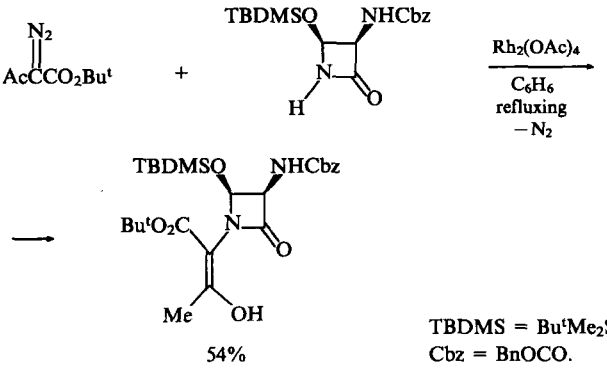
R = H, Me.

The intermolecular N–H insertion proceeds so readily that the catalytic dediazotisation of 2-alkylaminoethyl diazoacetates, even in the presence of olefins, leads not to cyclopropane adducts but exclusively to oligomers, which are formed as a result of the insertion of the carbene centre in the N–H bond of another molecule.[71]

The use of rhodium(II) acetate as the catalyst makes it possible to achieve the intermolecular N–H insertion reactions with labile products such as azetidinones. In the case of 3-aminoazetidinones, this reaction is exclusively selective, involving only the ring nitrogen atom, and leads to *N*-alkylated azetidinones — synthons for the preparation of β-lactam antibiotics (Scheme 47).[72,73]

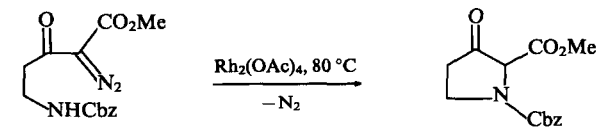
Scheme 47





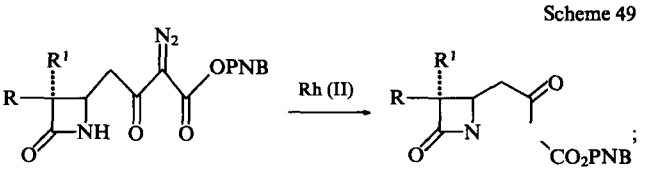
Examples of the intramolecular N–H insertion of carbenes, generated from diazoesters under the conditions of their dediazotisation by rhodium(II) compounds, are also known. However, these reactions take place effectively only in the case of compounds containing a N–H bond at a carbon atom in the δ-position. Thus the cyclisation of methyl 5-amino-2-diazo-3-oxopentanoate leads to methyl 3-oxopyrrolidine-2-carboxylate in 90% yield (Scheme 48).[74]

Scheme 48



The $Rh_2(OAc)_4$-catalysed intramolecular N–H insertion reaction with participation of the corresponding metal-carbene complexes derived from α-acyldiazoacetates containing an azetidinone fragment is used widely for the synthesis of β-lactam antibiotics (Scheme 49)[75] (for the references to studies up to 1985, see Maas[7]).

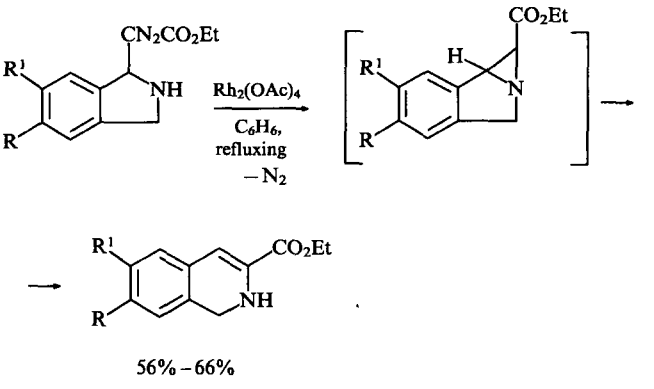
Scheme 49



PNB = $C_6H_4NO_2$-4. 50% – 100%

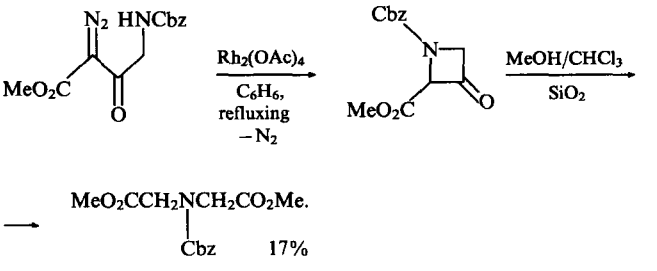
The number of examples of intramolecular cyclisation involving a more or less remote amino-group is extremely small. In particular, the cyclisation of β-aminodiazoesters has been described recently. The unstable aziridines formed initially in this case readily isomerise under the reaction conditions with the opening of the three-membered ring to give dihydroisoquinolinecarboxylates (Scheme 50).[76]

Scheme 50



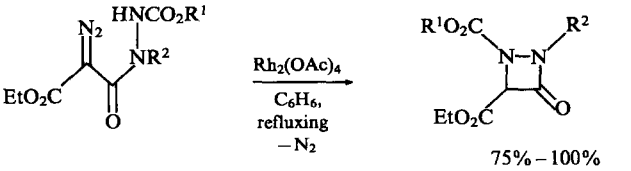
Intramolecular N–H insertion reactions with participation of a γ-amino-group are also known. For example, the $Rh_2(OAc)_4$-catalysed dediazotisation of the *N*-protected methyl 4-amino-2-diazo-3-oxobutanoate leads, admittedly with a low yield, to 3-oxoazetidine-2-carboxylate, which readily isomerises during isolation to a glycine derivative (Scheme 51).[74]

Scheme 51



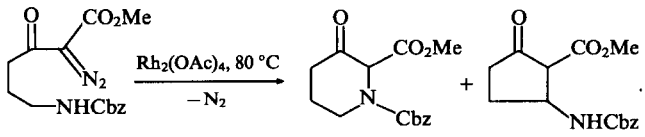
The monocarbazides of diazomalonates cyclise significantly more readily under these conditions, forming 1,2-diazetidinones in high yields (Scheme 52).[77]

Scheme 52



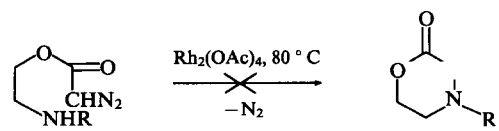
The intramolecular N–H insertion reaction involving diazoesters with an ε-amino-group is frequently complicated by the formation of side products of insertion in a C–H bond in the γ-position (Scheme 53)[74] or it does not occur at all, as happens in the reactions of 2-aminoethyl esters of diazoacetic acid (Scheme 54).[71]

Scheme 53



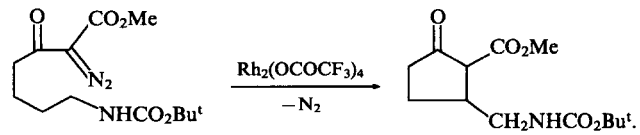
70% 10%

Scheme 54



The available information about the possibility of the N–H insertion with participation of more remote amino-groups is contradictory. Thus the cyclisation of methyl 7-*tert*-butoxycarbonylamino-2-diazo-3-oxoheptanoate leads exclusively to the products of insertion in a C–H bond at the ε-carbon atom (Scheme 55).[78]

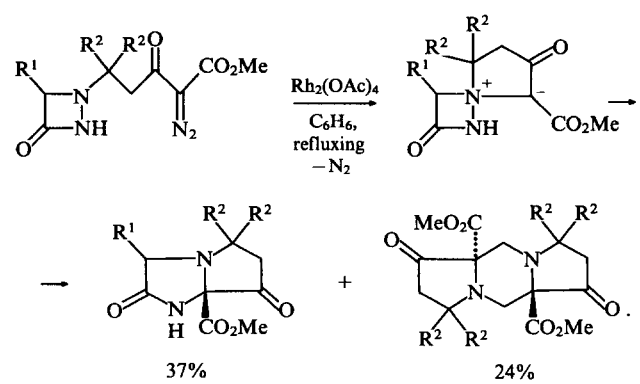
Scheme 55



73%

On the other hand, in the absence of C–H bonds at the ε-atom, as happens, for example, in methyl 2-diazo-5-(3-oxo-2*H*-1,2-diazetidinyl)-3-oxopentanoate, the products of insertion in a ring C–N bond of the diazetidine are formed, apparently via the intermediate formation of ylides (Scheme 56).[79]

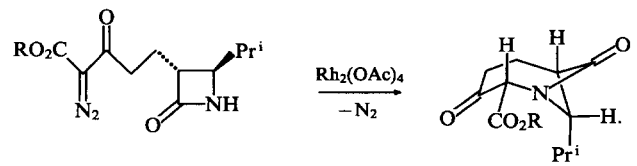
Scheme 56



37% 24%

However, the intramolecular insertion of the carbene centre in a N–H bond separated by a chain of five carbon atoms has been recently observed (Scheme 57).[80]

Scheme 57



50%

2. O–H bonds

The reactions of alkyl diazoacetates with hydroxyl-containing compounds, leading to the formation of the products of the insertion of the corresponding carbenes in the O–H bonds, are fairly varied. Thus certain organic acids, for example, trifluoromethanesulfonic acid, are capable of reacting with ethyl diazoacetate in liquid SO_2 even at −78 °C with formation of the corresponding sulfonate of glycolic acid in 73% yield (Scheme 58).[81]

Scheme 58

$$CF_3SO_2OH + N_2CHCO_2Et \xrightarrow[-78\,^\circ C/-N_2]{\text{liquefied } SO_2} CF_3SO_2OCH_2CO_2Et.$$

However, other hydroxylated compounds (water, alcohols, carboxylic acids) afford the O–H insertion products only in the photolytic, pyrolytic, or catalytic dediazotisation of alkyl diazoacetates[68,82] or their α-metallated derivatives (Scheme 59).[83]

Scheme 59

$$ROH + N_2CR^1CO_2R^2 \xrightarrow[-N_2]{h\nu,\ \Delta,\ Cat} ROCHR^1CO_2R^2;$$

R = H, Alk, Ac; R^1 = H, HgMe; R^2 = Alk.

This reaction acquired preparative importance only after the discovery of catalysts based on rhodium compounds, which ensure preparative yields (in excess of 80%) of the products in the case of various diazoesters and a wide range of hydroxylated compounds.[7]

The high efficiency of these catalysts makes it possible to carry out reactions also with diazoacetic acid esters having a complex structure (Scheme 60).[84]

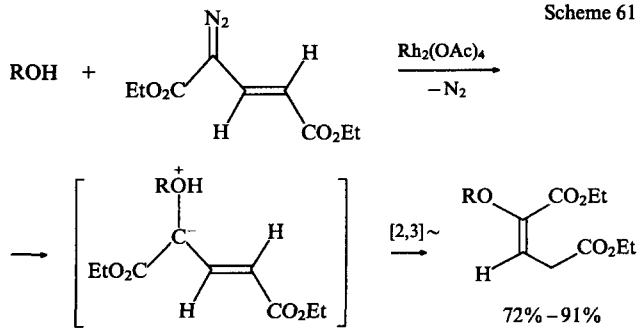
Scheme 60

$$H_2O + N_2CHCO_2CH_2C{\equiv}CH \xrightarrow[CH_2Cl_2/-N_2]{Rh_2(OAc)_4,\ 20\,^\circ C} HOCH_2CO_2CH_2C{\equiv}CH + O(CH_2CO_2CH_2C{\equiv}CH)_2.$$

15% 20%

In the case of carbenes containing an allyl fragment, for example, the metal-carbene complex formed on dediazotisation of ethyl α-(2-ethoxycarbonylvinyl)diazoacetate on treatment with $Rh_2(OAc)_4$, the insertion reaction is accompanied by a [2,3]-sigmatropic rearrangement (Scheme 61).[85]

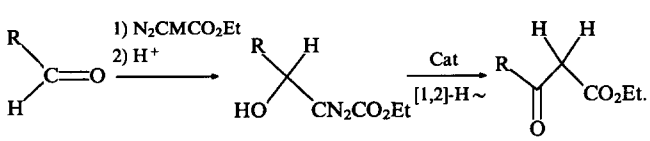
Scheme 61



R = Me, Et, Pr^i, Bu^t.

Instances of intramolecular reactions of diazoesters with participation of O–H bonds are known. However, these have a number of characteristic features compared with the analogous N–H insertion reactions. Thus the dediazotisation of α-diazo-β-hydroxyacetates, catalysed by rhodium(II) carboxylates, leads not to three-membered heterocycles (oxirans in the given instance), of the kind observed in the reactions involving β-amino-α-diazoacetates (Scheme 50), but to acyl acetates as a result of a [1,2]-H shift (Scheme 62).[36,86–89]

Scheme 62

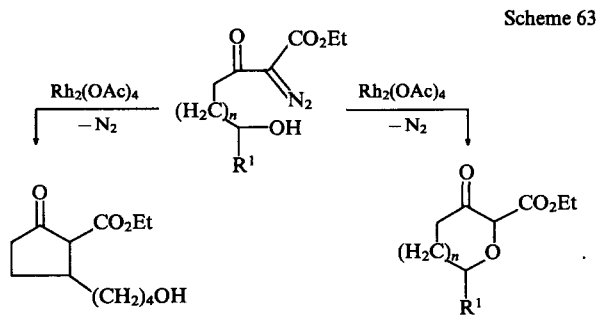


M – metal; Cat = Rh_2L_4; SnX_2;

R = H, Alk, Ph, $H_2C{=}CH$, *trans*-PhCH=CH.

Furthermore, similar cyclisations involving hydroxylated diazoesters lead readily to six-, seven-, and eight-membered cyclic esters in satisfactory yields,[90,91] whereas heterocycles containing more than six atoms cannot be obtained as a rule with the aid of similar N–H insertion reactions. However, the attempts to obtain oxygen-containing heterocycles with more than eight atoms by this procedure have led to the formation of cyclopentanones — the products of the competing C–H insertion (Scheme 63).[90]

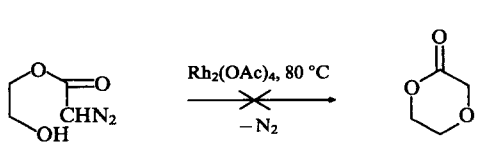
Scheme 63



n = 5, R^1 = H. *n* = 1–3, 24%–78%.

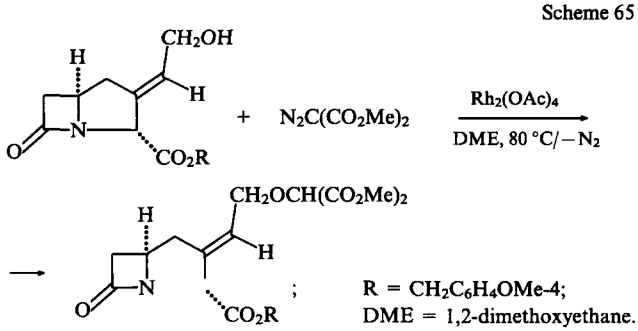
The attempt to obtain 1,4-dioxanone by the cyclisation of 2-hydroxyethyl diazoacetate was also unsuccessful. The dediazotisation of this diazoacetate led to the formation of oligomers, apparently as a result of intermolecular O–H insertion (Scheme 64).[92]

Scheme 64



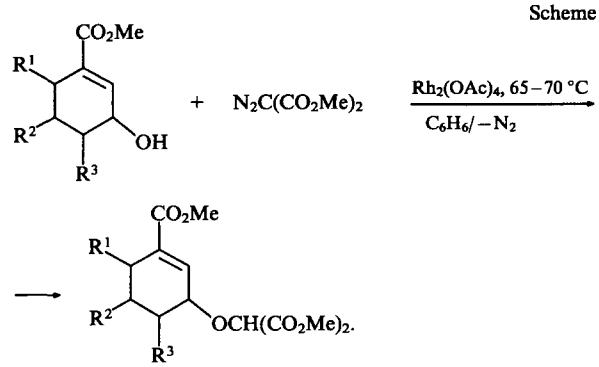
Special mention should be made of the reactions of carbenes, generated from diazoesters, with allyl and propargyl alcohols, because in this case the ACC are capable both of being inserted in the O–H bonds and of adding to the multiple bond with formation of cyclopropane or cyclopropene adducts.[93,94] However, instances are known where the interaction with allyl alcohol in accordance with the O–H insertion mechanism proceeds with a high selectivity and high yields of the corresponding esters (Schemes 65 and 66).[95–98]

Scheme 65



R = $CH_2C_6H_4OMe$-4;
DME = 1,2-dimethoxyethane.

Scheme 66

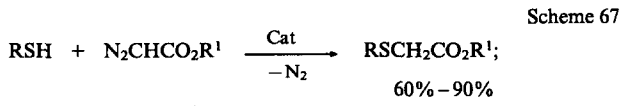


R^1	R^2	R^3	Yield (%)	Ref.
H	H	OCH_2CH_2OMe	75	96
H	H	$NHCO_2Bu^t$	94	97
H	–O–		82	98

3. S–H, Si–H, Ge–H, and P–H bonds

Isolated examples of the reactions of diazoesters with the S–H bond, leading to the formation of esters of thioglycolic acid, have been described in the literature. In the reactions with thiols, both CuCl[67] and $Rh_2(OAc)_4$ are used as the catalysts of the dediazotisation of alkyl diazoacetates (Scheme 67).[99]

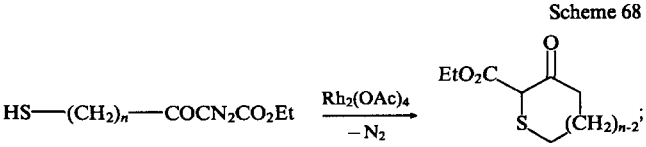
Scheme 67



Cat = CuCl, $Rh_2(OAc)_4$.

However, rhodium(II) compounds are usually employed for theintramolecular reactions of mercaptodiazoesters (Scheme 68).[73,77]

Scheme 68



n = 3 (73%), *n* = 4 (35%).

The reactions of diazoesters with mono-, di-, and trisubstituted hydrosilanes, leading to esters of acetic acids, are of preparative importance. The reactions proceed with high yields both under the conditions of the thermal decomposition of alkyl diazoacetates (Scheme 69) and on treatment with catalysts — copper compounds and $Rh_2(OAc)_4$ (Scheme 70).[100-102]

Scheme 69

$$PhMe_nSiH_{3-n} + N_2CHCO_2Et \xrightarrow[-N_2]{130-140\ ^\circ C} PhMe_nSiH_{2-n}CH_2CO_2Et;$$

n = 0 (59%), 1 (92%), 2 (94%).

Scheme 70

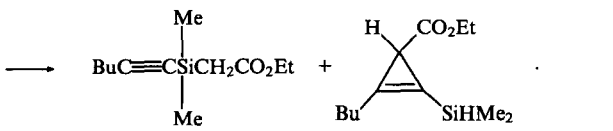
$$RR^1R^2SiH + N_2CHCO_2R^3 \xrightarrow[-N_2]{Cat} RR^1R^2SiCH_2CO_2R^3;$$

Cat = Cu, 94 °C (< 90%);
$Rh_2(OAc)_4/CH_2Cl_2$ (90%-94%).

Under these conditions, the addition to the triple bond in hydroxyacetylenes competes to only a slight extent with the Si–H insertion reactions (Scheme 71).[103]

Scheme 71

$$BuC{\equiv}CSiMe_2H + N_2CHCO_2Et \xrightarrow[-N_2]{150\ ^\circ C\ (or\ CuCl,\ 80\ ^\circ C)}$$



50%–60% 5%–15%

There are data indicating the possibility of the insertion of carbenes, generated by the dediazotisation of α-triethylgermyldiazoacetates, in the Ge–H bond of triethylgermane and in the Sn–H bond of trineopentylstannane (Scheme 72).[104] In the case of stannanes, this reaction proceeds in the absence of catalysts (Scheme 73).

Scheme 72

$$Et_3GeCN_2CO_2Et + Et_3GeH \xrightarrow[C_6H_6/-N_2]{Cu,\ 100\ ^\circ C} (Et_3Ge)_2CHCO_2Et.$$

66%

Scheme 73

$$(neo\text{-}C_5H_{11})_3SnCN_2CO_2Et + (neo\text{-}C_5H_{11})_3SnH \xrightarrow[C_6H_6/-N_2]{100\ ^\circ C}$$

$$\longrightarrow [(neo\text{-}C_5H_{11})_3Sn]_2CHCO_2Et.$$

It has been established recently that products of P–H insertion may be formed in 16%–39% yields under the conditions of the benzophenone-sensitised photolysis of certain diazoesters in the presence of dimethyl phosphorothioite (Scheme 74).[105,106]

This reaction proceeds more selectively under the conditions of catalytic dediazotisation of diazoesters by $Cu(acac)_2$; the yields of the corresponding P–H insertion products reach 83%.[107]

Scheme 74

$$N_2CRCO_2R^1 + (R^2O)_2\overset{\overset{S}{\|}}{P}H \xrightarrow[-N_2]{h\nu\ (Cat)} (R^2O)_2\overset{\overset{S}{\|}}{P}CHRCO_2R^1;$$

R = H, Ph, Ac, CO_2Me; R^1 and R^2 = Me, Et.

IV. Carbon–carbon bonds

The dediazotisation of certain α-diazocarboxylates may be accompanied not only by a [1,2]-H-shift (Section II, 1) but also by the [1,2]-shift of the carbon atom to the carbene centre generated with formation of the products of the formal insertion of the carbene in the C–C bond. Rearrangements of this type usually occur in the catalytic and photolytic decomposition of diazoacetates containing a cyclic substituent in the α-position. The dediazotisation of such diazoesters leads to ring expansion by one carbon atom and may serve as a convenient method for the formation of higher homologues of alicyclic compounds. The data concerning the [1,2]-carbon shift in a series of α-cyclyldiazoacetates are in Table 3.

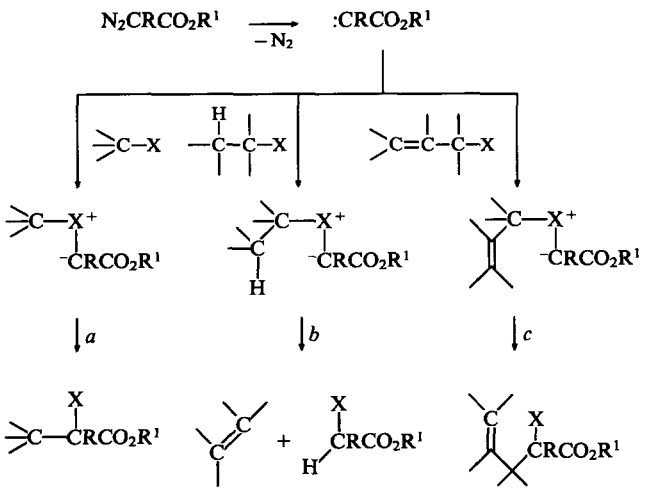
The [1,2]-carbon shift reactions are frequently accompanied by other reactions, for example, the [1,2]-hydride shift (Table 4, example 1). Combination of the [1,2]-H and [1,2]-C shifts in the transition metal-catalysed dediazotisation of certain α-diazo-β-hydroxycarboxylates without a hydrogen atom in the α-position leads to a mixture of α-acyl-α-alkylacetates (Table 4). In the case of cyclic α-diazo-β-hydroxycarboxylates (Table 4, examples 1–5), the analogous reactions are accompanied by the unexpected migration of the less substituted carbon atom and lead to the formation of 2-oxocyclocarboxylates.

High and in certain cases quantitative yields of target products as well as the availability of the initial α-diazo-β-hydroxycarboxylates, obtained by the reaction of carbonyl compounds with alkyl diazoacetates, make this reaction a convenient preparative method for the formation of higher homologues of carbonyl compounds.

V. Carbon–heteroatom bonds

Under the conditions of their dediazotisation, diazoesters react with various compounds containing carbon–heteroatom bonds. A common feature of this large group of reactions is the mechanism of the primary step, which consists in the attack by the carbene on the lone pair of the heteroatom with formation of an ylide. The subsequent reactions of these ylides, determined by the structure of the substrate, are fairly varied. The [1,2]-shift of the carbene fragment from the heteroatom to a neighbouring carbon atom occurs most frequently (the Stevens rearrangement) with formation of the product of the formal insertion of the carbene in the C–X (Scheme 75, pathway *a*), which is sometimes complicated by the elimination of a hydrogen atom attached to the β-carbon atom with transfer of the HX fragment from the substrate to the carbene (pathway *b*). In the case of allyl derivatives, the [2,3]-sigmatropic rearrangement of the ylide takes place effectively and leads to the insertion product (pathway *c*).

Scheme 75



All these processes, which lead to significant changes in the carbon skeleton of the initial molecule, take place selectively in many instances and constitute an effective pathway to the introduction of functional groups into acyclic heteroatomic compounds and the synthesis of carbofunctional heterocycles. Numerous studies devoted to the mechanistic aspects of the insertion reactions of this type have been described in detail in a number of reviews.[3,7,118–120] We shall deal with the synthetic possibilities of these reactions.

It has now been established that diazoesters are able to interact with C–Hal, C–N, C–O, and C–S bonds; individual examples of reactions involving C–Se are known; in conformity with the logic adopted for the presentation of data, they are considered in the Section devoted to the C–S insertion (Section V.4).

1. Carbon–halogen bonds

The interaction with monohaloalkanes leads to esters of monochloroacetic and ω-haloalkanoic acids as a result of β-elimination and C–H insertion respectively and usually proceeds nonselectively, as a result of which the reaction has no preparative value. The reaction of ethyl diazoacetate with bromotrinitromethane, which leads to the product of C–Br insertion in 67% yield, is an exception (Scheme 76).[121]

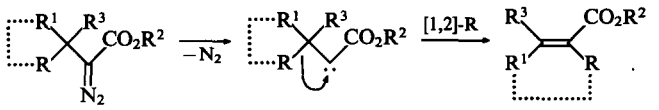
Scheme 76

$$(O_2N)_3CBr + N_2CHCO_2Et \xrightarrow[-N_2]{\text{ether, 20 °C}} (O_2N)_3CCHBrCO_2Et.$$

The reactions of diazoesters with allyl halides, which contain two reaction centres in the molecule (the double bond and the C–Hal bond), have been investigated quite vigorously. It was established that carbenes in the singlet state are equally involved in the addition to the double bond with formation of cyclopropane adducts and in the reaction with the C–Hal bond with formation of ylides, undergoing the [2,3]-rearrangement to the C–Hal insertion products; on the other hand, triplet carbenes add preferentially to the multiple bond.[3] This finding enabled Ando[119] to propose allyl halides as test reagents for the spin state of carbenes generated by the dediazotisation of alkyl diazoacetates.

The reaction of alkyl diazoacetates with allyl halides has acquired preparative importance after the appearance of catalysts based on rhodium(II) carboxylates, which make it possible to increase significantly the selectivity of the processes involving the insertion of carbenes in the C–Hal bond. The use of $Rh_2(OAc)_4$ for the dediazotisation of ethyl diazoacetate in the reaction with allyl iodide makes is possible to obtain the ester of 2-iodobut-3-enoic acid in a virtually quantitative yield (Scheme 77).[122]

Table 3. The formation of higher homologues of cyclic compounds via the [1,2]-carbon shift in alkoxycarbonylcarbenes.



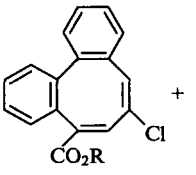
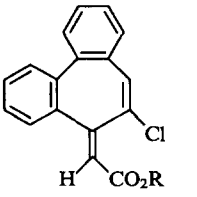
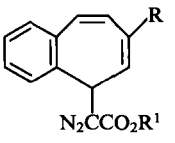
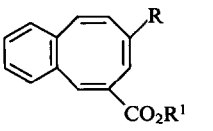
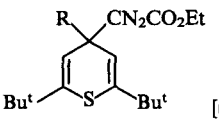
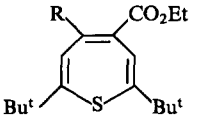
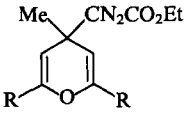
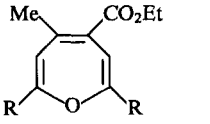
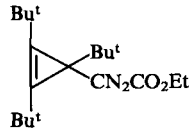
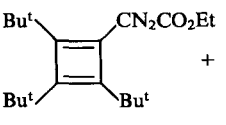
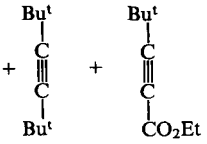
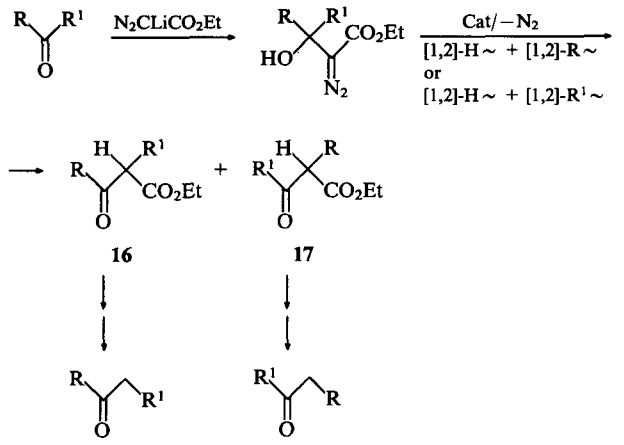
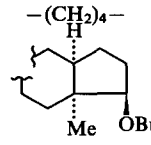
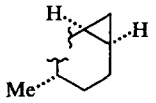
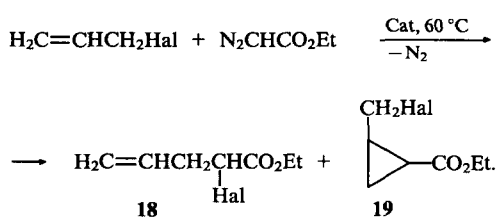
Diazoester	Dediazotisation conditions	Products (yield (%))	Ref.
 (R = Me, Et)	Cu (acac)$_2$, PhMe, refluxing	 (25) +  (10)	120
	Cu (acac)$_2$, PhMe, refluxing	 R = Br, R^1 = Me, Bu^t (70–86); R = Cl, R^1 = Me (64)	109, 110
	[(η^3-C$_3$H$_5$)PdCl]$_2$ CHCl$_3$, 0 °C	 R = CO$_2$Et; R = Me (99)	129, 112
	[(η^3-C$_3$H$_5$)PdCl]$_2$ C$_6$H$_6$, 0 °C	 R = Bu^t (92); R = Me, Ph (97–98)	128, 130
	*hv* C$_5$H$_{12}$, 20 °C	 +  54:23:23	98

Table 4. The formation of higher homologues of ketones by the successive [1,2]-H and [1,2]-C shifts in alkoxycarbonylcarbenes.



R	R¹	Catalyst[a]	Yield (%) (16 : 17 ratio)	Ref.
Et	Me	A	87 (6:5)	87
Bu	Me	B	86 (7:5)	87
Bu^t	Me	B	59 (1:0)	87
$PhCH_2$	Me	C	73 (5:8)	87
Ph	Ph	C	70 (cm[b])	87
$-(CH_2)_4CHMe-$		B	82 (1:0)	87
$-(CH_2)_4-$		A	~100 (cm[b])	116
		C	~100 (1:0)	87
		A	55 (cm[b])	117

Scheme 77

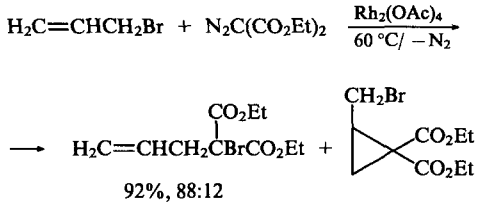


Cat	Hal	Yield (%)	
		18	**19**
$Rh_2(OAc)_4$	I	98%	–
$Rh_2(OAc)_4$	Cl	<2%	95%
$Rh_2(OAc)_4$	Br	30%	46%
Cu bronze	Br	50%	6%

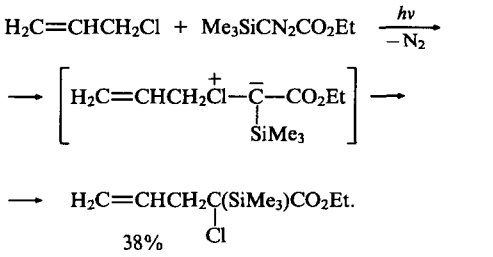
However, in the case of allyl bromide and chloride, the cyclopropane formation reaction is the main one; the decrease in the fraction of the C–Hal insertion products under these conditions in favour of cyclopropane adducts takes place in parallel with the decrease in nucleophilicity in the sequence I > Br > Cl, which confirms the ylide mechanism of the reaction. Thus allyl chloride affords the ester of 2-chloromethylcyclopropanecarboxylic acid in a yield exceeding 95% in the reaction with ethyl diazoacetate in the presence of $Rh_2(OAc)_4$. Nevertheless, when the same catalyst is used in the reaction with allyl bromide, the process proceeds nonselectively and leads to the formation of almost equal amounts of cyclopropane adducts and α-bromobutenoates, the use of copper bronze permitting some increase in the process selectivity as regards the insertion product.

Metal–carbene complexes generated from dimethyl diazomalonate on treatment with rhodium catalysts[122] and carbenes formed on photolysis of ethyl α-trimethylsilyldiazoacetate[123] show an even greater tendency to form ylides with allyl halides. In the first case (Scheme 78), the product of insertion in the C–Br bond of allyl bromide predominates even when $Rh_2(OAc)_4$ is used, whilst in the second (Scheme 79) the corresponding cyclopropane adduct is not formed at all.

Scheme 78

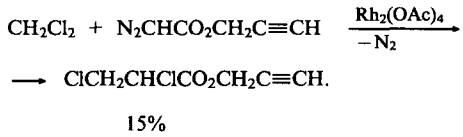


Scheme 79



The photolytic decomposition reactions of diazoesters in the presence of polyhaloalkanes, which were investigated vigorously in the 1950s,[3] have not found preparative applications because of their low selectivity. The synthetic possibilities of catalytic processes have been scarcely studied, although examples of such processes, described recently, yielded promising results. Thus, the ability of propargyl diazoacetate to afford the product of insertion in the C–Cl bond of methylene chloride in the presence of $Rh_2(OAc)_4$ has been established recently (Scheme 80).[84]

Scheme 80

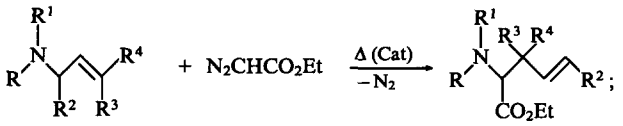


The analogous reaction does not take place with methyl diazoacetate.

2. C–N bonds

The number of examples of preparative syntheses based on the reactions of alkyl diazoacetates with amines, leading to products of the insertion of alkoxycarbonylcarbenes in the C–N bond, is limited. The interaction of ethyl diazoacetate with tertiary allyl amines on heating to 144–175 °C or on treatment with catalysts based on rhodium(II), copper(II), cobalt(II), and nickel(II), or zirconium(IV) compounds at 60 °C leads, as a result of the [2,3]-rearrangement, to esters of unsaturated *N,N*-dialkylamino-acids in high yields (Scheme 81).[124]

Scheme 81



30%–99%

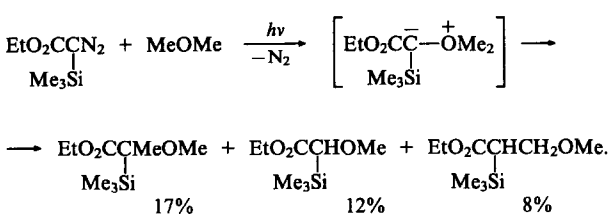
R, R^1 = alkyl or $R+R^1 = (CH_2)_n$ (n = 5–6) or $CH_2OCH_2CH_2$; R^2 = alkyl; R^3, R^4 = alkyl or R^3+R^4 = α,ω-alkenyl.

The reaction is extremely sensitive to the catalyst concentration. The highest yields have been achieved for a catalyst : amine molar ratio of 1 : 800; with increase in catalyst concentration, there is an appreciable increase in the contribution of the competing addition of the carbene to the double bond.[125]

3. C–O bonds

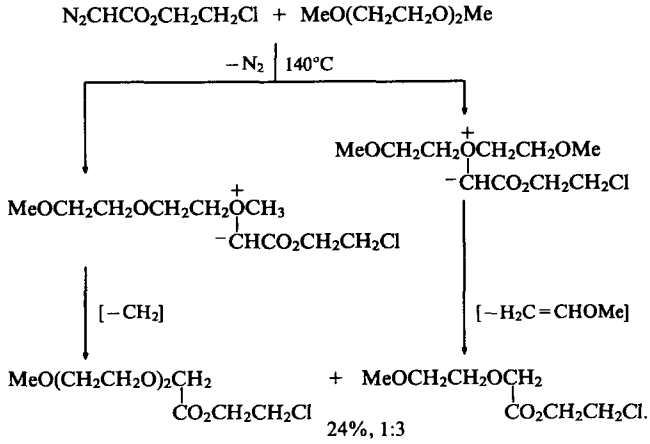
The reactions of diazoesters with acyclic ethers, initiated by irradiation (Scheme 82),[123] heating (Scheme 83),[126] or treatment with $Rh_2(OAc)_4$ (Scheme 84),[124] usually proceed nonselectively, leading to esters of alkoxyacetic acids as a result of the β-elimination reaction of the O ylides formed initially. The formation of C–O insertion products is observed in exceptional instances.

Scheme 82



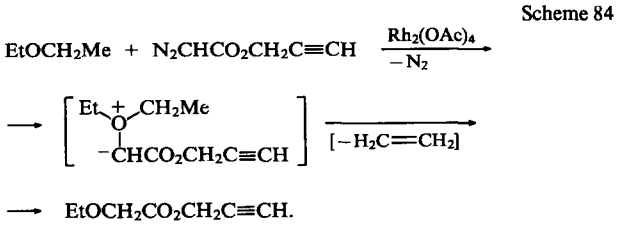
17% 12% 8%

Scheme 83



24%, 1:3

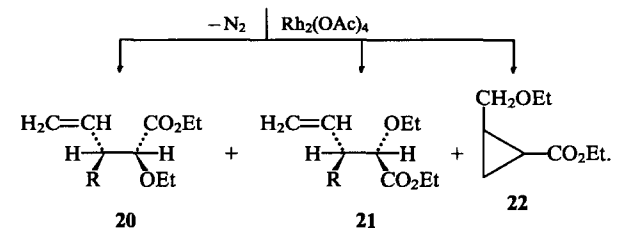
Scheme 84



30%

Although the reaction of ethyl diazoacetate with allyl ethyl ether in the presence of $Rh_2(OAc)_4$ does lead to C–O insertion products as a result of the [2,3]-rearrangement of the ylide, it too is complicated by the competing formation of cyclopropane adducts, the fraction of which may reach 30% (Scheme 85).[127]

Scheme 85

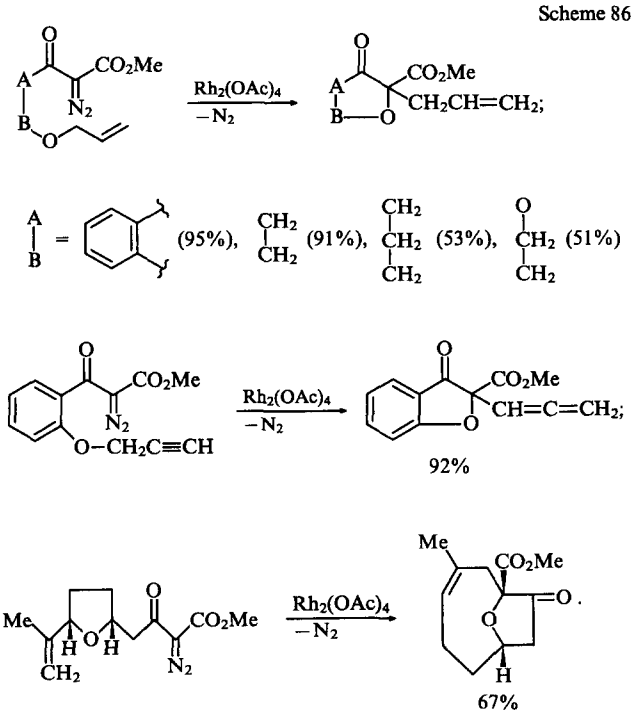


R	Configuration of double bond	Overall yield (%)	Product ratio		
			20	21	22/(20+21)
Ph	E	95	83	17	27
Ph	Z	95	6	94	26
Me	E	86	79	21	8
Me_3Si	E	68	97	3	6

The [2,3]-rearrangement itself then proceeds with a high degree of diastereoselectivity.

The $Rh_2(OAc)_4$-initiated intramolecular cyclisation of α-acyldiazoesters containing an allyloxy- or propargyloxy-fragment takes place with a high selectivity (Scheme 86).[128]

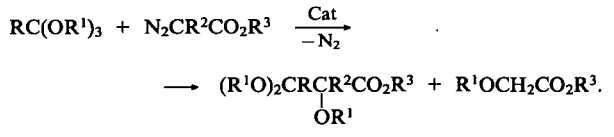
Scheme 86



These reactions lead to five- and six-membered oxacyclanones as a result of C–O insertion and the [2,3]-rearrangement.

The formation of products of the formal C–O insertion has been noted also in the reactions of ethyl diazoacetate with acetals and orthoesters. On treatment with BF_3 etherate, the reactions of diazoesters with orthoesters lead under these conditions exclusively to C–O insertion products. The metal-catalysed processes are less selective and are accompanied by β-elimination (Scheme 87).[129]

Scheme 87

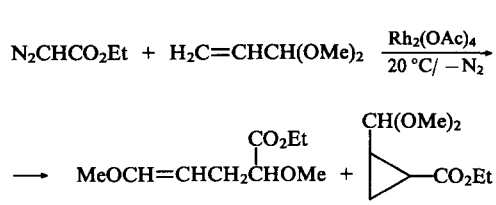


$BF_3 \cdot OEt_2$(Cat), 25 °C	45%–85%	< 5%
$Rh_2(OAc)_4$, 60 °C	3%–20%	11%–27%
$Cu(OTf)_2$, 20 °C	38%–46%	6%–20%

R = H, Me, Et; R^1 = Me, Et;
R^2 = H, CO_2Me; R^3 = Me, Et.

In the presence of $Rh_2(OAc)_4$, ethyl diazoacetate reacts with acrolein dimethyl acetal to form the product of the [2,3]-rearrangement of the O ylide together with the cyclopropane adducts (Scheme 88).[130]

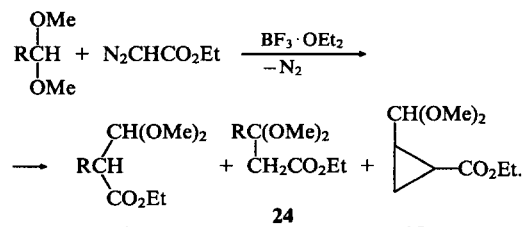
Scheme 88



76 : 24, overall yield 47%.

However, when this reaction is initiated by BF_3 etherate, the main and sometimes the only products are those of the formal C–C insertion — the diacetals of derivatives of formylacetic acid (together with small amounts of cyclopropane adducts) (Scheme 89).[131]

Scheme 89

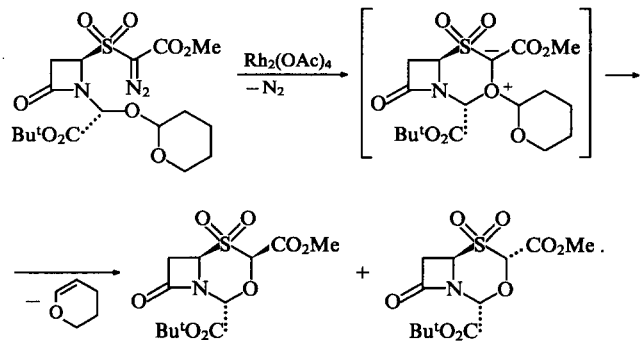


23 **24** **25**

R	T/°C	Overall yield (%)	Product ratio 23	24	25
$H_2C=CH$	−15	70	75	10	15
(*E*)-PhCH=CH	0	70	~100	< 1	< 1
Ph	25	85	~97	3	–
PhC≡C	25	22	~100	< 1	–

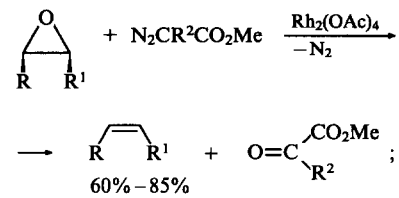
The β-elimination reaction of an endocyclic O ylide has been used recently for the preparative synthesis of antibiotics of the 3-oxacepham series (Scheme 90).[132]

Scheme 90



The reaction of diazoesters with cyclic oxa-compounds has a number of characteristic features, the decisive factor being the ring size. Dimethyl diazomalonate and methyl α-trimethylsilyldiazoacetate induce the deoxygenation of oxirans in the presence of $Rh_2(OAc)_4$, which proceeds with retention of the configuration of the initial oxirans in the olefins formed and with high yields of the latter (Scheme 91).[133]

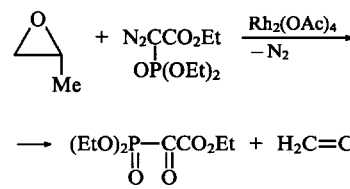
Scheme 91



R^2 = CO_2Me, $SiMe_3$.

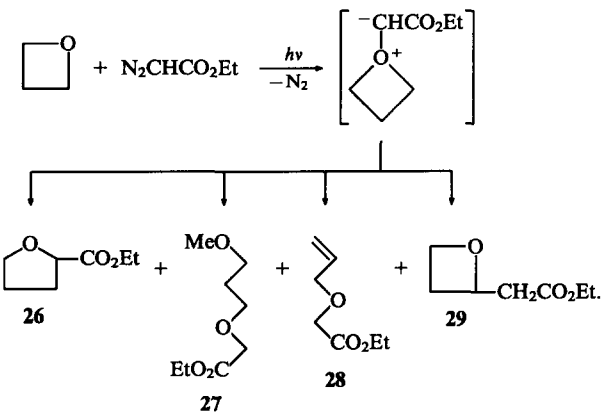
The analogous reaction of α-phosphoryldiazoacetate with methyloxiran has been used to synthesise oxophosphonates (Scheme 92).[134]

Scheme 92



On photolysis of ethyl diazoacetate in oxetan, the ylide formed is converted into the ester of tetrahydrofuran-2-carboxylic acid as the main product as a result of the Stevens rearrangement (Scheme 93).[135] However, in methanol the main process becomes the solvolysis of the ylide, which leads to ring opening and the formation of the ester of alkoxyacetic acid.

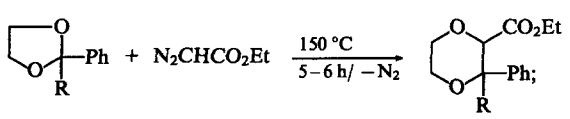
Scheme 93



Solvent	Overall yield (%)	Product ratio			
		26	27	28	29
Oxetan	54	70.3	–	12.2	17.5
MeOH	54	23.6	51.9	6.3	18.2

The interaction of ethyl diazoacetate with 1,3-dioxolans leads to 1,4-dioxanecarboxylates—the products of the formal C–O insertion of ethoxycarbonylcarbene—apparently as a result of the Stevens rearrangement of the corresponding O ylides (Scheme 94).[134]

Scheme 94



R = H (48.5%); Me (6.5%).

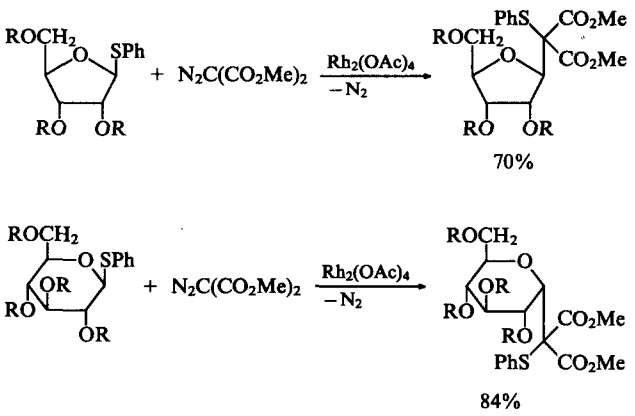
The low yields of the products formed (less than 50%) are due to the fairly severe reaction conditions (150 °C), but there are no literature data concerning the possibility of using milder conditions, for example, dediazotisation in the presence of $Rh_2(OAc)_4$.

4. C–S and C–Se bonds

The greater nucleophilicity of the sulphur atom compared with nitrogen or oxygen atoms is responsible for the high reactivity of sulphur-containing compounds and hence for the greater variety of the synthetic possibilities of their reactions with carbenes. This explains the special interest in the study of the reactions of diazoesters with compounds containing C–S bonds, which has been reflected in the large number of studies described in the literature. Furthermore, in the reactions of diazoesters with sulphur-containing compounds, it has been possible to isolate stable S ylides and to investigate the reactions of the latter, obtaining thereby direct evidence for their involvement in the formation of the final products.

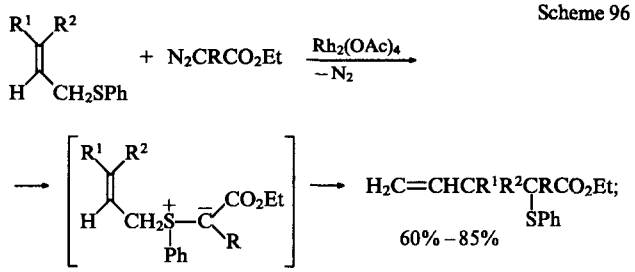
Diazoesters react with virtually any acyclic sulfides to form the C–S insertion products as a result of the [1,2]-shift of the carbene fragment in the S ylide formed initially (Scheme 95).[137]

Scheme 95

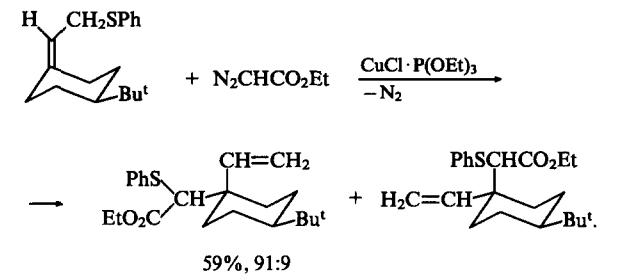


Allyl sulfides react under these conditions with a [2,3]-rearrangement (Scheme 96).[138,139]

Scheme 96



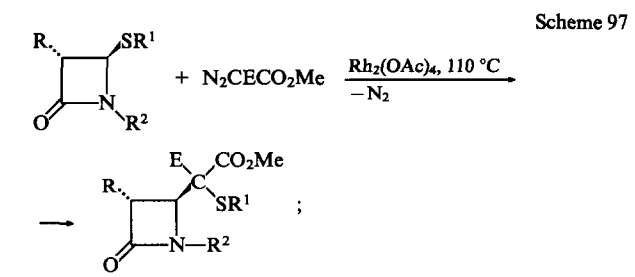
R = CO_2Et, $P(O)(OEt)_2$.



59%, 91:9

The attack on the sulfur atom in the carbenes generated from diazoesters takes place preferentially even in the presence in the substrate molecule of other heteroatoms, for example, oxygen or nitrogen (Scheme 97).[140]

Scheme 97

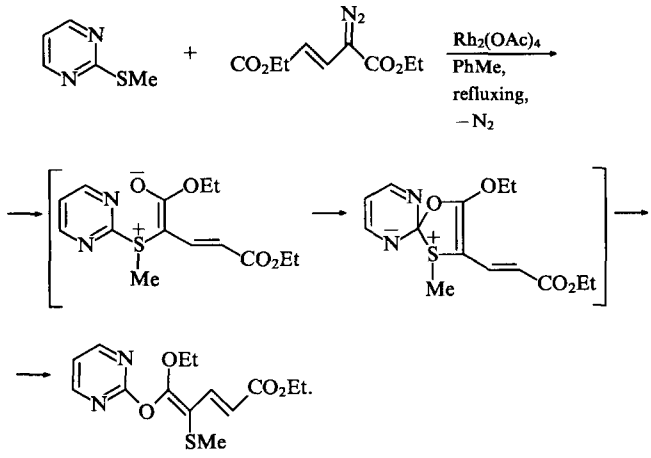


R, R^1 – Alk, Ph, CH_2Ph;
R^2 = H, $CH_2CO_2R^3$, $SiMe_2Bu^t$;
E = CO_2R^4, $P(O)(OEt)_2$.

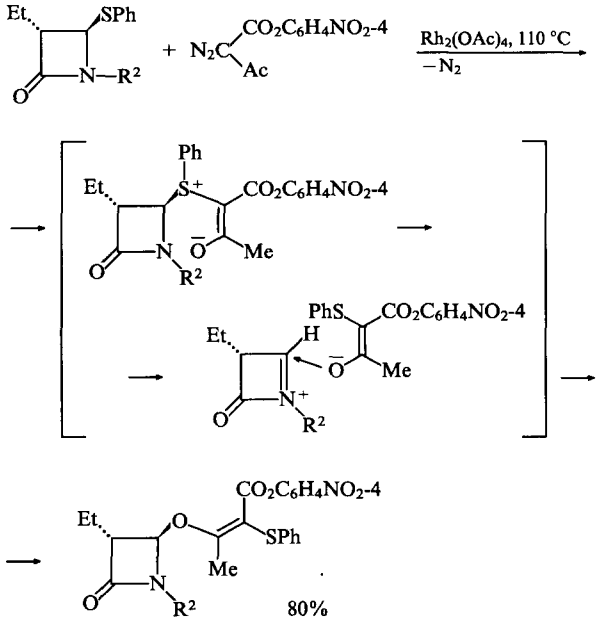
Furthermore, the interaction of such polyheteroatomic molecules with certain diazoesters, for example with ethyl α-(2-ethoxycarbonylvinyl)diazoacetate (Scheme 98)[141] or with 4-nitrophenyl α-acetyldiazoacetate (Scheme 99),[142] gives rise to

the possibility of the additional stabilisation of the cationic and ionic centres in the resulting S ylide which promotes its [1,4]-rearrangement with formation of an *O*-alkylated product.

Scheme 98

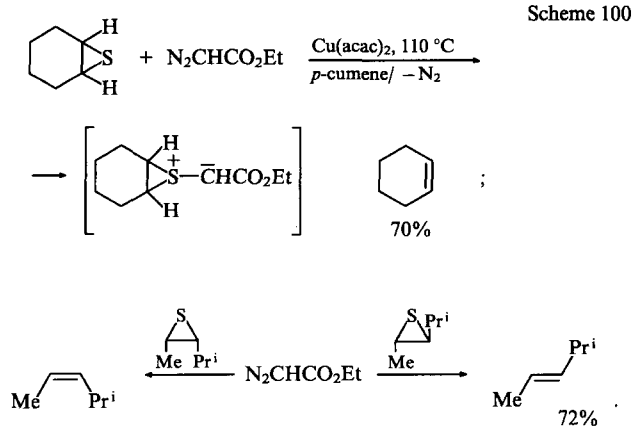


Scheme 99



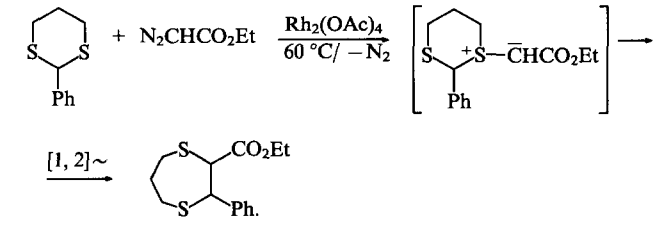
The carbene decomposition of alkyl diazoacetate in the presence of cyclic thioethers also leads to the formation of S ylides, the subsequent reactions of which are usually accompanied by a change in ring size. For example, as in the reactions with oxirans, the interaction of ethyl diazoacetate with thiirans is accompanied by selective desthiylation with formation of olefins retaining the initial configuration of the three-membered heterocycle (Scheme 100).[143]

Scheme 100



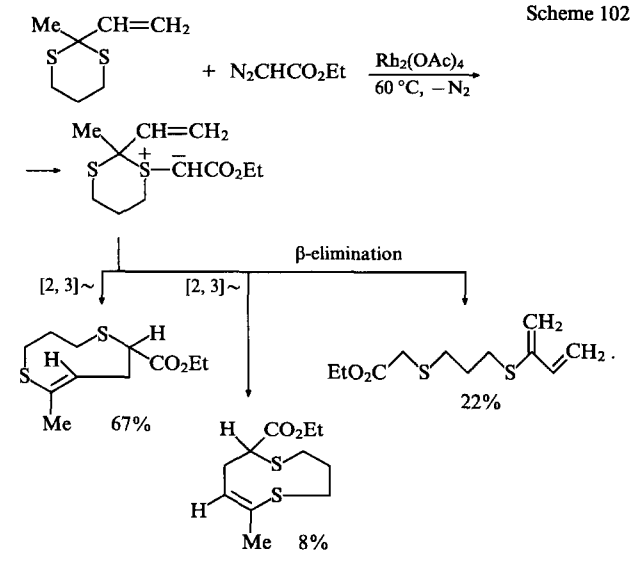
On the other hand, the $Rh_2(OAc)_4$-catalysed interaction of ethyl diazoacetate with 2-phenyl-1,3-dithiane is accompanied by the insertion of the ethoxycarbonylmethylene fragment into the six-membered ring as a result of the Stevens rearrangement of the S ylide formed initially and leads to the corresponding 1,4-dithiepan (Scheme 101).[129]

Scheme 101

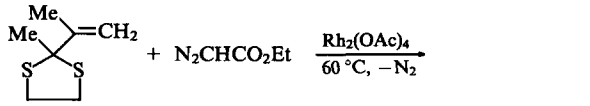


The interaction of alkyl diazoacetates with thiacyclanes containing an unsaturated fragment involves either the substrate ring expansion or ring contraction depending on whether the double bond is in the side chain or in the ring. Thus the $Rh_2(OAc)_4$-catalysed interaction of diazoesters with 2-vinyl-1,3-dithiane (Scheme 102),[129] 2-isopropenyl-2-methyl-1,3-dithiolan (Scheme 103),[129] and 2-vinyltetrahydrothiophene (Scheme 104)[144] leads, as a result of the [2,3]-sigmatropic rearrangement of the S ylides, to nine- and eight-membered thiacyclanes together with the acyclic β-elimination products.

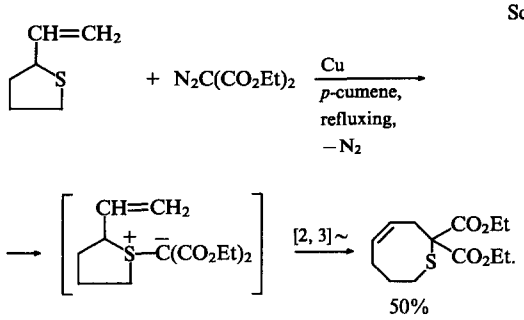
Scheme 102



Scheme 103

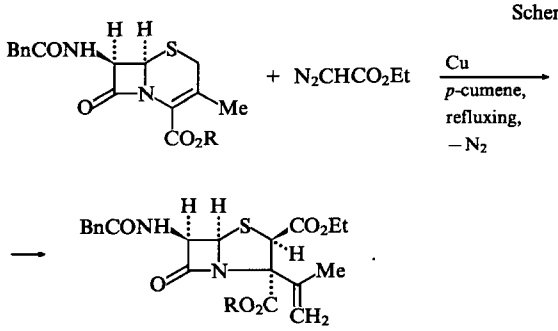


Scheme 104



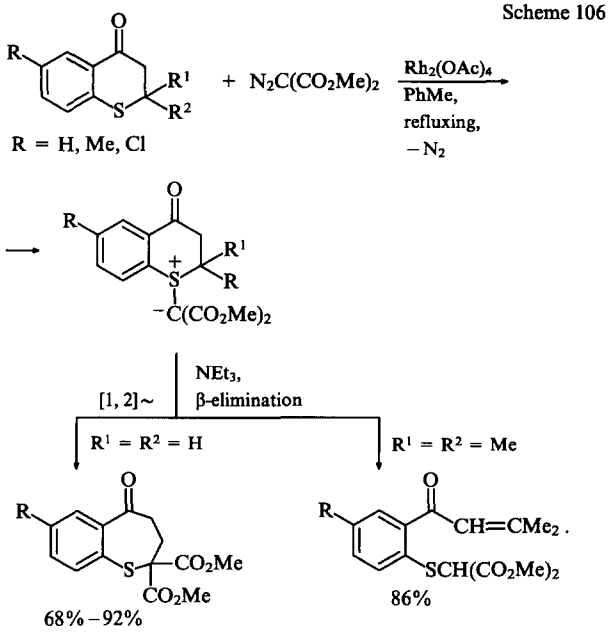
On the other hand, the reaction of ethyl diazoacetate with the esters of cephalosporanic acid, containing a double bond in the heterocycle, is accompanied by ring contraction with formation of the esters of 3-isopropenylpenicillanic acid (Scheme 105).[145]

Scheme 105



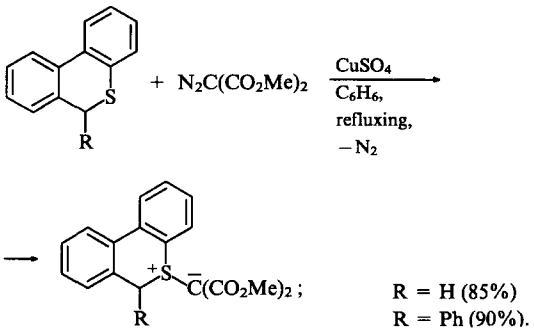
In contrast to alkyl diazoacetates, diazomalonates and diazomalononitriles react with thiacyclanes to form fairly stable S ylides, which can be isolated in a pure form as the main or even the only reaction products, which makes it possible to investigate their subsequent reactions. For example, the $Rh_2(OAc)_4$-catalysed decomposition of dimethyl diazomalonate in the presence of thiachromones leads to stable S ylides, the decomposition of which takes place only on treatment with triethylamine and leads to homothiachromones or thiobenzophenone as a result of the [1,2]-shift and β-elimination respectively (Scheme 106).[146]

Scheme 106

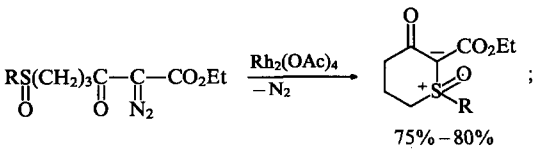


The S ylides formed are sometimes so stable that they do not rearrange even on fusion at temperatures above 100 °C (Schemes 107–109).[147–149]

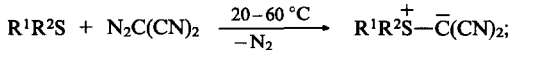
Scheme 107



Scheme 108

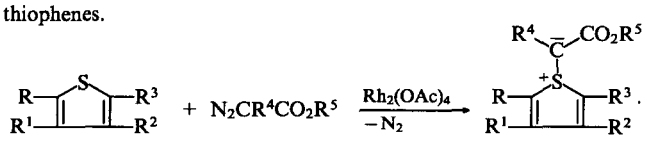


Scheme 109



As already mentioned above, stable ylides are also formed in yields up to 98% in $Rh_2(OAc)_4$-catalysed reactions of diazomalonates with thiophenes at 20 °C (Table 5).

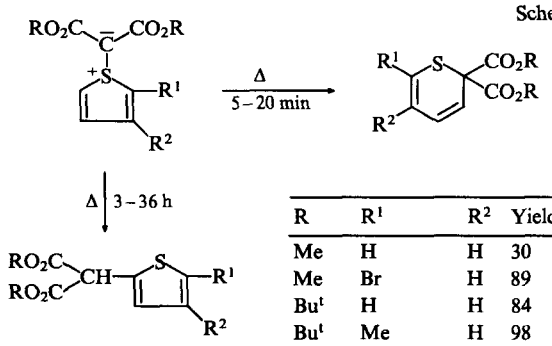
Table 5. The formation of ylides in the reactions of diazoesters with thiophenes.



R	R^1	R^2	R^3	R^4	R^5	Yield of ylide (%)	Ref.
H	H	H	H	CO_2Me	Me	95	150
Cl	H	H	Cl	CO_2Me	Me	~100	151
$HOCH_2$	H	H	H	CO_2Me	Me	92	151
Br	Me	H	H	CO_2Me	Me	86	151
Me	H	H	H	CO_2Me	Me	90	151
Br	H	H	H	CO_2Me	Me	95	151
Cl	Cl	Cl	Cl	SO_2CH_2Ph	Et	53	151
Cl	Cl	Cl	Cl	CONHTs	Et	88	72
CH=CHCH=CH	H	H		CO_2Me	Me	97	72
CH=CHCH=CH	Br	Br		Ac	Et	71	152
CH=CHCH=CH	H	H		Ac	Et	58	152
CH=CHCH=CH	H	H		Ac	Bu^t	88	152
CH=CHCH=CH	Cl	Cl		Ac	Et	84	152
CH=CHCH=CH	Br	Br		Ac	Bu^t	41	152
CH=CHCH=CH	Br	Br		CO_2Me	Me	65	152
$CH=CMe_2$	H	H	H	CO_2Me	Me	40	153

The thermal rearrangement of such ylides leads to acceptable yields of C–S insertion products (2*H*-thiopyrans), which are subsequently converted into the thermodynamically more stable (2-thienyl)malonates (Section II. 2).[154,155] The final composition of the products of the thermal isomerisation of S ylides is determined by the nature of the substituents, temperature, and duration of heating (Scheme 110). Thus brief heating (for less than 20 min) of thiophenium bis(*tert*-butoxycarbonyl)methylides leads to the corresponding 2*H*-thiopyrans in yields up to 98%. After more prolonged heating of the ylides, 2-substituted thiophenes are formed.

Scheme 110



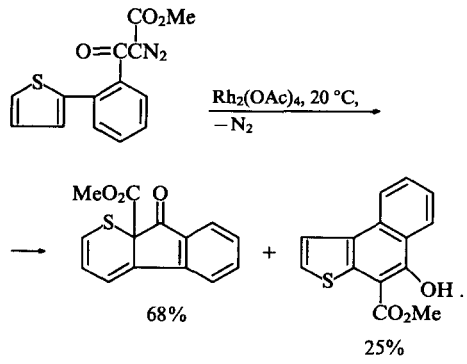
R	R^1	R^2	Yield (%)
Me	H	H	82
Me	Me	H	94

R	R^1	R^2	Yield (%)
Me	H	H	30
Me	Br	H	89
Bu^t	H	H	84
Bu^t	Me	H	98
Bu^t	I	H	60
Bu^t	$PhOCH_2$	H	97
Bu^t	Br	H	75
Bu^t	H	Br	22

The ease with which ylides rearrange to 2*H*-thiopyrans depends on the nature of the substituents. Thus the 2-phenoxymethyl-substituted ylide is converted into the corresponding 2*H*-thiopyran during crystallisation from methylcyclohexane, while the 3-bromo-substituted ylide is converted *in situ*.

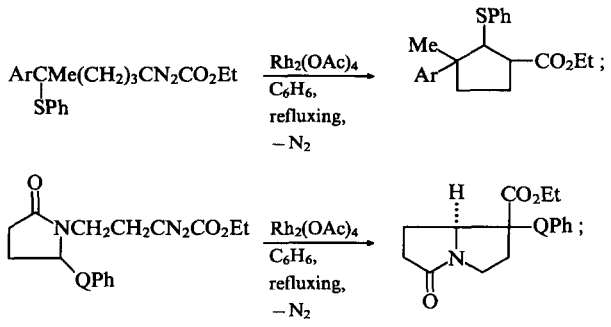
The formation of 2*H*-thiopyrans together with 2-substitution products has been observed also in the isomerisation of cyclic S ylides formed during the rhodium(II)-catalysed dediazotisation of the thienyl-substituted α-acyldiazoester (Scheme 111).[156]

Scheme 111



Similar intramolecular reactions of sulphur- and selenium-containing diazoesters constitute an effective synthetic method for the preparation of cyclic and condensed systems. For example, the metal-carbene complexes generated by the dediazotisation of 6-phenylthiodiazoalkanoates in the presence of $Rh_2(OAc)_4$ readily cyclise to five-membered rings (Scheme 112).[157,158]

Scheme 112

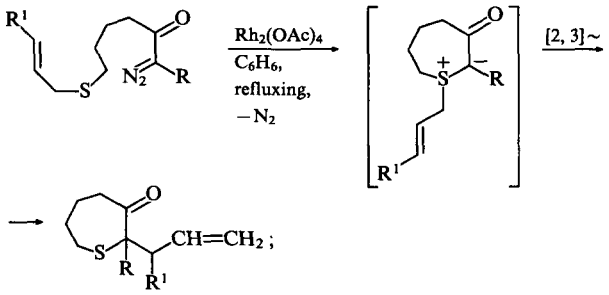


Q = S (55%), Se (36%).

Unfortunately, cyclic compounds containing six and more atoms in the ring cannot be obtained in this way because of the active competition by the C–H insertion reaction.[150]

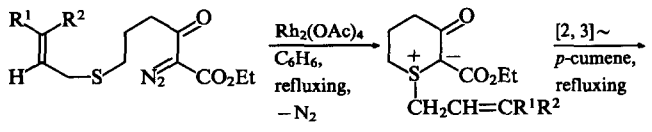
The formation of heterocycles containing more than five atoms in the ring is observed in the intramolecular reactions of the carbenes generated from diazoesters containing an allyl fragment. Thus the $Rh_2(OAc)_4$-catalysed dediazotisation of 7-allylthio-2-diazo-3-oxoheptanoates and 6-allylthio-2-diazo-3-oxohexanoates results in the formation of 3-thiepanones and 3-thianones in high yields (Schemes 113 and 114);[149] the C–H insertion products were not detected under these conditions.

Scheme 113



R = CO_2Et, R^1 = Ph (29%).

Scheme 114

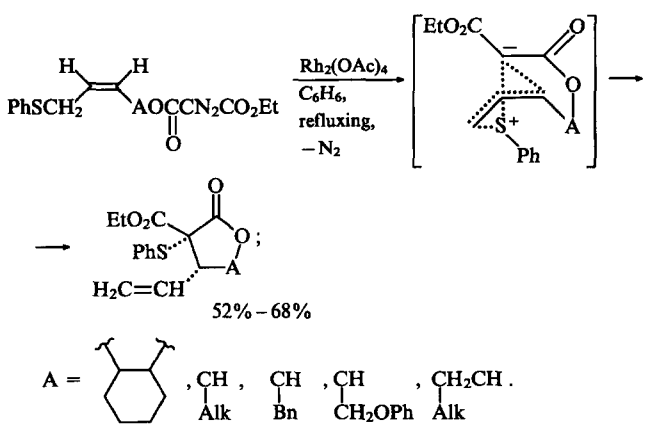


55–85%

R^1	R^2	Yield (%)
Me	Me	66
H	H	59
Ph	H	78
Me	H	71

The presence of the allyl fragment in the alcoholic component of the monoethyl diazomalonate molecule also makes it possible to synthesise vinyl-substituted five- and six-membered cyclic lactones as a result of the stereoselective [2,3]-rearrangement of the S ylide arising on cyclisation of the carbenes stabilised on rhodium(II) (Scheme 115).[149,160]

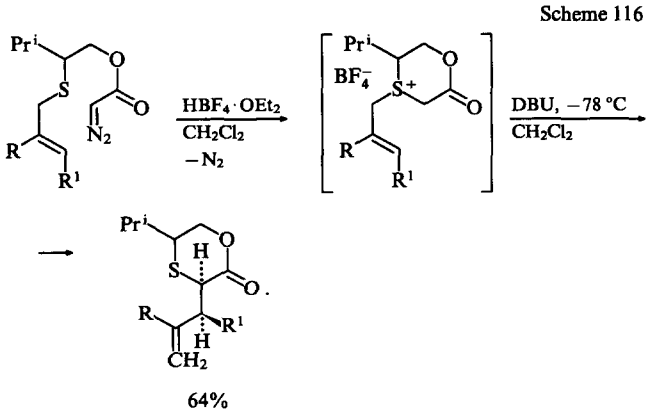
Scheme 115



52%–68%

The diastereoselectivity of this reaction can be increased significantly by using $HBF_4 \cdot Et_2O$ as the agent promoting the heterocyclisation of diazaesters and subsequently treating the resulting thiooxonium salt with 1,8-diazobicyclo[5.4.0]-undec-7-ene (DBU). Thiooxanones were obtained in this way from allylthioalkyl diazoacetates in satisfactory yields and with a high diastereoselectivity (in excess of 93%) (Scheme 116).[161]

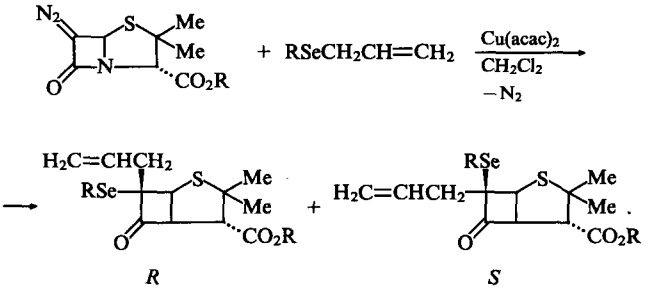
Scheme 116



64%

There are only isolated examples of reactions involving insertion in the C–Se bond. Thus the reaction of a cyclic diazoamide with allyl phenyl selenide in the presence of $Cu(acac)_2$ leads to a mixture of equal amounts of the corresponding isomeric C–Se insertion products with an overall yield of 64% (Scheme 117).[162]

Scheme 117



The analogous reaction of this diazoamide with allyl sulfides proceeds more selectively with the (*R*)-isomer predominating. Its fraction can reach 87%.

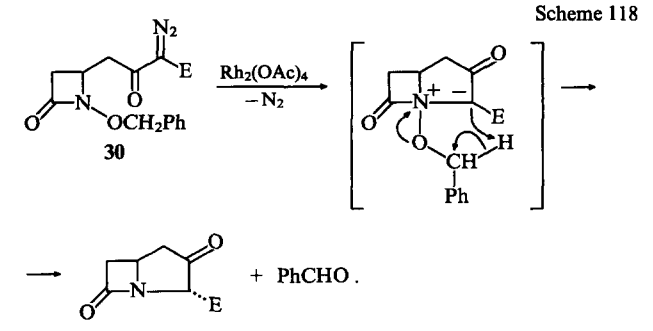
VI. Heteroatom–heteroatom bonds

The reactions of diazoesters involving the insertion of the carbene fragment in a heteroatom–heteroatom bond are presented in Table 6.

These reactions also take place with the intermediate formation of ylides. In the carbene reactions of diazoesters with organosilicon compounds (examples 5–7, Table 6), β-elimination and C–H insertion processes take place in the ylides formed apart from the [1,2]-shift, which lowers the preparative value of these reactions.

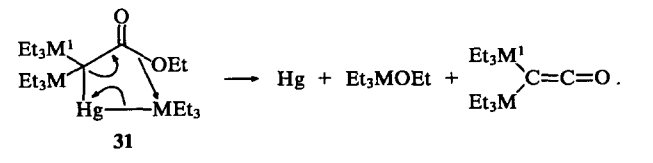
The reactions of ylides do not always lead to the products of the insertion of the carbene in the bond being attacked. Thus the intramolecular attack by the carbene centre on the N–O bond in the diazolactam **30** (E = CO_2Me) leads to an N ylide, the rearrangement of which is accompanied by the dissociation of the N–O bond and the formation of a N–C bond (Scheme 118).[178]

Scheme 118



It is suggested that the formation of organoelement ketenes as a result of the interaction of α-metallated diazoesters with bis-(triethylsilyl)- or bis(triethylgermyl)-mercury (examples **20**–**22**) takes place owing to the decomposition of the unstable product **31** of the insertion of the carbene in the Hg–Si or Hg–Ge bond formed initially (Scheme 119).

Scheme 119



It is noteworthy that the formation of the formal insertion products is not always associated with the reactions of diazoesters via the carbene pathway. For example, although the interaction of ethyl diazoacetate with *tert*-butyl hypochlorite does lead to the product of the insertion of the carbene fragment $CHCO_2Et$ in the O–Cl bond (examples **1** and **2**, Table 6), the attempts to achieve

Table 6. Reactions of diazoesters with element–element bonds.

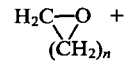
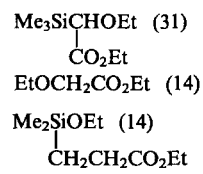
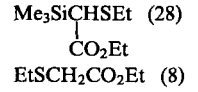
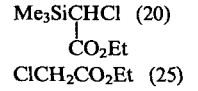
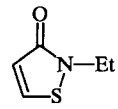
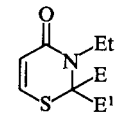
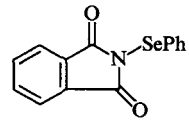
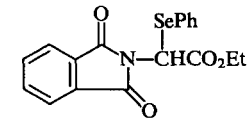
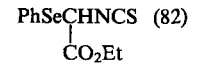
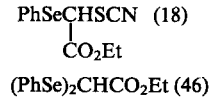
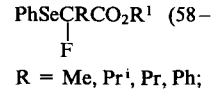
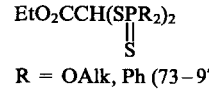
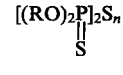
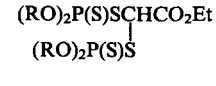
No.	Bond	Substrate	Diazoester	Reaction conditions	Products (yield (%))	Ref.
1	O–Cl	Bu^tOCl	EDA	−10 °C, CH_2Cl_2	$Bu^tOCHClCO_2Et$ (36)	163
2	O–Cl	Bu^tOCl	EDA	−10 °C, CH_2Cl_2/ROH	$(RO)_2CHCO_2Et$[a] R = Bu^t (36), Et (57)	163
3	O–Cl	$ROR^1 + SO_2Cl_2$	EDA	0 °C, darkness, CH_2Cl_2	$ROCHClCO_2Et$ R = R^1 = Et (75), R = Me, R^1 = $CH(OMe)_2$ (64) R = Me, R^1 = CH_2CH_2OMe (76)	164
4	O–Cl		EDA	0 °C, darkness, CH_2Cl_2	$Cl(CH_2)_nOCHClCO_2Et$ n = 1–4 (67.5–73)	164
5	Si–O	Me_3SiOEt	EDA	*hv*, MeCN	 $Me_3SiCHOEt$ (31) CO_2Et $EtOCH_2CO_2Et$ (14) Me_2SiOEt (14) $CH_2CH_2CO_2Et$	165
6	Si–S	Me_3SiSEt	EDA	*hv*, MeCN	 $Me_3SiCHSEt$ (28) CO_2Et $EtSCH_2CO_2Et$ (8)	165
7	Si–Cl	Me_3SiCl	EDA	Cu/NEt_3, 80 °C	 $Me_3SiCHCl$ (20) CO_2Et $ClCH_2CO_2Et$ (25)	166
8	N–S		N_2CEE^1	$Rh_2(OAc)_4$, C_6H_6, refluxing	 E = E^1 = CO_2Et (70); E = Ac, E^1 = CO_2Et (74); E+E^1 = $COCMe_2OC(O)$ (74)	167
9	N–Se		EDA	20 °C, CH_2Cl_2	 (58)	168
10	S–Se	PhSeSCN	EDA	20 °C, CH_2Cl_2	 $PhSeCHNCS$ (82) CO_2Et  $PhSeCHSCN$ (18) CO_2Et	169
11	Se–Se	PhSeSePh	EDA	Cu bronze, *p*-cumene, 100 °C	$(PhSe)_2CHCO_2Et$ (46)	169
12	Se–Se	PhSeSePh	MDM	100 °C	$(PhSe)_2C(CO_2Me)_2$ (32) $PhSeCH(CO_2Me)_2$ (12)	169
13	Se–F	PhSeF		CH_2Cl_2, 20 °C	 $PhSeCRCO_2R^1$ (58–85) F R = Me, Pr^i, Pr, Ph; R^1 = Me, Et	170
14	S–S	$[R_2P(S)S]_2$	EDA	Cu, 80 °C	 $EtO_2CCH(SPR_2)_2$ S R = OAlk, Ph (73–97)	171
15	S–S		EDA	Cu, 80 °C	 $(RO)_2P(S)SCHCO_2Et$ (86) $(RO)_2P(S)S$	172

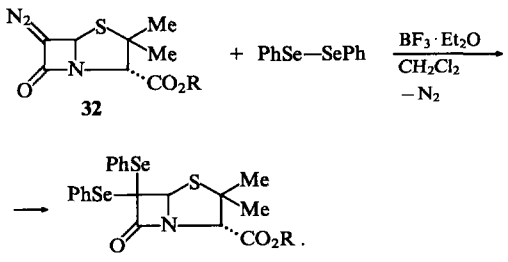
Table 6. (continued)

No.	Bond	Substrate	Diazoester	Reaction conditions	Products (yield (%))	Ref.
16	S–S	$[(RO)_2\overset{\overset{O}{\|}}{P}S]_2$	EDA	Cu, 80 °C	$(RO)_2P(O)SCHCO_2Et$ (67) $(RO)_2P(O)S$ $[(RO)_2P(O)CHS]_2$ (< 7) CO_2Et	173
17	S–P	$[(RO)_2\overset{\overset{O}{\|}}{P}S]_2$	EDA	80 °C, C_6H_6	$[(RO)_2P(O)CHS]_2$ CO_2Et R = Alk (11)	174
18	S–P	$[(RO)_2\overset{\overset{O}{\|}}{P}S]_2$	EDA	120 °C	$(RO)_2\overset{\overset{S}{\|}}{P}OCHSP(O)(OR)_2$ [b] CO_2Et	174
19	S–P	$[(RO)_2\overset{\overset{O}{\|}}{P}]_2S_n$	EDA	70–100 °C	$(RO)_2P(O)SCHCO_2Et$ (> 80) $(RO)_2P(O)S_n$	172
20	Hg–Si Hg–Ge	$Hg(MEt_3)_2$	N_2CCO_2Et $SiEt_3$	Cu, 100 °C, C_6H_{14}	Et_3Si $C{=}C{=}O$ Et_3M M = Si (58), Ge (92)	175
21	Hg–Ge	$Hg(GeEt_3)_2$	N_2CCO_2Et $SnEt_3$	Cu, 100 °C, C_6H_{14}	Et_3Sn $C{=}C{=}O$ (73) Et_3Ge	175
22	Hg–Ge	$Hg(GeEt_3)_2$	N_2CCO_2Et $GeEt_3$	Cu, 100 °C, C_6H_{14}	Et_3Ge $C{=}C{=}O$ (72) Et_3Ge	176

[a] Formed as a result of the solvolysis of the O–Cl insertion product.
[b] The yield is not indicated.

the capture of the carbene by the olefin under these conditions were unsuccessful. The formation of the O–Cl insertion products was observed also in the reaction of ethyl diazoacetate with ethers in the presence of SO_2Cl_2 (examples **3** and **4**, Table 6). Yet another example of reactions of this type is the $BF_3 \cdot Et_2O$-catalysed interaction of the cyclic diazoamide **32** with diphenyldiselenium, which leads to 6,6-di(phenylselenyl)penicillanate in a satisfactory yield (Scheme 120).[178]

Scheme 120



32

* * *

The data presented in this review clearly demonstrate, in relation to insertion reactions, the considerable potential possibilities of the use of the chemistry of diazoesters in organic synthesis. Quite recently, the principal application of diazoesters was still the reaction involving the conversion of olefins into cyclopropane derivatives. At the present time, progress in the field of homogeneous catalysis has made it possible to include in practical preparative organic synthesis also reactions which seemed to be exotic in earlier studies, such as the insertion of alkoxycarbonylcarbenes in a carbon–carbon or carbon–heteroatom bond. Study of the literature shows that the development of this branch of the chemistry of diazoesters has proceeded in two directions, which are of key importance for the expansion of the applications of these reagents in organic synthesis.

The first of these is associated with the increase in the selectivity of the reactions with participation of diazoesters. It involves mainly studies on the enantioselective and stereoselective synthesis of cyclic compounds by the catalytic dediazotisation of diazoesters. The aim of the second aspect was to expand the applications of insertion reactions with participation of diazoesters in organic synthesis. It has developed, in its turn, both in connection with the search for new reactions of diazoesters and their involvement in reactions with compounds of new classes such as the synthesis of new diazoesters for the construction of specified structures, in particular natural products.

The successful development of these two types of studies will depend, in our view, on the progress in the development of synthetic methods for the introduction of the functional diazo-group into the molecules of organic acid esters and also on the search for new effective and selective catalysts of the dediazotisation of diazoesters and the advances in the elucidation of the mechanisms of catalytic reactions undertaken to allow the regulation of such reactions.

References

1. E A Shapiro, A B Dyatkin, O M Nefedov *Diazoefiry* (Diazoesters) (Moscow: Nauka, 1992)
2. V Dave, E Warnhoff, in *Organic Reactions* Vol. 18 (Ed. W G Dauben) (New York: Wiley, 1970) p. 217
3. A P Marchand, N McBrockway *Chem. Rev.* **74** 431 (1974)
4. S D Burke, P A Grieco, in *Organic Reactions* Vol. 26 (Ed. W G Dauben) (New York: Wiley, 1979) p. 361
5. D S Wulfmann, G Linstrumelle, C F Cooper *The Chemistry of Diazonium and Diazo Groups* Vol. 2 (Ed. S Patai) (New York: Wiley, 1978)
6. M P Doyle *Chem. Rev.* **86** 919 (1986)
7. G Maas, in *Topics in Current Chemistry* Vol. 137 (Berlin: Springer, 1987) p. 77
8. J Adams, D M Spero *Tetrahedron* **47** 1765 (1991)
9. A J Hubert, A F Noel, A J Anciaux, P Teyssiè *Synthesis* **9** 600 (1976)
10. O G Kulinkovich *Usp. Khim.* **58** 1233 (1989) [*Russ. Chem. Rev.* **58** 711 (1989)]
11. A Demonceau, A F Noels, A J Hubert, P Teyssiè *Tetrahedron* **14** 688 (1981)
12. A Demonceau, A F Noels, A J Hubert, P Teyssiè *Bull. Soc. Chim. Belg.* **93** 945 (1984); A Demonceau, A F Noels, P Teyssiè, A J Hubert *J. Mol. Catal.* **49** L13 (1988); A Demonceau, A F Noels, A J Hubert *J. Mol. Catal.* **57** 149 (1989); A Demonceau, A F Noels, J-L Costa, A J Hubert *J. Mol. Catal.* **58** 21 (1990)
13. M E Alonso, M del C Garcia *Tetrahedron* **45** 69 (1989)
14. M Aglietto, R Alterio, R Bertani, F Galleschi, G Ruggeri *Polymer* **30** 1133 (1989)
15. G Lowe, J Parker *J. Chem. Soc., Chem. Commun.* 577 (1971)
16. E Buchner, M Fritsch, A Papendieck, H Witter *Liebigs Ann. Chem.* **278** 214 (1893)
17. I E Dolgii, E A Shapiro, G V Lun'kova, O M Nefedov *Izv. Akad. Nauk SSSR, Ser. Khim.* 7 1652 (1979)
18. H Ledon, G Linstrumelle, S Julia *Tetrahedron Lett.* **14** 25 (1973)
19. D F Taber, R E Ruckle *J. Am. Chem. Soc.* **108** 7686 (1986)
20. D F Taber, E H Petty *J. Org. Chem.* **47** 4808 (1982)
21. D F Taber, K J Raman *J. Am. Chem. Soc.* **105** 5935 (1983)
22. D F Taber, E H Petty, K J Raman *J. Am. Chem. Soc.* **107** 196 (1985)
23. D F Taber, M J Hennessy, J P Louey *J. Org. Chem.* **57** 436 (1992)
24. P Ceccherelli, M Curini, M C Marcotullio, O Rosati, E Wenkert *J. Org. Chem.* **55** 311 (1990)
25. V G S Box, N Marinovic, G P Yiannikouros *Heterocycles* **32** 245 (1991)
26. D F Taber, J L Schuchardt *Tetrahedron* **43** 5677 (1987)
27. D E Cane, P J Thomas *J. Am. Chem. Soc.* **106** 5295 (1984)
28. D F Taber, R E Ruckle *Tetrahedron Lett.* **26** 3059 (1985)
29. D F Taber, K J Raman, M D Gaul *J. Org. Chem.* **52** 28 (1987)
30. M P Doyle, V Bagheri, M M Pearson, J D Edwards *Tetrahedron Lett.* **30** 7001 (1989)
31. M P Doyle, A van Oeveren, L J Westrum, M N Protopopova, T W Clayton Jr *J. Am. Chem. Soc.* **113** 8982 (1991)
32. M P Doyle, M Y Eismont, D E Bergbreiter, B Chen *J. Am. Chem. Soc.* in press (1993)
33. M P Doyle, M N Protopopova, W R Winchester, K L Daniel *J. Am. Chem. Soc.* in press (1993)
34. A Padwa, D J Austin, S F Hornbuckle, M A Semones, M P Doyle, M N Protopopova *J. Am. Chem. Soc.* **114** 1874 (1992)
35. A G Wee, B Liu, L Zhang *J. Org. Chem.* **57** 4404 (1992)
36. E Wenkert, P Ceccherelli, R A Fugiel *J. Org. Chem.* **43** 3982 (1978)
37. N Ikota, N Takamura, S D Young, B Canem *Tetrahedron Lett.* **22** 4163 (1981)
38. W Ando, S Kondo, K Nakayama, K Ichibori, H Kohoda, H Yamato, I Imai, S Nakaido, T Migita *J. Am. Chem. Soc.* **94** 3870 (1972)
39. N Takamura, T Mizoguchi, S Yamada *Tetrahedron Lett.* **14** 4267 (1973)
40. M Regitz, S G Khbeis *Chem. Ber.* **117** 2233 (1984)
41. M Jones Jr, W Ando, A Kulczycki Jr *Tetrahedron Lett.* **8** 1391 (1967); W von Doering, T Mole *Tetrahedron* **10** 65 (1960)
42. D F Taber, J C Amedio Jr, R G Sherrill *J. Org. Chem.* **51** 3382 (1986)
43. M E Alonso, R Fernandez *Tetrahedron* **45** 3313 (1989)
44. M E Alonso, M del C Garcia *J. Org. Chem.* **50** 988 (1985)
45. M Vidal, F Massot, P Arnaud *C. R. Acad. Sci.* **268C** 423 (1969)
46. M Vidal, M Vincens, P Arnaud *Bull. Soc. Chim. Fr.* **2** 657 (1972)
47. E A Shapiro, I E Dolgii, C M Nefedov *Izv. Akad. Nauk SSSR, Ser. Khim.* **9** 2096 (1980)
48. M Hrytsak, T Durst *J. Chem. Soc., Chem. Commun.* 1150 (1987)
49. N Etkin, S D Babu, C J Fooks, T Durst *J. Org. Chem.* **55** 1093 (1990)
50. M P Doyle, M S Shanklin, H Q Pho, S N Mahapatro *J. Org. Chem.* **53** 1017 (1988)
51. A Padwa, D J Austin, S F Hornbuckle, M A Semones, M P Doyle, M N Protopopova *J. Am. Chem. Soc.* **114** 1874 (1992)
52. M Matsumoto, N Watanabe, H Kobayashi *Heterocycles* **26** 1479 (1987)
53. E C Taylor, H M L Davies *Tetrahedron Lett.* **24** 5453 (1983)
54. S D Babu, M D Hrytsak, T Durst *Can. J. Chem.* **67** 1071 (1989)
55. D S Wulfmann, B Poling, in *Reactive Intermediates* Vol. 1. (Ed. R A Abramovitch) (New York: Plenum, 1980) p. 321
56. B E Marianoff *J. Org. Chem.* **44** 4410 (1979)
57. B E Marianoff *J. Org. Chem.* **47** 3000 (1982)
58. H M L Davies, W B Young, H D Smith *Tetrahedron Lett.* **30** 4653 (1989)
59. W Herz, R L Settine *J. Org. Chem.* **24** 201 (1959)
60. V M Shostakovskii, A U Musaev, A E Vasil'vitskii, A M Gumilev, O M Nefedov *Izv. Akad. Nauk SSSR, Ser. Khim.* 715 (1989); V M Shostakovsky, A E Vasilvitsky, A U Musaev, O M Nefedov *VI International Conference on Organic Synthesis, Moscow: Abstracts* (Moscow: Izd. Akad. Nauk SSSR, 1986) p. 176
61. US P. 2 079 416; *Chem. Abstr.* **91** 4343 (1937); J R Piper, F J Stevens *J. Heterocycl. Chem.* **3** 95 (1966); C A Payne, F J Stevens *J. Chem. Ind. Data* **10** 71 (1975)
62. A E Vasil'vitskii, A B Sheremet'ev, T S Novikova, L I Khmel'nitskii, O M Nefedov *Izv. Akad. Nauk SSSR, Ser. Khim.* 2876 (1989)
63. E Galeazzi, A Gurzmann, A Pinedo, A Saldana, D Torre, J M Muchowski *Can. J. Chem.* **61** 454 (1983)
64. R A Franich, G Lowe, J Parker *J. Chem. Soc., Perkin Trans. 1* **16** 2034 (1972)
65. A E Vasilvitsky, O M Nefedov, in *Chemistry of Carbenes and Small-sized Cyclic Compounds* (Ed. O M Nefedov) (Moscow: Mir, 1989) p. 142
66. R J Gillespie, A E A Porter, W E Willmott *J. Chem. Soc., Chem. Commun.* **1** 85 (1978)
67. T Bowles, R J Gillespie, A E A Porter, J A Rechka, H S Rzepa *J. Chem. Soc., Perkin Trans. 1* **4** 803 (1988)
68. T Saegusa, Y Ito, S Kobayashi, K Hirota, T Shimizu *Tetrahedron Lett.* **7** 6131 (1966); *J. Org. Chem.* **33** 544 (1968)
69. R J Chorvat, K J Rorig *J. Org. Chem.* **53** 5779 (1988)
70. B Doma, B Vercek, B Stanovnik, M Tisler *Chimia* **28** 235 (1974)
71. E A Shapiro, T N Romanova, T A Bunkina, I E Dolgii, O M Nefedov *Izv. Akad. Nauk SSSR, Ser. Khim.* 1344 (1987)
72. R J Gillespie, A E A Porter *J. Chem. Soc., Perkin Trans. 1* **11** 2624 (1979)
73. M Hrytsak, T Durst *Heterocycles* **26** 2393 (1987)
74. M P Moyer, P L Feldman, H Rapoport *J. Org. Chem.* **50** 5223 (1985)
75. T J Sowin, A I Meyers *J. Org. Chem.* **53** 4155 (1988); D Häbich, H Hartwig *Tetrahedron Lett.* **28** 781 (1987); J Fetter, K Lempert, T Gizur, J Nyitrai, M Kajtar-Peredy, G Simig, G Hornyak, G Doleschall *J. Chem. Soc., Perkin Trans. 1* **2** 221 (1986); J D Buynak, M N Pao, H Pajouhesh, R Y Chandrasekaran, K Finn *J. Org. Chem.* **50** 4245 (1985); M Aratani, H Hirai, K Sawada, A Yamada, M Hashimoto *Tetrahedron Lett.* **26** 223 (1985)
76. J-M Liu, J-J Yong, Y-J Li, Ch-K Sha *J. Org. Chem.* **51** 1120 (1986)
77. C J Moody, C J Pearson, G Lawton *Tetrahedron Lett.* **26** 3171 (1985); *J. Chem. Soc., Perkin Trans. 1* **4** 899 (1987)
78. C J Moody, R J Taylor *Tetrahedron Lett.* **28** 5351 (1987)
79. E C Taylor, H M L Davies *J. Org. Chem.* **49** 113 (1984)
80. R M Williams, B H Lee, M M Miller, O P Anderson *J. Am. Chem. Soc.* **111** 1073 (1989)
81. E Vedejs, D A Engler, M J Mullins *J. Org. Chem.* **42** 3109 (1977)
82. H Chaimovich, R J Vaugham, F H Westheimer *J. Am. Chem. Soc.* **90** 4088 (1968); O P Strausz, T DoMinh, H E Gunning *J. Am. Chem. Soc.* **90** 1660 (1968); E A Shapiro, I E Dolgii, O M Nefedov *Izv. Akad. Nauk SSSR, Ser. Khim.* 2096 (1980)
83. S J Valenty, P S Skell *J. Org. Chem.* **38** 3937 (1973)
84. E A Shapiro, A B Dyatkin, O M Nefedov *Izv. Akad. Nauk SSSR, Ser. Khim.* 1051 (1991)
85. H M L Davies, H D Smith, O Korkov *Tetrahedron Lett.* **28** 1853 (1987)
86. R Pelliciari, R Fringuelli, E Sisani, M Curini *J. Chem. Soc., Chem. Commun.* 959 (1979)
87. K Nagao, M Chiba, S-W Kim *Synthesis* **3** 197 (1983); C R Holmquist, E J Roskamp *J. Org. Chem.* **54** 3258 (1989)

88. A Padwa, J S Kulkarni, Z Zhang *J. Org. Chem.* **55** 4144 (1990)
89. R Pellicciari, B Natalini, S Cecchetti, R Fringuelli *J. Chem. Soc., Chem. Commun.* 493 (1985)
90. C J Moody, R J Taylor *J. Chem. Soc., Perkin Trans. 1* **4** 721 (1989)
91. J C Heslin, C J Moody *J. Chem. Soc., Perkin. Trans. 1* **6** 1417 (1988)
92. J P Greenstein, M Winitz, in *Chemistry of the Amino Acids* Vol .2 (New York: Wiley, 1961) p. 925
93. A F Noels, A Demonceau, N Petiniot, A J Hubert, P Teyssiè *Tetrahedron* **38** 2733 (1982)
94. W Ando, I Imai, T Migita *J. Org. Chem.* **37** 3596 (1972)
95. B.P. 1 572 259 *Chem. Abstr.* **94** 103 343j (1981)
96. B Ganem, N Ikota, V B Muralidharan, W S Wade, S D Young, Y Yukimoto *J. Am. Chem. Soc.* **104** 6787 (1982)
97. C-Y Teng, B Ganem, S Z Doktor, B P Nichols, R K Bhatnagar, L C Vining *J. Am. Chem. Soc.* **107** 5008 (1985)
98. J H Hoare, P P Policastro, G A Berchthold *J. Am. Chem. Soc.* **105** 6264 (1983)
99. R Paulissen, H Reimlinger, E Hayez, A J Hubert, P Teyssiè *Tetrahedron Lett.* **14** 2233 (1973)
100. V Bagheri, M P Doyle, J Taunton, E E Claxton *J. Org. Chem.* **53** 6158 (1988)
101. H Watanabe, T Nakano, Y Araki, H Matsumoto, Y Nagai *J. Organomet. Chem.* **69** 389 (1974)
102. L P Danilkina, O V Dorokhova, Ya M Slobodin *Zh. Obshch. Khim.* **45** 2677 (1975)
103. V E Baikov, L P Danilkina, K A Ogloblin *Zh. Obshch. Khim.* **51** 2156 (1981)
104. O A Kruglaya, I B Fedot'eva, B F Fedot'ev, I D Kalikhman, E I Brodskaya, N S Vyazankin *Izv. Akad. Nauk SSSR, Ser. Khim.* 1887 (1976)
105. A M Polozov, N A Polezhaeva, B A Arbuzov *Zh. Obshch. Khim.* **57** 2200 (1987)
106. A M Polozov, A Ya Levin, E I Goldfarb, N A Polezhaeva, A Kh Mustafin *Zh. Obshch. Khim.* **59** 1262 (1989)
107. A M Polozov, N A Polezhaeva, A H Mustafin, A V Khotinen, B A Arbuzov *Synthesis* **6** 515 (1990)
108. S Arenz, M Böhshar, M Regitz *Chem. Ber.* **119** 1755 (1986)
109. M Böhshar, H Heydt, M Regitz *Chem. Ber.* **117** 3093 (1984)
110. M Böhshar, G Maas, H Heydt, M Regitz *Tetrahedron* **40** 5171 (1984)
111. K Yamamoto, A Matsukawa, I Murata *Chem. Lett.* **8** 1119 (1985)
112. K Nishino, S Yano, Y Kohashi, K Yamamoto, I Murata *J. Am. Chem. Soc.* **101** 5059 (1979)
113. K-L Hoffmann, G Maas, M Regitz *Chem. Ber.* **118** 3700 (1985)
114. K-L Hoffmann, G Maas, M Regitz *J. Org. Chem.* **52** 3851 (1987)
115. P Eisenbarth, M Regitz *Chem. Ber.* **115** 3796 (1982)
116. S Padwa, G S Kulkarni, Z Zhang *J. Org. Chem.* **55** 4144 (1990)
117. R Baudouy, J Gore, L Ruest *Tetrahedron* **43** 1099 (1987)
118. W Ando *Acc. Chem. Res.* **10** 179 (1977)
119. W Ando, in *The Chemistry of Diazonium and Diazo Group* (Ed. S Patai) (New York: Wiley, 1978) p. 341
120. A Padwa, S F Hornbuckle *Chem. Rev.* **91** 263 (1991)
121. A L Fridman, F A Gabitov, A D Nikolaeva *Zh. Org. Khim.* **7** 1126 (1971)
122. M P Doyle, W H Tamblyn, V Bagheri *J. Org. Chem.* **46** 5094 (1981)
123. A Sekiguchi, W Ando *J. Synth. Org. Chem. Jpn.* **35** 897 (1977)
124. U N Dzhemelev, R N Fakhretdinov, R M Marvanov, O M Nefedov *Izv. Akad. Nauk SSSR, Ser. Khim.* 588 (1984); R M Marvanov, R N Fakhretdinov, U M Dzhemelev *Izv. Akad. Nauk SSSR, Ser. Khim.* 1680 (1985); T V Mandel'shtam, A V Balycheva *Zh. Org. Khim.* **19** 232 (1983)
125. R M Marvanov, Candidate's Thesis in Chemical Sciences, Institute of Chemistry, Ufa, 1988
126. E A Shapiro, G V Lun'kova, I E Dolgii, O M Nefedov *Izv. Akad. Nauk SSSR, Ser. Khim.* 2529 (1984)
127. M P Doyle, V Bagheri, N K Harn *Tetrahedron Lett.* 5119 (1988)
128. M C Pirrung, J A Werner *J. Am. Chem. Soc.* **108** 6060 (1986)
129. M P Doyle. M L Trudell *J. Org. Chem.* **49** 1196 (1984); A Schönberg, K Praefcke *Tetrahedron Lett.* **5** 2043 (1964)
130. M P Doyle, J H Griffin, M S Chinn, D van Leusen *J. Org. Chem.* **49** 1917 (1984)
131. M P Doyle, M L Trudell, J W Terpstra *J. Org. Chem.* **48** 5146 (1983)
132. P H Crackett, P Sayer, R J Stoodley, C W Greengrass *J. Chem. Soc., Perkin Trans. 1* **5** 1235 (1991)
133. M G Martin, B Ganem *Tetrahedron Lett.* **25** 251 (1984)
134. C E McKenna, J N Levi *J. Chem. Soc., Chem. Commun.* 246 (1989)
135. K Friedrich, U Jansen, W Kirmse *Tetrahedron Lett.* **26** 193 (1985)
136. C D Gutsche, M Hillman *J. Am. Chem. Soc.* **76** 2236 (1954)
137. T Kametani, K Kawamura, T Honda *J. Am. Chem. Soc.* **109** 3010 (1987)
138. S Takano, S Tomita, M Takahashi, K Ogasawara *Chem. Lett.* **8** 1569 (1987)
139. G Andrews, D A Evans *Tetrahedron Lett.* **13** 5121 (1972)
140. K Prasad, P Kneussel, G Shulz, P Stütz *Tetrahedron Lett.* **23** 1247 (1982)
141. T Kametani, K Kawamura, T Akaji, C Fujita, T Honda *Heterocycles* **27** 2531 (1988)
142. T Kametani, N Kanaya, T Mochizuki, T Honda *Heterocycles* **19** 1023 (1982); *Tetrahedron Lett.* 221 (1983)
143. Y Hata, M Watanabe, S Inoue, S Oae *J. Am. Chem. Soc.* **97** 2553 (1975)
144. E Vedejs, J P Hagen *J. Am. Chem. Soc.* **97** 6878 (1975)
145. M Yoshimoto, S Ishihara, E Nakayama, N Soma *Tetrahedron Lett.* **13** 2923 (1972)
146. Y Tamura, Y Takebe, C Mukai, M Ikeda *Heterocycles* **15** 875 (1981)
147. L Benati, P C Montevecchi, P Spagnolo *J. Chem. Soc., Perkin Trans. 1* **4** 917 (1982)
148. C J Moody, R J Taylor *Tetrahedron* **46** 6524 (1990)
149. K Friedrich, J Rieser *Liebigs. Ann. Chem.* **4** 641 (1976)
150. R J Gillespie, J Murray-Rust, P Murray-Rust, A Porter *J. Chem. Soc., Chem. Commun.* 83 (1978)
151. O Meth-Cohn, E Vuorinen, T A Modro *J. Org. Chem.* **54** 4822 (1989)
152. E Vuorinen, A A Chalmers, J L M Dillen, T A Modro *Tetrahedron* **47** 8611 (1991)
153. V M Shostakovskii, A E Vasil'vitskii, V L Zlatkina, O M Nefedov *Izv. Akad. Nauk SSSR, Ser. Khim.* 2180 (1980)
154. R J Gillespie, A E A Porter, W E Willmott *J. Chem. Soc., Chem. Commun.* 85 (1978)
155. T Bowles, R J Gillespie, A E A Porter, J A Rechka, H S Rzepa *J. Chem. Soc., Perkin Trans. 1* **4** 803 (1988)
156. H Storflor, J Skramstrad, S Nordenson *J. Chem. Soc., Chem. Commun.* 208 (1984)
157. T Kametani, K Kawamura, M Tsubuki, T Honda *J. Chem. Soc., Chem. Commun.* 1324 (1985)
158. T Kametani, H Yukawa, T Honda *J. Chem. Soc., Perkin Trans. 1* **4** 833 (1988)
159. H M L Davies, van T Crisco *Tetrahedron Lett.* **28** 371 (1987)
160. F Kido, S C Sinha, T Abiko, M Watanabe, A Yoshikoshi *Tetrahedron* **46** 4887 (1990)
161. M J Kurth, S H Tahir, M M Olmstead *J. Org. Chem.* **55** 2286 (1990)
162. P J Giddings, D I John, E J Thomas *Tetrahedron Lett.* **21** 395 (1980)
163. B Zwanenburg, W Middelbos, G J K Hemke, J Strating *Recl. Trav. Chim. Pays-Bas* **90** 429 (1971)
164. W Middelbos, B Zwanenburg, J Strating *Recl. Trav. Chim. Pays-Bas* **90** 435 (1971)
165. W Ando, K Konishi, T Hagiwara, T Migita *J. Am. Chem. Soc.* **96** 1601 (1974)
166. E A Shapiro, I E Dolgii, O M Nefedov *Izv. Akad. Nauk SSSR, Ser. Khim.* 1915 (1979)
167. W D Grow, I Gosney, R A Ormiston *J. Chem. Soc., Chem. Commun.* 643 (1983)
168. T G Back, R G Kerr *J. Organomet. Chem.* **286** 171 (1985)
169. N Furukawa, F Takahashi, T Yoshimura, S Oae *Tetrahedron Lett.* **28** 3633 (1977)
170. R Pellicciari, M Curini, P Ceccherelli, R Fringnelli *J. Chem. Soc., Chem. Commun.* 440 (1979)
171. Y Usuki, M Iwaoke, Sh Tomoda *J. Chem. Soc., Chem. Commun.* 1148 (1992)
172. B A Khaskin, O D Sheluchenko, N A Torgasheva *Zh. Obshch. Khim.* **50** 1990 (1980)
173. B A Khaskin, N A Tolmacheva, T I Koroleva *Zh. Obshch. Khim.* **53** 1219 (1983)
174. B A Khaskin, O D Sheluchenko, N A Torgasheva *Zh. Obshch. Khim.* **53** 780 (1983)
175. B A Khaskin, O D Sheluchenko, N A Torgasheva *Zh. Obshch. Khim.* **52** 597 (1982)
176. O A Kruglaya, I B Fedot'eva, B V Fedot'ev, I D Kalikhman, V V Keiko, N S Vyazankin *Zh. Obshch. Khim.* **46** 930 (1976)
177. O A Kruglaya, I B Fedot'eva, B V Fedot'ev, I D Kalikhmann, E I Brodskaya, N S Vyazankin *J. Organomet. Chem.* **142** 155 (1977)
178. M A Williams, M J Miller *Tetrahedron Lett.* **31** 1807 (1990)
179. P J Giddings, D I John, E J Thomas *Tetrahedron Lett.* **21** 399 (1980)