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The Interaction of Carbenes and Nitrenes with Azo-compounds

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A critical analysis of the literature on the interaction of carbenes and nitrenes with azo-compounds is presented, attention being concentrated on the reactions of aminonitrenes.
The bibliography includes 83 references.

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I. INTRODUCTION

The study of the reactions of unstable intermediate species is one of the most fruitful "growth points" in modern organic chemistry. Its branches, such as the chemistry of carbonium ions, carbanions, and free radicals, have already become classical but at the same time it continues to develop vigorously. During the last decades, very much attention has been devoted to the study of the reactions of carbenes, nitrenes, and their analogues—neutral intermediates incorporating an atom with an incomplete six-electron (sextet) electron shell. Owing to the exceptional wide variety of reactions of such compounds, which has stimulated both applied, synthetic development and numerous studies by theoreticians (see, for example, the corresponding chapters in the annual reviews "Organic Reaction Mechanisms" or "Annual Reports on the Progress in Chemistry").

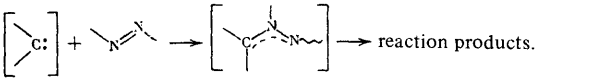
The most important trend in this field concerns the study of the interaction of carbenes and nitrenes with unsaturated groups. Their addition to the C=C, C≡C, and C=X (X is a heteroatom) bonds constitutes an effective general method of synthesis of three-membered rings, strained polycyclic systems, and a very great variety of products of further reactions. This is why thousands of papers and tens of reviews and monographs have been devoted to the above branch of chemistry of carbenes and their analogues and their number continues to grow.

Azo-compounds have been one of the few exceptions in this field and the interaction of carbenes and nitrenes with compounds containing the N=N group has not been investigated systematically until recently. However, since the beginning of the 1970s, a whole series of studies have been carried out in which it has been demonstrated that the usually fairly inert azo-group reacts smoothly with these sextet species to form new classes of unusual polynitrogen compounds. So far, fairly extensive data have accumulated in this field requiring a survey, which has been the reason why this review, in which we have tried to cover the literature until the beginning of 1985, has been written.

II. THE ADDITION OF CARBENES TO AZO-COMPOUNDS

In contrast to the majority of other reactions, the reaction with azo-compounds has been investigated in less detail for carbenes than for nitrenes. Furthermore, it has been found that certain reactions, assigned to this type, in reality proceed without the participation of carbenes. Thus investigation of the kinetics of the reactions of diazo-compounds with a series of azo-compounds, in the first place with azodicarbonyl compounds, showed that the initial diazo-compound itself usually reacts with the azo-group and that only then is the nitrogen molecule split off[1] (among the later studies in this field see, for example, Korobitsyna and co-workers[2,3] and the literature quoted therein).

Nevertheless, it has been suggested that in many instances it is precisely carbenes that react with azo-compounds. This entails the formation, as a rule, of the corresponding 1:1 adducts to which the structure of diaziridines or the isomeric 1,3-dipolar compounds—azomethineimines (I)—was attributed in early studies. Later it was demonstrated that in reality the reaction products have a different structure and can be usually formally regarded as a result of the 1,4-addition of the carbene to the N=N–C=X fragment (X = O, N, or C) of the initial conjugated azo-compound. However, although the azomethineimines (I) are not in fact the final products in any of the reactions of carbenes with azo-compounds known at the present time, their involvement as intermediates has been suggested:

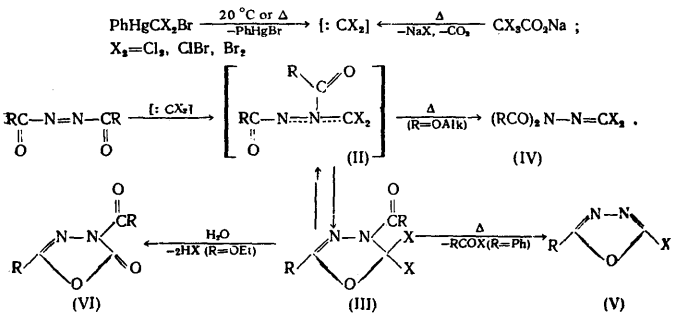


(I)

The reactions of carbenes with azo-compounds can be divided into several types: interaction of dihalogeneocarbenes with azo-compounds; the addition of methylene and its aromatic derivatives to 2,2'-azopyridine and its analogues; the addition of alkylidenecarbenes to aromatic azo-compounds and the reaction of alkoxyalkylcarbenes with oxadiazolines.

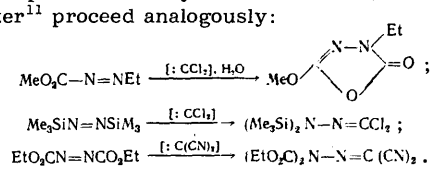
1. The Reactions of Dihalogenocarbenes with Azo-Compounds

In reactions with various azo-compounds dihalogeneocarbenes were usually generated by the thermal decomposition of trihalogenomethylphenylmercury[4-8] or sodium trichloroacetate.[4,5,9] The addition of dihalogeneocarbenes to azodicarbonyl compounds has been studied in greatest detail:

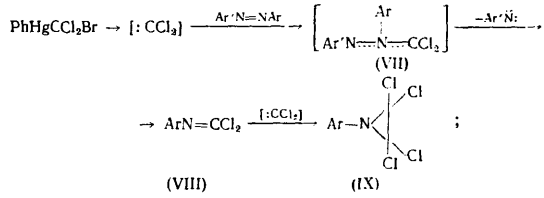


At room temperature, the products in this instance are oxadiazolines (III), which are apparently formed as a result of the cyclisation of the intermediate azomethineimines (II).[4-8] If the reaction is carried out with heating, then, depending on the nature of the substituent, the oxadiazolines (III) are either rearranged to the hydrazones (IV), probably again via the azomethineimines (II),[4,5] or they split off the RCOX molecule with formation of the oxadiazoles (V);[6,7] in the presence of water, the main reaction products are the oxadiazolinones (VI).[9]

The addition of dichlorocarbene to methyl ethylazocarboxylate (in the presence of water)[9] and to bis(trimethylsilyl)diimide[10] and also the addition of dicyanocarbene, generated by the decomposition of dicyanodiazomethane, to azodicarboxylic ester[11] proceed analogously:

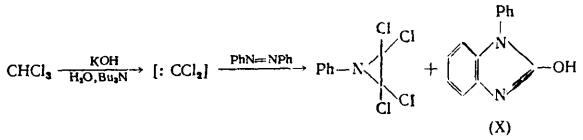


Dichlorocarbene reacts significantly differently with azoarenes. In this case, the phosgeneimines (VIII) and the products of the further addition of the carbene (IX) are formed in this reaction:[4,8]



Ar = Ph, *p*-Tol, *p*-ClC$_6$H$_4$.

When dichlorocarbene was generated by the phase transfer method, the formation of phosgeneimine in the reaction with azobenzene was not noted, but 2-hydroxy-1-phenylbenzimidazole (I) was islated as an additional product:[12]

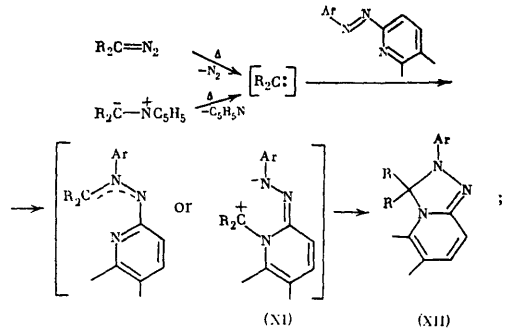


It has been suggested that the azomethineimines (VII)[8] (or the isomeric diaziridines[8,12]) are formed initially in this instance and then lose an arylnitrene[8] or rearrange to benzimidazole derivatives (cf. the Section below). The mechanism of the elimination of the arylnitrene was not discussed.[8] It may be that the intermediate azomethineimines (VII) react with a second molecule of dichlorocarbene to form two phosgeneimine molecules.

The same products are obtained also in the reaction of dichlorocarbene with azoxyarenes, probably as a result of the intermediate formation of azo-compounds.[8,12]

2. The Addition of Methylene and Arylcarbenes to 2,2'-Azopyridine and Its Analogues

The reactions of methylene and its aryl-substituted derivatives with 2,2'-azopyridine, 2-phenylazopyridine, and 2,2'-azoquinoline involve the formation, like the reactions of dihalogeneocarbenes with azodicarbonyl compounds, of (formally) the products of the 1,4-addition of the carbene to the N=C–N=N fragment, namely the triazolopyridines (XII).[13,14] The carbenes were generated by the thermolysis of the corresponding diazo-compounds or pyridinium ylides:

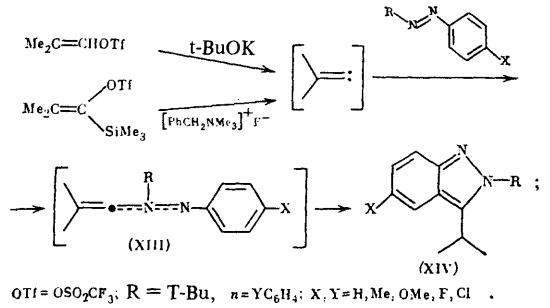


R = H, Ph; R$_2$C = PhCH, 9-fluorenylidene;
Ar = Ph, 2-pyridyl, 2-quinolinyl.

The authors of the first studies of this reaction[15,16] assumed that carbenes are not formed in the course of the reaction. However, it was shown later[13] that the interaction of diazo-compounds with 2,2'-azopyridine and its analogues proceeds only under these conditions when the diazo-compounds are unstable and decompose with formation of carbenes. The rate of reaction then varies with temperature, like the rate of decomposition of the initial diazo-compound in the absence of substrates, which indicates the carbene mechanism of this reaction.[13] However, it is noteworthy that, apart from the azo-group, the molecules of 2,2'-azopyridine and its analogues contain yet another potential reaction centre—the nitrogen atom of the pyridine ring and it is not known whether the initial attack is in fact directed to the azo-group or whether an alternative mechanism with formation of the intermediates (XI) operates.[13]

3. The Addition of Alkylidenecarbenes to Azoarenes

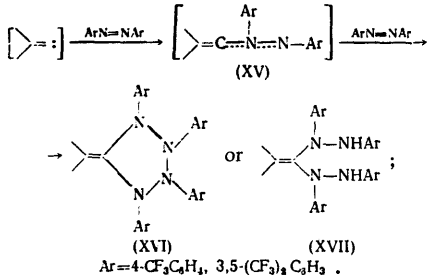
The reaction of 2-propylidenecarbene with a number of azoarenes and t-butylazobenzene results in the formation of, formally, the products of the 1,4-addition of the carbene to the N=N–C=C system, probably via the intermediate azomethineimines (XIII):[17-20]



OTf = OSO$_2$CF$_3$; R = T-Bu, *n*=YC$_6$H$_4$; X, Y=H, Me, OMe, F, Cl.

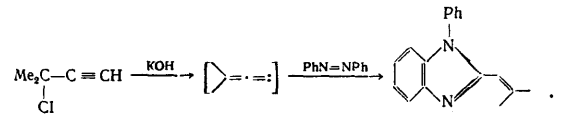
The reactions with asymmetric substrates yield comparable amounts of both possible isomeric benzopyrazoles (XIV).[18,19]

In the reactions with azoarenes containing strong electron-accepting substituents, the 2:1 adducts (XVI) or (XVII), regarded as the results of the 1,3-dipolar addition of the intermediate azomethineimines (XV) to the initial azo-compound, were isolated in low yields:[19,20]



Ar=4-$CF_3C_6H_4$, 3,5-$(CF_3)_2C_6H_3$.

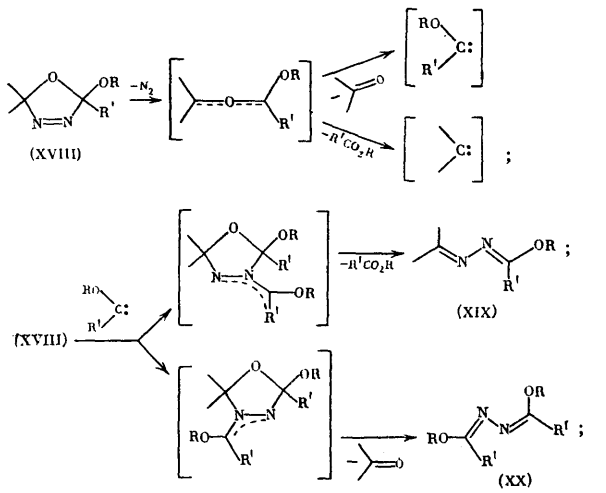
The initial adducts of dimethylvinylidenecarbene with azobenzene rearrange with dissociation of the nitrogen–nitrogen bond:[21]



The reaction of fluorenylidenecarbene with azobenzene leads to the formation of a small amount of a 1:1 adduct, whose structure has not, however, been established.[22]

4. The Reaction of Alkoxycarbenes with 1,3,4-Oxadiazol-3-ines

The thermal decomposition of a series of 2-alkoxy-1,3,4-oxadiazol-3-ines (XVIII) results in the formation of dialkyl- and alkylalkoxy-carbenes, which react with the initial compounds:[23]



R = Me, Et, CH_2CF_3, CH_2CCl_3; R' = Me, Et, iso-Pr; RR' = $(CH_2)_3$.

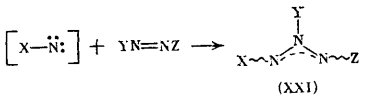
The main reaction pathway involves the intermediate formation of alkoxycarbenes and the subsequent addition to the nitrogen atom in the 3-position in the oxadiazoline ring, which ultimately leads to the asymmetric azines (XIX).[23] However, the reaction mixtures usually contain also the azine (XX) and dimethylketazine, which the authors[23] regard as a result of the participation in the reaction of not only the alkoxycarbene but also of dimethylcarbene.

III. THE ADDITION OF NITRENES TO AZO-COMPOUNDS

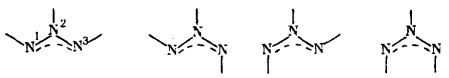
A fairly large range of examples of the interaction of nitrenes with azo-compounds has now been investigated. It has been found that the addition takes place only in those cases where the substituents in the nitrene and in the azo-compound differ greatly in their electronic nature. On the other hand reactions with participation of many nitrenes such as aryl-, perfluoroalkyl-, amino-, and imido-nitrenes as well as others frequently result in the formation of their formal dimers—azo-compounds[24]—in high yields, but there have been no communications about the products of further addition of nitrenes to these compounds. This indicates most probably the inertness or low reactivity of nitrenes in relation to azo-compounds having the same substituents (although one cannot rule out also the possibility that nitrenes do nevertheless add in this instance by the resulting adducts are unstable and decompose with formation of the initial azo-compound).

In our view, this type of dependence of the reactivity of nitrenes in relation to azo-compounds on the electronic nature of the substituents justifies the assumption that, when the nitrene molecule contains electron-donating substituents and the azo-compound molecule contains electron-accepting substituents (as in the reactions of dialkylamino- and diarylamino-nitrenes with azodicarboxylic acid derivatives), the addition of the nitrene to the azo-group is nucleophilic, while in the opposite case (the addition of phthalimidonitrene and alkoxycarbonylnitrenes to azoalkanes and azoarenes) this interaction is electrophilic.

In contrast to the addition of carbenes, where the formation of azomethineimines as intermediates is usually postulated, almost all the known reactions of nitrenes with azo-compounds lead to stable 1,3-dipolar compounds—the azimines (XXI):



E,Z-isomerism is possible in relation to both partially double nitrogen–nitrogen bonds and the azimines containing different substituents at the terminal nitrogen atoms can exist in principle in the form of four stereoisomers:

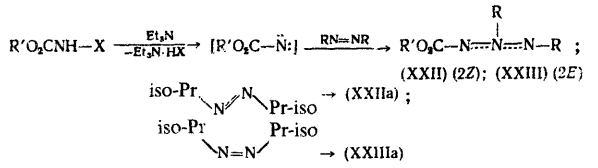


A non-empirical calculation of the relative stabilities of the isomers of the simplest azimine N_3H_3 [25] showed that the *Z,Z*-isomer is the most stable, that the energy of the *E,Z*-configuration is slightly higher, and that the *E,E*-structure is energetically extremely unfavourable. Taking into account steric factors, one may expect that the *E,Z*- and *Z,E*-isomers will be the most stable for the substituted azimines and that in all the known acyclic azimines the two nitrogen–nitrogen bonds do indeed have the opposite configurations.

1. The Addition of *C*-Nitrenes to the Azo-Group

As mentioned above, arylnitrenes and a series of other *C*-nitrenes apparently do not react with azo-compounds containing the same substituents as those in the nitrene molecule. In particular, the reaction of azocycarbonylnitrene with diethyl azodicarboxylate could not be achieved.[26,27]

On the other hand, alkoxycarbonylnitrenes add to nitrogen-containing compounds without electron-accepting substituents—azoalkanes and azoarenes—with formation of the esters of the corresponding azimine-1-carboxylic acids (XXII) or (XXIII):[28,29]



(XXII) (2Z); (XXIII) (2E)

(XXIIa);

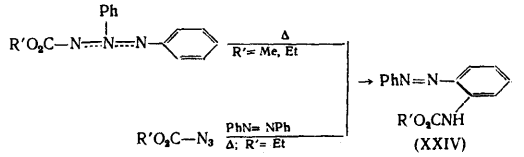
(XXIIIa)

$X = OSO_2C_6H_4NO_2$-*p*; R′ = Me, Et; R = iso-Pr (a), Ph (b), *p*-Tol (c); R_2 = 1,3-cyclopentylene (d).

The alkoxycarbonylnitrenes were generated under mild conditions by the α-elimination of *p*-nitrobenzenesulphonic acid from the corresponding sulphonyloxycarbamates in the presnece of an equimolar amount or an excess of the azo-compound.

The reaction with *E*- and *Z*-2,2′-azopropanes proceed with retention of the configuration of the azo-group and lead respectively to 2*Z*- and 2*E*-azimines (XXIIa) and (XXIIIa).[28,29] On the other hand, the same product, whose geometry has not been established, is formed from the isomeric *E*- and *Z*-azoarenes.[29]

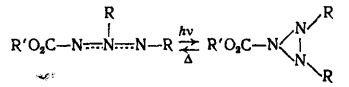
The adducts of alkoxycarbonylnitrenes with azobenzene rearrange on heating with migration of the alkoxycarbonylimino-group to the *ortho*-position in the benzene ring and the formation of the products (XXIV).[29] The same substances are formed on thermolysis of ethoxycarbonyl azide in the presence of azobenzene:[30,31]



(XXIV)

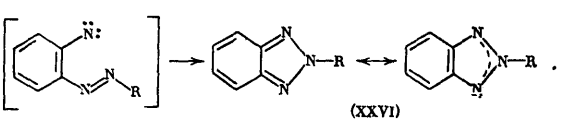
Probably ethoxycarbonylnitrene adds in this instance to azobenzene with subsequent thermal rearrangement of the adduct (XXIIb) or (XXIIIb).[30,31]

It is of interest to note that derivatives of a three-membered ring with three nitrogen atoms, namely triaziridines (XXV), were obtained for the first time by the cyclisation of the azimines (XXIIa) and (XXIIId).[28,32] These compounds are comparatively unstable and gradually recyclise to the initial azimines even at room temperature:[28,32]



(XXIIa), (XXIIIg)

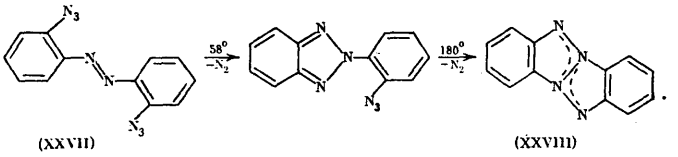
In contrast to carbonylnitrenes, alkyl- and aryl-nitrenes have been much more rarely introduced into intermolecular reactions[24] and there are no examples in the literature of their interaction with azo-compounds. However, a series of reactions which can be formally treated as intermolecular addition of arylnitrenes to the azo-group, usually located in the *ortho*-position, have already been known for more than 100 years:



(XXVI)

The oxidation of *o*-aminoazo-compounds by various oxidants,[33-39] the reduction of *o*-nitroazo-compounds,[40-44] and the thermolysis and photolysis of the corresponding azides[31,34,45-50] belong to these reactions. Their products are 2*H*-benzotriazoles (XXVI), related to azimines, or the initial heterocyclic compounds containing the azimine chain in their structure.

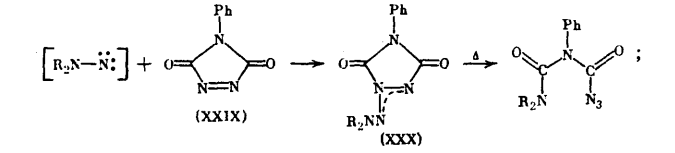
However, in the majority of cases the reactions enumerated above apparently proceed via intermediate species other than nitrenes[38] and also as concerted processes.[45] The involvement of nitrenes is assumed in this instance by analogy with other reactions,[41-43] is regarded as one of the possible variants, and as a rule has not been reliably demonstrated (cf. for example, Butler[38] and Dyall,[39] Spagnolo et al.,[47] Spagnolo et al.,[48] etc.); at the same time even formally very similar compounds can have different mechanisms. As an illustration, one may quote a series of syntheses of tetraazapentalene systems of type (XXVIII),[51-55] where it has been demonstrated, in relation to the thermolysis of *oo*′-diazidoazobenzene (XXVII), that the elimination of the first nitrogen molecule is a concerted process and that the nitrene mechanism is possible only for the second stage (but has not been demonstrated):



(XXVII) (XXVIII)

2. The Interaction of Dialkylamino- and Diarylamino-nitrenes with Derivatives of Azodicarboxylic Acid

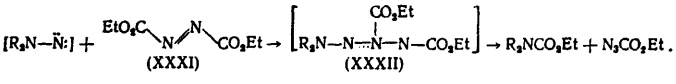
The first communication about the reaction of aminonitrenes and nitrenes in general with nitrogen-containing compounds was published in 1970.[56] In this and in a series of later studies it was shown that dialkylamino- and diarylamino-nitrenes add to 4-phenyl-1,2,4-triazoline-3,5-dione (XXIX), a cyclic derivative of azodicarboxylic acid, with formation of the stable adducts (XXX),[56,57] the azimine structure of which has been confirmed by ^{1}H NMR, IR, and UV spectra, as well as mass spectra and, in the case of the adduct of diphenylaminonitrene (XXXa), also by X-ray diffraction.[58] On heating, the aminoazimines (XXX) rearrange with the opening of the five-membered ring:[56,59]



(XXIX) (XXX)

R = Ph (a), CH_2Ph (b), Me (c), Et (d); R_2N– = MePhN– (e), $(CH_2)_5N$–(f).

The reaction of the same aminonitrenes with diethyl azodicarboxylate (XXXI) leads in each instance to a mixture of the corresponding urethane with ethoxycarbonyl azide, but the full analogy of this set of substances with the products of the thermolysis of the azimines (XXX) makes it possible to postulate also the intermediate formation of the aminoazimines (XXXII):[56,60,61]



(XXXI) (XXXII)

The high thermal stability of the cyclic aminoazimines (XXX) has been explained by the fact that the migration of the carbonyl group to the amino-nitrogen atom is hindered in this instance by steric factors.[60]

The aminonitrenes were generated in these reactions by oxidising the corresponding 1,1-disubstituted hydrazines using azodicarbonyl compounds as oxidants;[56,60,61] in addition, dibenzylaminonitrene was obtained by decomposing dibenzylamino-*N*-azide:[57]

$$R_2N{-}NH_2 \xrightarrow[-XNHNHX]{XN=NX} [R_2N{-}\ddot{N}{:}] \xleftarrow[R=CH_2Ph]{-N_2} R_2N{-}N_3 .$$

The involvement of aminonitrenes in the reaction is indicated by the following data. Firstly, the same aminoazimine (XXXb) is formed from both 1,1-dibenzylhydrazine and from dibenzylaminoazide in the reaction with triazolinedione (XXIX) and in the latter case the rate of decomposition of the azide (the rate of evolution of nitrogen) is independent of the presence of the azo-compound (XXIX) in the mixture.[56] Secondly, in the reaction of 1,1-disubstituted hydrazines with azodicarboxylic ester (XXXI) the formation of a small amount of tetrazenes—typical products of the interaction of aminonitrenes with the initial hydrazines—was observed and the yield of the tetrazenes increased greatly (sometimes by a factor of hundreds) when the azo-compound was added to hydrazine instead of *vice versa*.[56,60,61]

3. The Interaction of Phthalimidonitrene with Azo-Compounds

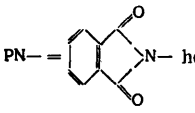
Among all the sextet species, phthalimidonitrene (XXXIII) has been studied in greatest detail in its reaction with azo-compounds. Its addition to the azo-group was first reported in 1971 [62] and since then many studies have been devoted to this reaction and its products.[62-81]

In all cases, phthalimidonitrene (XXXIII) was generated by oxidising *N*-aminophthalimide with lead tetraacetate in the presence of an equimolar amount of an azo-compound:

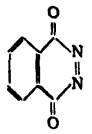
$$PN{-}NH_2 \xrightarrow[-Pb(OAc)_2,\ -2AcOH]{Pb(OAc)_4} [PN{-}\ddot{N}{:}] \xrightarrow{RN=NR'} PN{-}\underset{R}{N}{-}\underset{R}{N}{-}R' \ ;$$

(XXXIII) (XXXIV)

$$[PN{-}NH{-}NH{-}NP] \xrightarrow{-N_2} 2PNH \ ;$$

PN— =  N— here and henceforth.

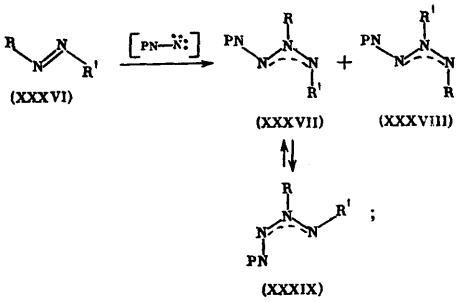
Phthalimidonitrene (XXXIII) adds readily and with high yields (up to 95%) to substrates containing hydrocarbon substituents at the azo-group with formation of 2,3-disubstituted 1-phthalimidoazimines (XXXIV), but it does not react with the azodicarbonyl compounds (XXXI) and (XXXV).[30,31]



(XXXV)

Phthalamide, formed apparently as a result of the interaction of the nitrene (XXXIII) with the initial *N*-aminophthalimide, is usually a side product of the reaction.[82] The structure of the reaction products has been established by spectroscopic methods (^1H and ^{13}C NMR, UV, etc.) and also by X-ray diffraction for 1*E*, 2*Z*- and 1*Z*, 2*E*-2,3-dimethyl-1-phthalimidoazimines (XXXVIIa) and (XXXIXa).[64,65]

The addition of phthalimidonitrene (XXXIII) to *E*-azoalkanes (XXXVI) proceeds stereospecifically with retention of the configuration of the azo-group and fully stereoselectively,[67,68] leading to 1*E*, 2*Z*-2,3-dialkyl-1-phthalimidoazimines (XXXVIIa) and (XXVIIIa):[62,63,66-68]

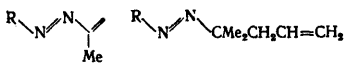


(XXXVI) (XXXVII) (XXXVIII) (XXXIX)

R = R′ = Me (a), Et (b), iso-Pr (c), CHMePh (d);
R = Me, R′ = Et (e), iso-Pr (f), t-Bu (g), $CH_2CH_2CH=CH_2$ (h);
R′ = iso-Pr, R = Et (i), $CH_2CH_2CH=CH_2$ (j), $CHMeCH_2CH=CH_2$ (k).

The asymmetric *E*-azoalkanes (XXXVI, e–g and I) give rise to mixtures of the regioisomeric 2,3-dialkyl-1-phthalimidoazimines (XXXVII) and (XXXVIII) with predominance of the isomer (XXXVII) containing a smaller substituent at the central nitrogen atom of the azimine system.[67,68] The regioselectivity of the reaction increases on passing from *E*-methylazoethane (XXXVIe) to the more asymmetric substrates (XXXVI, f and g).[67,68]

The reaction of phthalimidonitrene with γδ-unsaturated analogues of *E*-azoalkanes (XXXVI, h, j, and k) proceeds fully analogously.[69] The addition of the nitrene to the azo-group only is then observed; the products of addition to the C=C bond were not detected.[69] However, αβ-unsaturated azo-compounds—*E*-2-alkylazopropenes (XL)—proved to be extremely inert in relation to phthalimidonitrene.[69] The reasons for this are obscure.



(XL) (XLI)
R = Me, iso-Pr.

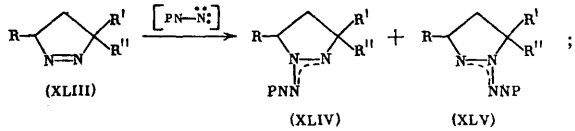
When a tertiary substituent is introduced at the azo-group, the reactivity of *E*-azoalkanes diminishes sharply.[67-69] The addition of phthalimidonitrene to *E*-2-methyl-2-methylazopropane (XXXVIg) can be achieved only by employing a special method whereupon the side reaction involving the formation of phthalimide is suppressed [even in this case most of the azo-compound (XXXVIg) is preserved in the course of the reaction[67,68]] and the reaction with unsaturated tertiary azo-compounds (XLI) could not be carried out at all.[69] The main product of the addition of phthalimidonitrene to *E*-2-methyl-2-methylazopropane (XXXVIg) is 1*E*, 2*Z*-3-t-butyl-2-methyl-1-phthalimidoazimine (XXXVIIg), but the reaction is overall more complex than that with the sterically unhindered *E*-azoalkanes (XXXVI, a–f and i) and small amounts of unstable products, whose structure has not been established, are formed.[67,68]

The reaction of phthalimidonitrene with *Z*-2,2′-azopropane (XLII) affords a high yield of 1*Z*, 2*E*-2,3-diisopropyl-1-phthalimidoazimine (XXXIXc), which, however, is configurationally extremely unstable and is readily converted into the 1*E*, 2*Z*-isomer (XXXVIIc):[66]

$$\underset{(XLII)}{iso\text{-}Pr{-}N{=}N{-}Pr\text{-}iso} \xrightarrow{[PN{-}\ddot{N}{:}]} (XXXIXc) \rightarrow (XXXVIIc).$$

The addition of phthalimidonitrene to cyclic analogues of azoalkanes with a fixed *Z*-configuration of the azo-group, namely 1-pyrazolines (XLIII, a–d)[67,69,70] and 2,3-diazabicyclo]2.2.1]hept-2-ene (XLIIIe),[66] leads to the corresonding 2,3-trimethylene-1-phthalimidoazimines (XLIV) and (XLV). The reaction with asymmetric 1-pyrazolines (XLIII, b–d) leads to the formation of two regioisomeric adducts (XLIV)

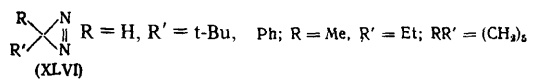
and (XLV), in each case with the sterically less hindered isomer (XLIV) predominating,[67,69,70] i.e. the influence of the bulk of the substituents on the mode of reaction is in this case qualitatively the same as in the series of acyclic *E*-azo-compounds. At the same time, the yields of the adducts with the cyclic azo-compounds (XLIII) are higher than for the adducts with the *E*-azoalkanes (XXXVI);[66,67,70] even for the adducts with 1-pyrazolines (XLIII, c and d), formally containing a tertiary substituent at the azo-group, the reaction proceeds without complications and leads to both regioisomeric adducts (XLIV, c and d) and (XLV, c and d).[67,70] This can apparently be accounted for by the greater steric accessibility of the azo-group when it has the *Z*-configuration



(XLIII) (XLIV) (XLV)

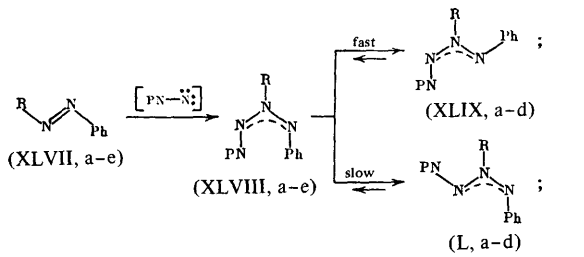
R = R′ = H, R″ = H (a), Me (b); R′ = R″ = Me, R = H (c), Me (d); RR′ = 1,3-cyclopentylene, R″ = H (e).

On the other hand, 3*H*-diazirines (XLVI), both mono- and di-substituted, proved be be almost inert in relation to phthalimidonitrene,[67,69] which is evidently associated with the relatively deep position of the highest occupied molecular orbital in these compounds:[83]



(XLVI)

The reaction of phthalimidonitrene with the markedly asymmetric *E*-alkylazobenzenes (XLVII)[67,71–76] takes place stereospecifically with retention of the configuration of the azo-group and usually fully regioselectively and stereoselectivity with formation of 1*Z*, 2*Z*-2-alkyl-3-phenyl-1-phthalimidoazimines (XLVIII).[67,74,76] With the exception of the t-butyl derivative (XLVIIIe), the latter are unstable at temperatures above approximately 0 °C and rapidly equilibrate in solution with 1*Z*, 2*E*-azimines (XLIX) and much more slowly with the 1*E*, 2*Z*-isomers (L). The principal components of the equilibrium mixtures of stereoisomers are 1*Z*, 2*E*-azimines (XLIX).[67,75,76] Their rapid formation from the intermediate 1*Z*, 2*Z*-isomers (XLVIII) leads to the apparent inversion of the configuration of the azo-group in the reaction of phthalimidonitrene with *E*-alkylazobenzenes (XLVII):[67,76]



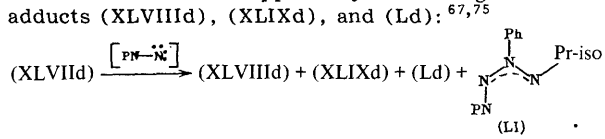
(XLVII, a-e) (XLVIII, a-e) (XLIX, a-d) (L, a-d)

R = Me (a), Et (b), Pr (c), iso-Pr (d), t-Bu (e).

With increase of the bulk of the alkyl substituent, the relative stability of the 1*Z*, 2*Z*-isomers (XLVIII) and hence their equilibrium content increase sharply.[67,75] As a result, 1*Z*, 2*Z*-2-t-butyl-3-phenyl-1-phthalimidoazimine (XLVIIIe) is configurationally completely stable and is the first example of a stable acyclic 1*Z*, 2*Z*-azimine.[67,74,75]

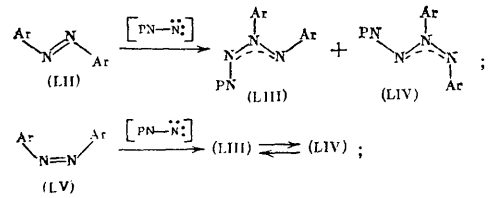
The kinetically controlled formation of 1*Z*, 2*Z*-azimines (XLVIII) in the reaction of phthalimidonitrene with *E*-alkylazobenzenes (XLVII) can probably be accounted for by secondary orbital interactions stabilising the *cis*-disposition of the phthalimide group of the nitrene and of the phenyl substituent of the azo-compound in the transition state.[67,76] One cannot rule out that the same interactions determine also the regioselectivity of the reaction.

The possible breakdown of regioselectivity in the addition process has been noted only for *E*-isopropylazobenzene (XLVIId). In this case, the regioisomeric 1*E*, 2*Z*-3-isopropyl-2-phenyl-1-phthalimidoazimine (LI) (25% of the overall amount of adducts) is apparently formed together with the adducts (XLVIIId), (XLIXd), and (Ld):[67,75]



(LI)

The reaction of phthalimidonitrene with *E*-azoarenes (LII) yielded mixtures of 1*Z*, 2*E*- and 1*E*, 2*Z*-2,3-diaryl-1-phthalimidoazimines (LIII) and (LIV),[31,62,63,77–81] between which equilibrium is gradually established at room temperature. Here the main reaction products are 1*Z*, 2*E*-azimines (LIII) and their content in the mixtures of isomers isolated exceeds somewhat the equilibrium value:[63,80]



(LII) (LIII) (LIV) (LV)

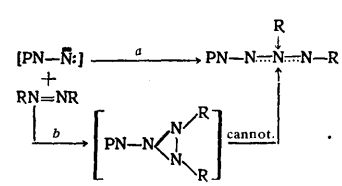
Ar = Ph (a), *p*-Tol (b).

The mechanism of the addition has not been investigated in detail, but, by analogy with *E*-alkylazobenzenes (XLVII), presumably the preferential inversion of the configuration of the azo-group can be explained in this case too by the rapid stereoisomerisation of the intermediate 1*Z*, 2*Z*-2,3-diaryl-1-phthalimidoazimines.[67,76]

The addition of phthalimidonitrene to *Z*-azoarenes (LV) leads to 1*Z*, 2*E*-2,3-diaryl-1-phthalimidoazimines (LIII) with a small admixture of the 1*E*, 2*Z*-isomers (LIV)[62,63,77–80] probably owing to the partial stereoisomerisation of the primary products (LIII). As for other types of azo-compounds, the yields of 1-phthalimidoazimines in the reaction with *Z*-azoarenes are much higher than in the reaction with the *E*-isomers.[62,63,77–80]

The reactions of phthalimidonitrene with both *E*- and *Z*-4-phenylazotoluenes result in the formation of both regioisomeric *p*-tolylphenyl-1-phthalimidoazimines in similar amounts (each in the form of a mixture of the 1*Z*, 2*E*- and 1*E*, 2*Z*-isomers).[31,80] Contrary to the initial communication,[81] the stereoisomerisation of these adducts is not accompanied by their interconversion (regioisomerisation).[80]

The most probable mechanism of the addition of phthalimidonitrene to azo-compounds, which can explain almost all the features of this reaction, involves electrophilic attack on the sextet nitrogen atom via the highest non-bonding orbital of the azo-group, in actual fact via the unshared electron pair of one of the nitrogen atoms. In this single-stage process, the azimine π-electron system is formed together with the N–N σ-bond; according to experimental data, the reaction should proceed with retention of configuration (pathway *a*):



The alternative two-stage mechanism with the intermediate formation of triaziridine (pathway *b*) is significantly less realistic.[67,68,76]

Within the framework of the single-stage mechanism, it is possible to explain satisfactorily the influence of electronic and steric factors on the course of the reaction of phthalimidonitrene with azo-compounds.[67,68,76] Furthermore, we we are justified to expect that the principal features of the reactant–substrate interaction will be retained also for the electrophilic addition of other sextet species via the azo-group, i.e. that this mechanism will prove valid for a wide range of related objects.

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