ELECTROPHILIC HETEROCYCLIZATION OF UNCONJUGATED DIENES (REVIEW)

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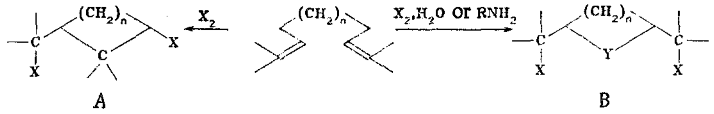
The results of research with the participation of unconjugated dienes in intramolecular electrophilic heterocyclization are presented. It is shown that this reaction can be used for the synthesis of heterocycles with one, two, or more heteroatoms. The stereochemistry of the resulting heterocycles and the mechanism of heterocyclization is examined.

The electrophilic heterocyclization of unconjugated dienes can be formally classified among reactions involving addition with the intermolecular formation of heterocycles [1-3].

The addition of electrophiles to unconjugated dienes leads to the formation of carbocyclic structures of the A type [4-6] if one of the double bonds participates in the reaction as an "internal" nucleophile or, on the other hand, it leads to the formation of heterocyclic structures of the B type if the reaction is carried out in the presence of "external" nucleophiles such as water, alcohols, amines, etc.



X_2=$HgCl_2$,$Hg(OAc)_2$,I_2,NBS,PhSeCl, PhSCl,SCl_2
Y=O,N,S .

A review was published in 1979 [5] dealing with reactions involving the intramolecular cyclization of unconjugated dienes that lead to the formation of carbocyclic compounds. In the present paper we examine reactions that proceed with the formation of structures of the B type with the participation of "external" nucleophiles.

The electrophilic heterocyclization of unconjugated dienes that proceed with the participation of "external" nucleophiles is widely used for the synthesis of heteroadamantanes. Appropriate sections in earlier reviews [7, 8] have been devoted to these reactions. In this connection we here present new data on the preparation of heteroadamantanes. However, in order to preserve the objectivity in our exposition on individual bases we also refer to previously published research.

In the present review we discuss the reactivities of 1,4-, 1,5-, and 1,6-dienes and the participation of various electrophiles and "external" nucleophiles and examine the stereochemistry of the resulting heterocycles and the mechanisms of the electrophilic heterocyclization of unconjugated dienes.

1. Heterocycles Containing One Heteroatom

1.1. Oxygen-Containing Heterocycles.

The addition of mercury salts to the double bond of ethylene compounds discovered in 1892 by M. G. Kucherov [9] was and remains the subject of extensive study, as attested to by a number of reviews [10-12] devoted to these transformations.

A. N. Nesmeyanov [13] and Brown and co-workers [14] subsequently showed that as a result of the chloromercuration of diallyl (I) in the presence of water, 2,5-dichloromercurimethyltetrahydrofuran (II) is obtained. In addition to a very small amount of 2,5-disubstituted tetrahydrofuran IV, 2,5-bis-(phenylselenomethyl)tetrahydrofuran (III) is primarily formed in the reaction of diallyl I with PhSeCl [15], PhSeCN [16, 17], and "PhSeOH" [18].

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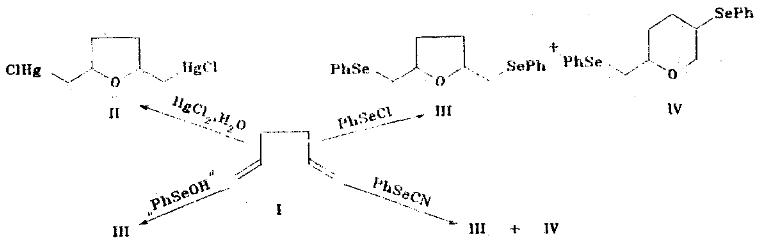
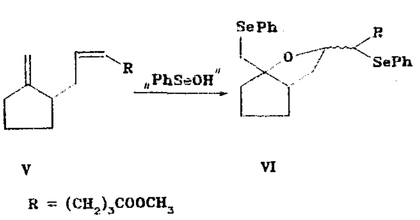
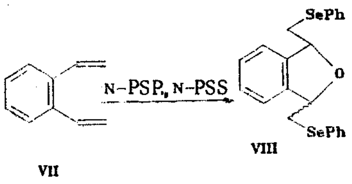
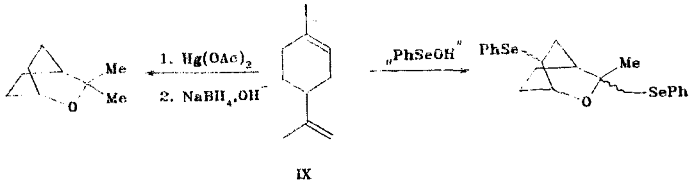


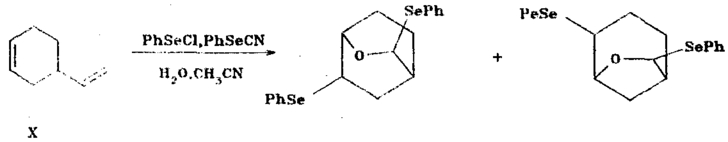
Tetrahydrofuran derivatives VI and VII were also obtained in the hydroxyselenization of hydrocarbons V by means of "PhSeOH" [18] and VII was obtained by means of N-phenylselenophthal- (N-PSP) and N-phenylselenosucinnimides (N-PSS) [19, 20].



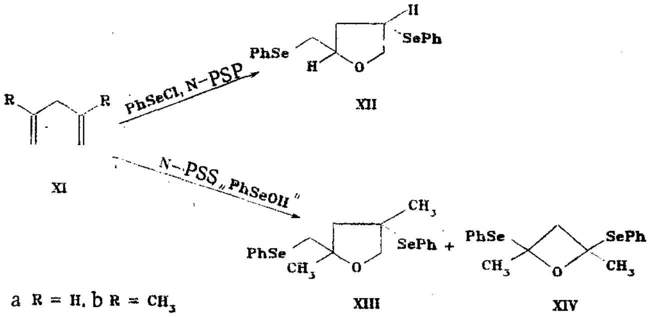


Depending on the structure of the starting 1,5-dienes, primarily tetrahydrofuran derivatives can be obtained as a result of hydroxyselenization and hydroxymercuration, as observed in the case of limonene (IX) [18, 21] and 4-vinylcyclohexene (X) [15-17].

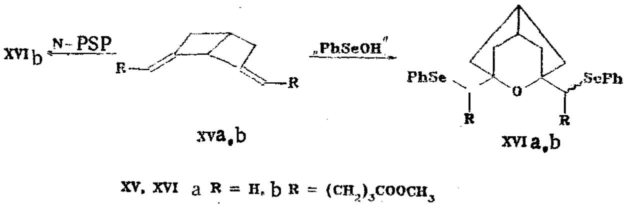




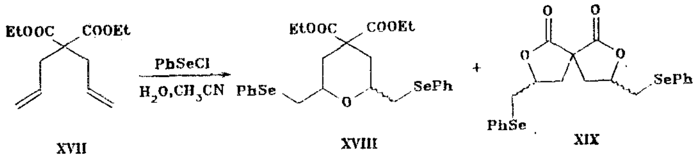
In addition to tetrahydrofuran derivatives XII and XIII, substituted oxetanes XIV are also obtained in the hydroxyselenization of 1,4-pentadiene (XIa) and 2,4-dimethyl-1,4-pentadiene (XIb) with phenylselenyl chloride [15] and N-PSP and N-PSS [19, 20].

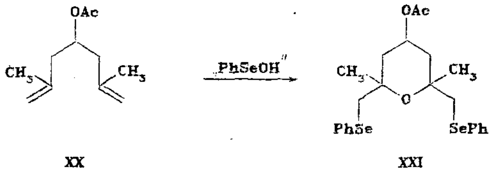


Tetrahydropyran derivatives XVIa, b are formed as a result of hydroxyselenization of 1,6-dienes XVa, b [18-20]:

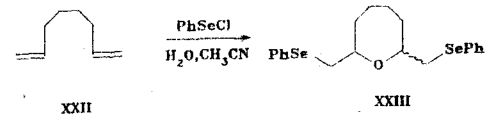


Diethyl diallylmalonate (XVII) reacts with PhSeCl [15] to give a mixture of tetrahydropyran XVIII and spiro-bislactone XIX, whereas ester XX reacts with "PhSeOH" to give tetrahydropyran XXI [18].

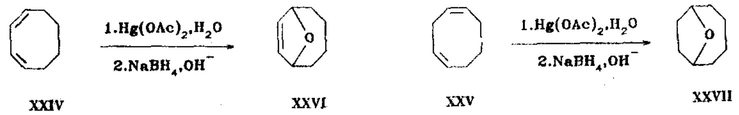




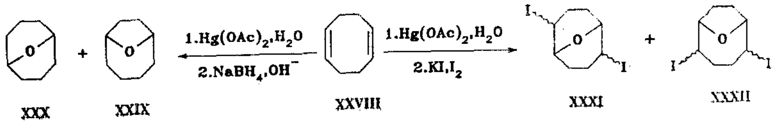
Under similar conditions, 1,7-octadiene (XXII) undergoes cyclization with PhSeCl [15] to give hexahydrooxepine XXIII.



In the case of acetoxymercuration and subsequent reduction of the reaction products with $NaBH_4$ [22], 1,3-cyclooctadiene (XXIV) and 1,4-cyclooctadiene (XXV) give, respectively, 9-oxabicyclo[4.2.1]non-7-ene (XXVI) and 9-oxabicyclo[4.2.1]nonane (XXVII) in low yields.

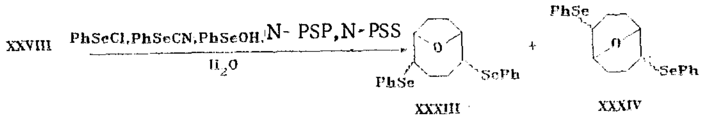


1,5-Cyclooctadiene (XXVIII) undergoes electrophilic heterocyclization readily to give bicyclic systems. Its acetoxymercuration and subsequent reduction of the mercury-containing reaction products with $NaBH_4$ [22] lead to the formation of a mixture of 9-oxabicyclo[4.2.1]nonane (XXIX) and 9-oxabicyclo[3.3.1]nonane (XXX) in a ratio of 1.2:1. Hydrocarbon XXVIII reacts with mercuric nitrate to give only XXX.



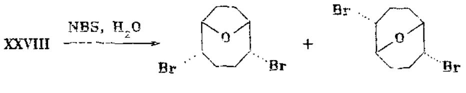
The acetoxymercuration of cyclooctadiene XXVIII with subsequent treatment of the mercuration products with KI and I_2 leads to 2,6-diiodo-9-oxabicyclo[3.3.1]nonane (XXXI) [24, 25]. Ganter and co-workers [26] were able to identify six possible stereoisomers of diiodo derivatives XXXI and XXXII (endo,endo-, endo,exo-, and exo,exo-). endo,endo-2,6-Diiodide XXXI is formed in 30% yield in the iodination of hydrocarbon XXVIII in methanol [27], whereas its iodocyclization in chloroform in the presence of HgO [28] leads to a mixture of diiodides XXXI and XXXII in a ratio of 3:2.

A mixture of 2,5-diphenylseleno-9-oxabicyclo[4.2.1]nonane (XXXIII) and 2,6-diphenylseleno-9-oxabicyclo[3.3.1]nonane (XXXIV) was obtained in the phenylselenylchlorination of diene XXVIII [15]. The isomer ratio depends on the reaction temperature and on the solvent used. The product of thermodynamic control XXXIV is primarily obtained at 76°C with XXXIII:XXXIV = 1:32, whereas this ratio is 7:1 at 24°C.



The hydroxyselenization of hydrocarbon XXVIII by PhSeCN in methanol or ethanol in the presence of $CuCl_2$ [16, 17] gives primarily XXXIV (XXXIII:XXXIV ratios 1:19 and 1:9, respectively), whereas only isomer XXXIII is obtained in a mixture of THF and H_2O. The latter isomer was isolated in good yields in the reaction of diene XXVIII with "PhSeOH" [18] and N—PSP and N—PSS [19, 20], as well as in low yields in the reaction with PhSeOSePh [18].

The formation of 2,5-dibromo-9-oxabicyclo[4.2.1]nonane (XXXV) and 2,6-dibromo-9-oxabicyclo[3.3.1]nonane (XXXVI) is observed in the hydroxybromination of hydrocarbon XXVII with N-bromosuccinimide (NBS) in the presence of water [25]:

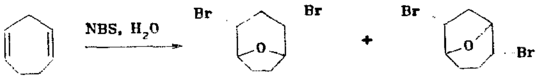


XXXV XXXVI

When Stetter and Heckel [29] treated diene XXVII with MBS in the presence of catalytic amounts of H_2SO_4, they obtained dibromide XXXV in 31% yield, whereas Zefirov and co-workers [25] obtained isomer XXXVI in 21% yield in the case of hydroxybromination of this compound with NBS in aqueous acetone.

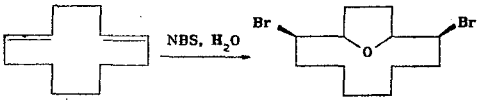
As a result of the reaction of diene XXVIII with MBS in aqueous dioxane [31] in the presence of H_2SO_4, a mixture of dibromides XXXV and XXXXVI in a ratio of 5:1 was isolated.

When 1,4-cycloheptadiene (XXXVII) is treated with NBS in aqueous dioxane [31], it gives a mixture of endo,endo-2,4-dibromo-8-oxabicyclo[3.2.1]octane (XXXVIII) and endo,endo-2,5-dibromo-8-oxabicyclo[3.2.1]octane (XXXIX), whereas Z,Z-cyclononadiene is converted to 2,6-dibromo-10-oxabicyclo[5.2.1]decane in very low yield [2].

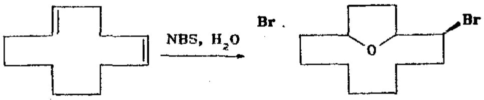


XXXVII XXXVIII XXXIX

Both E,E- and Z,E-1,5-dodecadienes (XL and XLI) react with NBS in methanol stereospecifically to give, respectively, exo,exo- and endo,exo-dibromo-13-oxabicyclo[8.2.1]tridecanes (XLII and XLIII) [33].

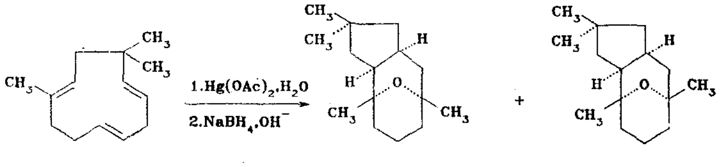


XL XLII



XLI XLIII

Humulene — 2,6,6,9-tetramethylcycloundecatri-1E,4E,8E-ene (XLIV) — reacts with $Hg(OAc)_2$ in aqueous tetrahydrofuran to give, after reduction of the mercury-containing products with $NaBH_4$ [34], tricyclic ethers XLV and XLVI; one of the three double bonds participates in the formation of the carbocyclic system.



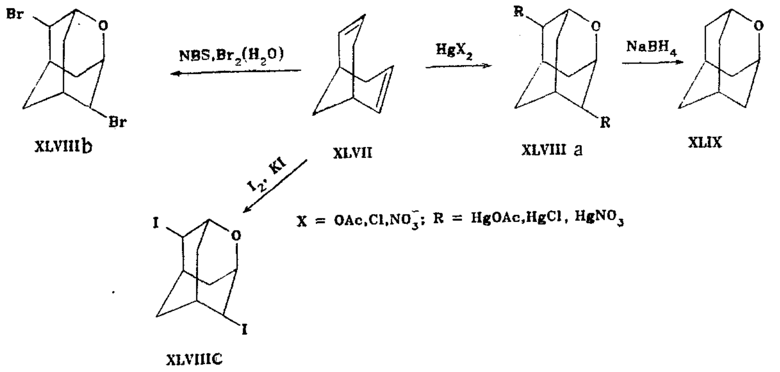
XLIV XLV XLVI

In the same way as cyclic dienes, bicyclo[3.3.1]nona-2,6-diene (XLVII) undergoes acetoxymercuration [35-38], chloromercuration in water [39], and bromination by NBS and bromine in water [25, 30] to give 4,8-disubstituted 2-oxaadamantanes XLVIIIa-c. 2-Oxaadamantane (XLIX) was obtained by reduction of XLVIIIa with $NaBH_4$.

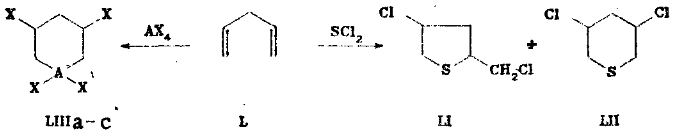
The acetoxymercuration of 9-acetoxybicyclo[3.3.1]nona-2,6-diene [40] and subsequent reduction of the reaction products with $NaBH_4$ leads to 2-oxaadamantan-6-ol.

1.2. Sulfur-, Selenium-, Tellurium-, Nitrogen-, and Phosphorus-Containing Heterocycles. The corresponding heterocyclic systems are formed in the reaction of polyenes with sulfur and selenium halides, as well as with sulfenyl halides.

2,3-Dimethylbutadiene reacts with sulfur dichloride to give 3,4-dichloro-3,4-dimethyltetrahydrothiophene [41], whereas butadiene gives only addition products.



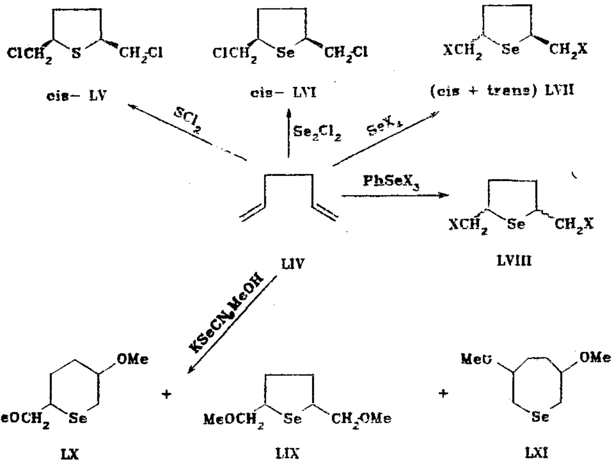
1,4-Pentadiene (L) reacts with SCl_2 to give a mixture of substituted tetrahydrothiophene (LI) and thiacyclohexane (LII), whereas 1,5-hexadiene (LIV) gives only cis-2,5-bis(chloromethyl)tetrahydrothiophene (LV) [42]:



a X = Br, A = Se; b X = Br, A = Te; c X = Cl, A = Te

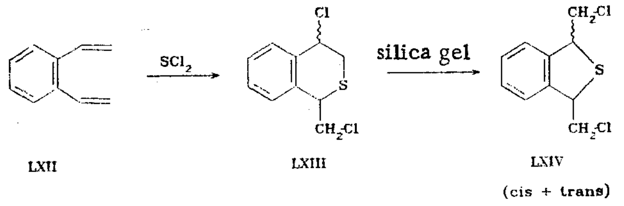
The reaction of diene L with tetrabromoselenium and tetrabromo(chloro)tellurium proceeds with great regioselectivity and leads only to 1,1,3,5-tetrahaloselenanes (telluranes) (LIIIa-c) [43].

The reaction of 1,5-hexadiene (LIV) with selenium monochloride [44] and selenium tetrahalides and phenylselenium tribromide (chloride) [45, 46] gives 2,5-bis(halomethyl)selenolanes (LVI, LVII) and 1-phenyl-1-halo-2,5-bis(halomethyl)selenolanes (LVIII).



LVII, LVIII X=Cl, Br

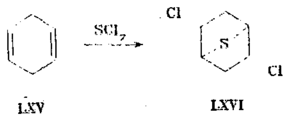
The reaction of diene LIV with potassium selenocyanide in methanol in the presence of $CuCl_2$ [47] leads to a mixture of five-, (LIX), six- (LX), and seven-membered (LXI) selenium-containing heterocycles. It has been shown that LIX is converted to isomer LX in an acidic medium.



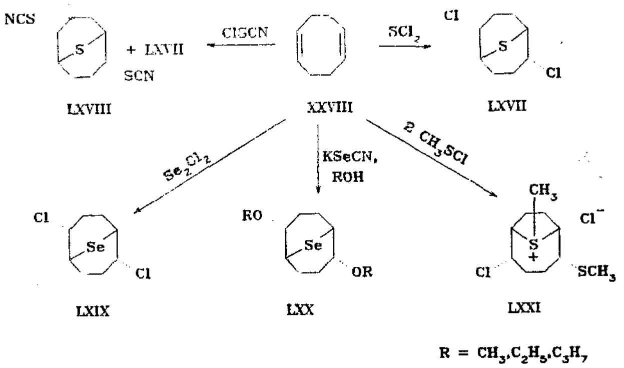
The reaction of divinylbenzene (LXII) with sulfur dichloride gave (in good yield) 3,4-dihydro-1-chloromethyl-4-chloro-1H-2-benzothiopyran (LXIII), treatment of which with silica gel gave 1,3-dihydro-1,3-bis(chloromethyl)benzo[c]thiophene (LXIV) in a stereoisomer ratio of 70:30 [48].

When 1.7-octadiene is treated with sulfur dichloride [42], it is converted to 2,7-bis-(chloromethyl)-1-thiacycloheptane in low yield.

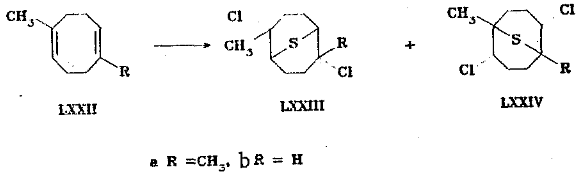
Cyclic dienes react with selenium- and sulfur-containing electrophiles to give the corresponding bi- or tricyclic heterocycles. 1,4-Cyclohexadiene (LXV) is converted to endo,endo-2,5-dichloro-7-thiabicyclo[2.2.1]heptane (LXVI) upon reaction with SCl_2 [49].



When 1,5-cyclooctadiene (XXVIII) is treated with SCl_2 [49-53], it gives 2,6-dichloro-9-thiabicyclo[3.3.1]nonane (LXVII). The latter was also obtained in the reaction of diene XXVIII with chlorothiocyanate [54], along with 2,6-dithiocyanato-9-thiabicyclo[3.3.1]nonane (LXVIII) and products of addition to the double bond. Treatment of hydrocarbon XXVIII with selenium monochloride [44] and potassium selenocyanate [47] leads to the formation of, respectively, 2,6-dichloro- (LXIX) and 2,6-dialkoxy-9-selenabicyclo[3.3.1]nonane (LXX). The reaction of methanesulfenyl chloride with diene XXVIII, gives, along with products of addition to the multiple bond, 2-chloro-5-methylthio-9-methyl-9-thioniabicyclo[4.2.1]nonane chloride (LXXI) [55, 56].

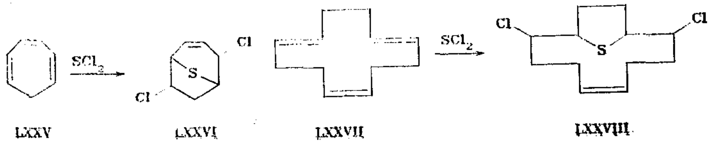


1,5-Dimethyl-1,5-cyclooctadiene (LXXIIa) is converted to a mixture of 2,6-dimethyl-(LXXIIIa) and 1,5-dimethyl-2,6-dichloro-9-thiabicyclo[3.3.1]nonanes (LXXIVa) in a ratio of 3:1 under the influence of SCl_2 [57]. 1-Methyl-1,5-cyclooctadiene (LXXIIb) gives a mixture of 1-methyl- (LXXIIIb) and 2-methyl-2,6-dichloro-9-thiabicyclo[3.3.1]nonanes (LXXIVb). The products of the reaction of LXXIIIa, b are kinetically controlled, whereas the products of the reaction of LXXIVa, b are thermodynamically controlled.



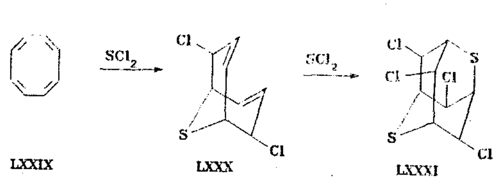
1,3-Cyclooctadiene reacts with SCl_2 to give 7,8-dichloro-9-thiabicyclo[4.2.1]nonane [51].

The reaction of SCl_2 with cycloheptatriene (LXXV) [58] leads to the formation of 2,6-dichloro-8-thiabicyclo[3.2.1]oct-3-ene (LXXVI).



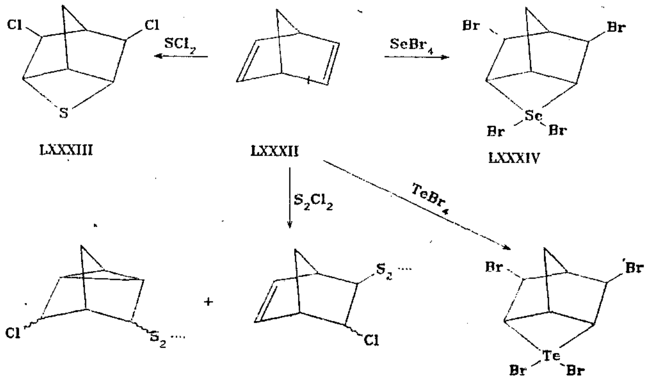
The reaction of trans,trans,cis-1,5,9-cyclododecatriene (LXXVII) [58] with SCl_2 gives 2,9-dichloro-13-thiabicyclo[8.2.1]tridec-5-ene (LXXVIII).

Transannular addition of sulfur dichloride to cyclooctatetraene (LXXIX) leads initially to the production of 2,6-dichloro-9-thiabicyclo[3.3.1]nona-3,7-diene (LXXX), which, upon adding another molecule of SCl_2, is converted to 3,5,7,9-tetrachloro-1,10-dithiaadamantene (LXXXI) [58].



LXXIX LXXX LXXXI

Bicyclo[2.2.1]hepta-2,5-diene (LXXXII) reacts with SCl_2 [42, 58-60] to give exo,exo-3,5-dichloro-8-thiatricyclo$[2.2.1^{2,6}]$octane (LXXXIII), whereas its reaction with selenium and tellurium tetrabromides [61] leads, respectively, to 3,5,8,8-tetrabromo-8-selena(tellura)-tricyclo$[2.2.1.1^{2,6}]$octane (LXXXIV, LXXXV). Sulfur monochloride reacts with diene LXXXII to give only products of addition to the multiple bonds, viz., LXXXVI and LXXXVII [62].

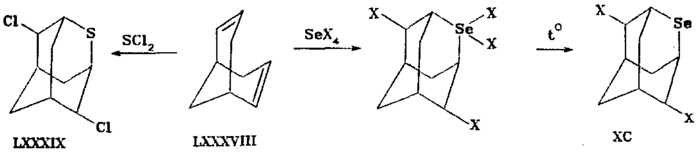


LXXXIII LXXXII LXXXIV

LXXXVII LXXXVI LXXXV

The reaction of bicyclo[3.3.1]nona-2,6-diene (LXXXVIII) with SCl_2 [35] and selenium tetrahalides [63] leads to the formation of, respectively, 4,8-dichloro-2-thiaadamantane (LXXXIX) and 4,8-dihalo-2-selenaadamantane (XC).

The transannular addition of sulfur dichloride to unconjugated dienes proceeds through the 1,2-thiiranium ion, which undergoes primarily trans-antiplanar opening, so that the chlorine atoms are trans-oriented with respect to the sulfur atom [50, 53].

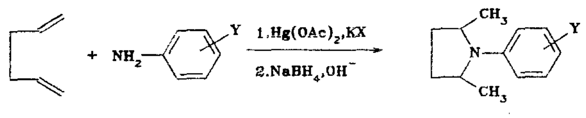


LXXXIX LXXXVIII XC

X=Cl,Br

Nitrogen-containing heterocycles are obtained in the reaction of unconjugated dienes with mercuric acetate in the presence of primary amines. Under these conditions and with subsequent reduction of the mercury-containing adducts with $NaBH_4$, 1,5-hexadiene (LIV) is converted to 2,5-dimethylpyrrolidines (XCI) [55].

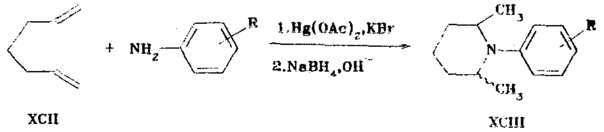
Under similar conditions, 1,6-heptadiene (XCII) gives piperidine derivatives XCIII [66]. The reaction is stereoselective and leads primarily to cis-2,5-dimethyl-N-arylpiperidines.



LIV XCI

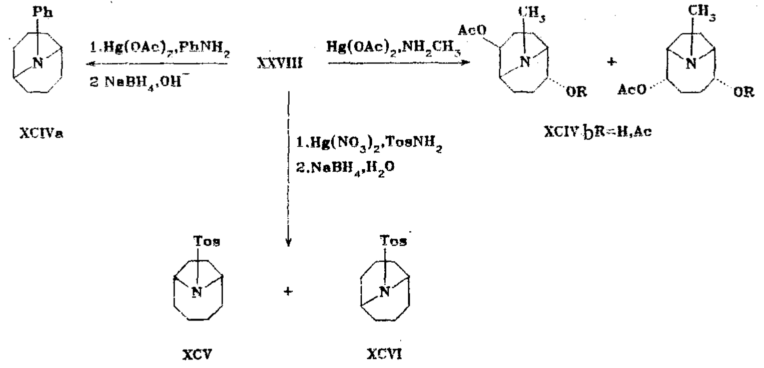
Y = H, CH_3COO, Cl, NO_2, CH_3, OCH_3, $COOC_2H_5$; X = OAc, Cl, Br

The stereoselectivity of the reaction decreases when substituents are introduced into the ortho position of the arylamine.

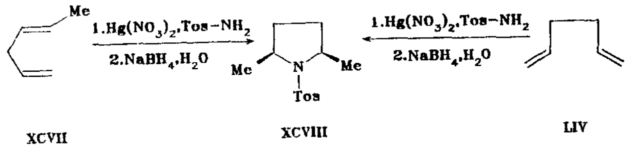


R=2-CH$_3$, 4-CH$_3$, 4-OCH$_3$, 4-Cl

1,5-Cyclooctadiene (XXVIII) reacts with mercuric acetate in the presence of primary amines [64, 67] to give primarily substituted 9-azabicyclo[3.3.1]nonane (XCIVa, b).

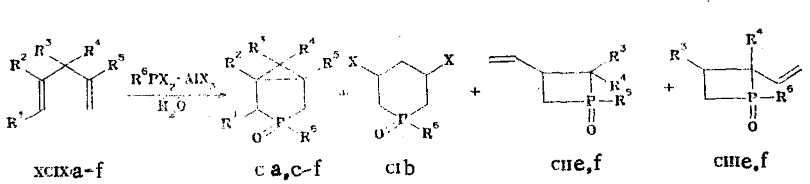


The reactions of 1-methyl-1,4-pentadiene (XCVII) and 1,5-hexadiene (LIV) with mercuric nitrate in the presence of toluenesulfonamide [68] and subsequent reduction of the reaction products with NaBH$_4$ lead to 1-tosyl-2,5-dimethylpyrrolidine (XCVIII). Under similar conditions, diene XXVIII is converted to a mixture of 9-tosyl-9-azabicyclo[3.3.1]nonane (XCVI) and 9-tosyl-9-azabicyclo[4.2.1]nonane (XCV) in a ratio of 44:56. The reaction does not take place with mercuric acetate.



The formation of nitrogen-containing heterocycles in the acetoxymercuration of dienes is realized in a stepwise manner. The initial product is the result of the addition of Hg(OAc)$_2$ and an amine residue to one double bond, after which the resulting unsaturated amine reacts with another molecule of mercuric acetate to give the final reaction product [2].

The electrophilic addition of $R^6PX_2 \cdot AlF_3$ complexes (R^6 = Ph or Me, X = Cl or Br) [69-72] to unconjugated dienes XCIX is a method for the synthesis of epimeric (with respect to the phosphorus atom) phosphabicyclo[3.1.0]hexanes (Ca, c, d).

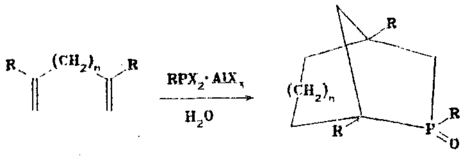


a $R^1=R^3=R^4=H$, $R^2=R^5=Me$; b $R^1=R^2=R^3=R^4=R^5=H$, c $R^1=R^2=-(CH_2)_4$, $R^3=R^4==R^5=H$, d $R^1=R^3=R^4=R^5=H$, $R^2=Me$, e $R^1=R^2=R^5=H$, $R^3=R^4=Me$, f $R^1=R^2=R^5=H$, $R^3=Me$, $R^4=Ph$

Under similar conditions, 1,4-pentadiene (XCIXb) gives two 3,5-dichloro(bromo)phosphorine epimers (CI) in low yields.

Substituted phosphetanes CII and CIII are obtained, along with Ce, f, in the phosphorylation of dienes XCIXe, f.

When 2,5-dimethyl-1,5-hexadiene (CIVa, n = 2) and 2,6-diphenyl-1,6-heptadiene (CIVb, n = 3) are treated with $RPX_2 \cdot AlX_3$ complexes, they are converted, respectively, to 1,4-dimethyl-2-phenyl(methyl)-2-oxo-2-phosphabicyclo[2.2.1]heptane (CVa, n = 0) and 1,4-diphenyl-2-methyl-2-oxo-2-phosphabicyclo[3.2.1]octane (CVb, n = 1).



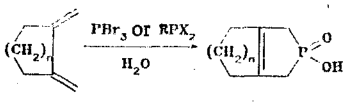
CIVa,b   CV a,b

a R=Me, b R=Ph

The phosphorylation of 9,9-bis(2-methallyl)fluorene gives two epimers (with respect to the phosphorus atom) of 1,4-dimethyl-6-(9-fluorenyl)-2-oxo-2-phenyl-2-phosphabicyclo[3.2.1]-octane [72].

Treatment of 1,7- and 1,14-dienes CIV (n = 4, 11) with the indicated complex does not lead to cyclic reaction products.

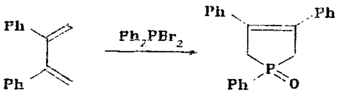
Bicyclic phospholenes CVII are formed in the reaction of 1,2-dimethylenecycloalkanes (CVI) with PBr_3 or RPX_2 [73].



CVI   CVII

n=1,2; X=Cl, Br

2,3-Diphenyl-1,3-butadiene (CVIII) reacts with Ph_2PBr_2 in the presence of copper stearate [74] to give 1,3,4-triphenyl-3-phospholene oxide (CIX):



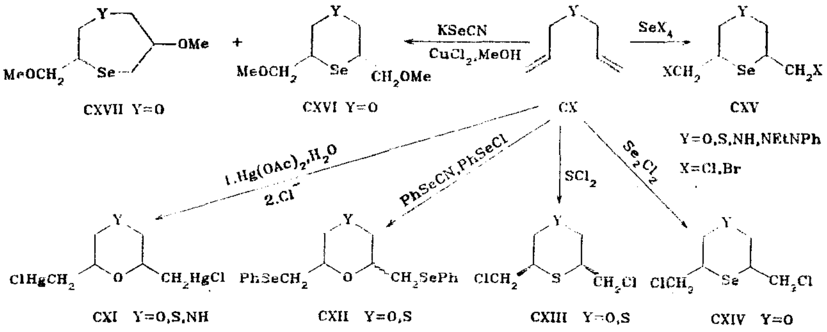
CVIII   CIX

2. Heterocycles Containing Two or More Heteroatoms

The electrophilic heterocyclization of unconjugated dienes can be used successfully for the synthesis of heterocyclic compounds that contain more than one heteroatom. The structures of the cyclic compounds are determined by the nature of the starting diene, the "external" nucleophile, and the electrophilic agent. By varying these factors one can obtain a heterocycle with a predesignated structure.

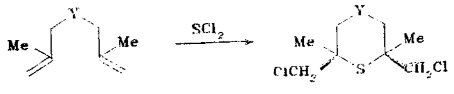
Allyl ether (CX, Y = O) and diallyl sulfide (CX, Y = S), as a result of mercuration in the presence of water [12, 62], are converted to 2,6-disubstituted 1,4-dioxanes and 1,4-oxathianes (CXI, Y = O, S). 2,3-Dihalo-substituted dioxanes are obtained as a result of the mercuration of 1,4-pentadiene in the presence of ethylene glycol [75].

2,6-Bis(phenylselenomethyl)1,4-dioxane (oxathiane) (CXII, Y = O, S) is obtained when ether or sulfide CX (Y = O, S) is treated with phenyl selenocyanide in the presence of $CuCl_2$ [16] and phenylselenyl chloride in aqueous acetonitrile [15].



2,6-Bis(chloromethyl)-substituted 1,4-oxathianes and 1,4-dithianes (CXIII, Y = O, S) are formed in the reaction of compounds of the CX type (Y = O, S) with SCl_2 [42].

When analogs of 2,6-dimethyl-1,6-heptadiene (CXVIII, Y = O, S, NH, NMe) are treated with sulfur dichloride [76], they are converted to derivatives of 1,4-oxathiane, 1,4-dithiane, and piperazine (CXIX, Y = O, S, NH, NMe).



CXVIII CXIX

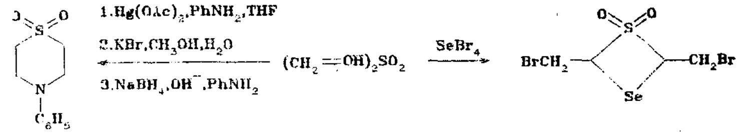
Y=O,S,NH,NMe

The reaction of dienes with SCl_2 proceeds stereoselectively and leads primarily to cis isomers, which are used for the synthesis of heteroadamantane compounds [42].

Selenium monochloride reacts with ether CX (Y = O) to give 2,6-bis(chloromethyl)-1,4-selenoxane (CXIV, Y = O) [44], whereas a mixture of 3,5-bis(methoxymethyl)-1,4-oxaselenane (CXVI, Y = O) and 3-methoxymethyl-6-methoxy-1,4-oxaselenepane (CXVII, Y = O) is formed with KSeCN in methanol with the same diene [47].

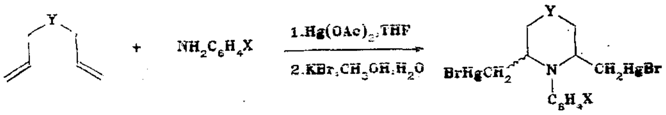
Substituted 1,4-selenoxanes, 1,4-selenothianes and 1,4-selenazines CXV (Y = O, S, NH, NEt, NPh) were obtained when dienes of the CX type (Y = O, S, NH, NEt, NPh) were treated with selenium tetrahalides [45].

The reaction of divinyl sulfone (CXX) with $SeBr_4$ [77] and $Hg(OAc)_2$ in the presence of primary aromatic amines [78], gives, respectively, substituted selenothietane (CXXI) and tetrahydro-1,4-thiazine (CXXII).



CXXII CXX CXXI

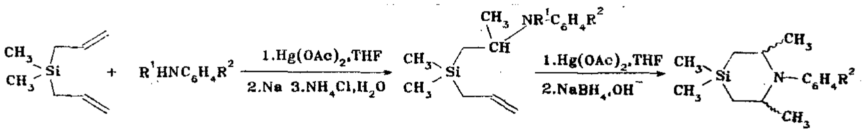
The mercuration of compounds of the CX type (Y = O, S, NH, NR) in the presence of primary arylamines [79, 80] leads to derivatives of morpholine, tetrahydro-1,4-thiazine, and piperazine (CXXIII). The ratio of cis and trans isomers in the substituted piperazines depends on the nature of R and substituent X:



CX CXXIII

X=H, 4-CH_3, 2-CH_3, 4-OCH_3, 2-OCH_3, 4-NO_2, 4-Cl; Y=O, S, NH, NR (R=CH_3, C_3H_7, $CH_2C_6H_5$, $COCH_3$, C_6H_5)

Heterocycles CXXVI, which contain nitrogen and silicon, were obtained in the aminomercuration of diallylsilanes (CXXIV) in the presence of primary and secondary amines [81]. It was demonstrated that their formation proceeds through intermediate aminoalkylsilanes CXXV, which subsequently undergo mercuration to give 1-aza-4-silacyclohexanes CXXVI.

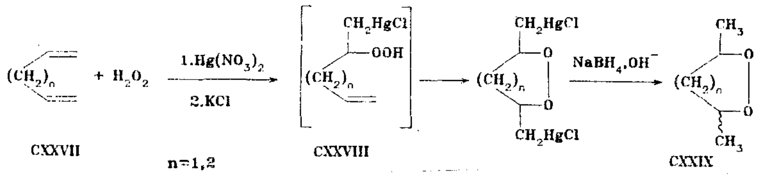


CXXIV CXXV CXXVI

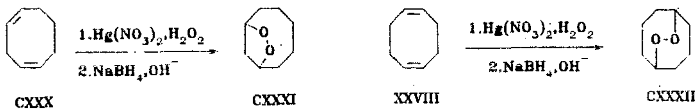
R^1=H, CH_3, C_2H_5; R^2=H, 4-Cl, 4-CH_3, 2-CH_3

Derivatives of cis- and trans-1,2-dioxolane (dioxane) CXXIX were obtained in the case of twofold treatment of 1,4- and 1,5-dienes CXXVII with mercuric nitrate or perfluoroacetate in the presence of hydrogen peroxide [82, 83] and subsequent reduction of the reaction products with $NaBH_4$.

In the case of similar treatment 4-methyl-, 3,4-dimethyl-, and 3,3-dimethyl-1,3-pentadienes give only substituted 1,2-dioxolanes [84]. 1,6-Heptadiene and 1,7-octadiene form cyclic peroxides in low yields [84].

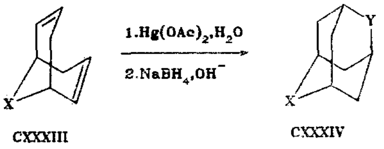


As a result of the reaction, 1,4-cyclooctadiene (CXXX) and 1,5-cyclooctadiene (XXVIII) are converted to 8,9-dioxabicyclo[5.2.1]decane (CXXXI) and 9,10-dioxabicyclo[3.3.2]decane (CXXXII) [85, 86]:



It is assumed that the formation of cyclic peroxides proceeds through intermediate unsaturated hydroperoxides CXXXIII, which, under the influence of a second molecule of the electrophile, give cyclic peroxides. This assumption is based on the facile transformation of unsaturated hydroperoxides in their reaction with mercuric nitrate or trifluoroacetate to the corresponding substituted 1,2-dioxabicyclopentanes (hexanes) [87], 1,2-dioxetanes [88], and 8,9-dioxabicyclo[5.2.1]decanes [86].

The heterocyclization of unconjugated dienes CXXXIII has been widely used for the synthesis of heteroadamantane structures CXXXIV. However, these studies are not examined in the present review, since special reviews [7, 8] have been devoted to them.



X=O,N;Y=O,N,S

Thus the electrophilic heterocyclization of unconjugated dienes is one of the methods used for the preparation of partially or completely hydrogenated heterocycles that contain O, S, Se, Te, N, and P atoms as the heteroatoms. As a rule, the mechanism of the formation of heterocycles reduces to initial addition of the electrophile, in the presence of an "external" nucleophile, to one of the double bonds of the unconjugated diene, after which the reaction proceeds via a scheme involving electrophilic heterocyclization of unsaturated alcohols, amines, etc. [1-3]. In the case of the addition of four-coordinated compounds of selenium and tellurium one may assume an associative mechanism that includes coordination of two unconjugated bonds of the dienes with the selenium or tellurium atoms. The electrophilic heterocyclization of dienes proceeds particularly readily in the case of strong electrophiles such as mercury salts, NBS, sulfenyl halides, selenium and tellurium halides, sulfur dichloride, etc. In the case of weak electrophiles such as iodine electrophilic heterocyclization proceeds only for reactive cyclic dienes.

LITERATURE CITED

1. V. I. Staninets and E. A. Shilov, Usp. Khim., 40, 491 (1971).
2. A. Latt, Khim. Geterotsikl. Soedin., No. 1, 7 (1975).
3. Yu. I. Gevaza and V. I. Staninets, Khim. Geterotsikl. Soedin., No. 11, 1443 (1982).
4. N. S. Zefirov, V. A. Tartakovskii, and N. V. Averina, Zh. Org. Khim., 7, 504 (1965).
5. G. Haufe and M. Mühlstädt, Z. Chem., No. 5, 170 (1979).
6. H. J. Günther, V. Jäger, and P. S. Skell, Tetrahedron Lett., No. 29, 2539 (1977).
7. N. V. Averina and N. S. Zefirov, Usp. Khim., 45, 1077 (1976).
8. Z. Kafka and V. Galik, Chem. Listy, 72, 509 (1978).
9. M. G. Kucherov, Zh. Russk. Fiz.-Khim. Ova., 24, 330 (1892).
10. N. S. Zefirov, Usp. Khim., 34, 1272 (1965).
11. J. Chatt, Chem. Rev., 48, 7 (1951).
12. L. G. Makarova and A. N. Nesmeyanov, in: Methods of Heteroorganic Chemistry. Mercury [in Russian], Nauka, Moscow (1965), p. 115.
13. A. N. Nesmeyanov and I. F. Lutsenko, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, 4, 296 (1943).
14. C. H. Brown, P. J. Geoghegan, G. J. Lynch, and J. T. Kurek, J. Org. Chem., 37, 1941 (1972).

15. S. Uemura, A. Toshimitsu, T. Aoai, and M. Okano, Tetrahedron Lett., 21, 1533 (1980).
16. S. Uemura, A. Toshimitsu, T. Aoai, and M. Okano, Chem. Lett., No. 10, 1359 (1979).
17. A. Toshimitsu, T. Aoai, S. Uemura, and M. Okano, J. Org. Chem., 46, 3021 (1981).
18. R. M. Scarborough, A. B. Smith, W. E. Barnette, and K. C. Nicolaou, J. Org. Chem., 44, 1742 (1979).
19. K. C. Nicolaou, D. A. Claremon, W. E. Barnette, and S. P. Seitz, J. Am. Chem. Soc., 101, 3704 (1979).
20. K. C. Nicolaou, Tetrahedron, 37, 4097 (1981).
21. M. Bambagiotti, F. F. Vincieri, S. A. Coran, J. Org. Chem., 39, 680 (1974).
22. S. Moon, J. M. Takakis, and B. H. Waxman, J. Org. Chem., 34, 2951 (1969).
23. F. G. Bordwell and M. S. Douglass, J. Am. Chem. Soc., 88, 993 (1966).
24. H. Stetter, H.-J. Meissner, and W.-D. Last, Chem. Ber., 101, 2889 (1968).
25. N. V. Averina, N. S. Zefirov, P. P. Kadzyauskas, S. V. Rogozina, N. K. Sadovaya, and N. M. Soldatov, Zh. Org. Khim., 10, 1442 (1974).
26. C. Ganter, K. Wicker, W. Zwahlen, and K. Schaffner-Sabba, Helv. Chim. Acta, 53, 1618 (1970).
27. J. N. Labows and D. Swern, J. Org. Chem., 37, 3004 (1972).
28. A. C. Cope, M. A. McKervey, and N. M. Weinschenker, J. Org. Chem., 34, 2229 (1969).
29. H. Stetter and K. Heckel, Chem. Ber., 106, 339 (1973).
30. G. Haufe, F. Kleinpeter, M. Mühlstädt, and J. Graefe, Monatsh. Chem., 109, 575 (1978).
31. G. Haufe and M. Mühlstädt, Z. Chem., 16, 100 (1976).
32. G. Haufe, M. Mühlstädt, and J. Graefe, Monatsh. Chem., 108, 1431 (1977).
33. J. Graefe, G. Haufe, and M. Mühlstädt, Z. Chem., 16, 180 (1976).
34. S. Misumi, U. Ohfune, A. Furusaki, H. Shirahama, and T. Matsumoto, Tetrahedron Lett., No. 33, 2865 (1976).
35. H. Stetter and F. F. Schwartz, Chem. Ber., 101, 2464 (1968).
36. N. V. Averina and N. S. Zefirov, Zh. Org. Khim., 5, 1991 (1969).
37. N. S. Zefirov and N. V. Averina, Zh. Org. Khim., 5, 190 (1969).
38. N. V. Averina and N. S. Zefirov, Chem. Commun., No. 6, 197 (1973).
39. N. S. Zefirov, V. A. Tartakovskii, and N. V. Averina, Zh. Org. Khim., 7, 504 (1971).
40. S. Moon, D. Wright, and A. L. Schwartz, J. Org. Chem., 41, 1899 (1976).
41. M. Mühlstädt and D. Martinetz, Z. Chem., 14, 297 (1974).
42. F. Lautenschlaeger, J. Org. Chem., 33, 2620 (1968).
43. Yu. V. Migalina, I. M. Balog, V. G. Lendel, and I. I. Ershova, in: The 14th Ukrainian Republic Conference on Organic Chemistry [in Russian], Odessa (1982), p. 182.
44. F. Lautenschlaeger, J. Org. Chem., 34, 4002 (1969).
45. Yu. V. Migalina, V. I. Staninets, V. G. Lendel, I. M. Balog, V. A. Palyulin, A. S. Koz'min, and N. S. Zefirov, Khim. Geterotsikl. Soedin., No. 1, 58 (1977).
46. Yu. V. Migalina, I. I. Gryadil', and V. I. Staninets, in: The 14th Ukrainian Conference on Organic Chemistry [in Russian], Odessa (1982), p. 184.
47. A. Toshimitsu, S. Uemura, and M. Ikano, J. Chem. Soc., Perkin Trans. I, No. 5, 1206 (1979).
48. T. S. Barton and R. C. Kippenhaw, J. Org. Chem., 37, 4194 (1972).
49. E. J. Corey and E. Block, J. Org. Chem., 31, 1663 (1966).
50. F. Lautenschlaeger, Can. J. Chem., 44, 2813 (1966).
51. E. D. Weil, K. J. Smith, and R. J. Gruber, J. Org. Chem., 31, 1669 (1966).
52. W. H. Mueller, Angew, Chem., 81, 475 (1969).
53. C. Ganter and J. F. Moser, Helv. Cim. Acta, 51, 300 (1968).
54. G. Haufe and M. Mühlstädt, J. Prakt. Chem., 323, 89 (1981).
55. W. H. Mueller, J. Am. Chem. Soc., 91, 1223 (1969).
56. L. P. Rasteikene, D. I. Greichute, M. G. Lin'kova, and I. L. Knunyants, Usp. Khim., 44, 1041 (1977).
57. G. A. Tolstikov, R. G. Kaptyukova, and L. V. Spirikhin, Zh. Org. Khim., 16, 1408 (1980).
58. F. Lautenschlaeger, J. Org. Chem., 33, 2627 (1968).
59. S. D. Ziman and B. M. Trost, J. Org. Chem., 38, 649 (1973).
60. D. J. H. Smith, J. D. Filnay, and C. R. Hall, J. Org. Chem., 44, 4757 (1979).
61. Yu. V. Migalina, V. G. Lendel, I. M. Balog, and V. I. Staninets, Ukr. Khim. Zh., 47, 1293 (1981).
62. N. S. Zefirov and S. V. Rogozina, Usp. Khim., 42, 423 (1973).
63. Yu. V. Migalina, V. I. Staninets, V. G. Lendel, A. S. Koz'min, and N. S. Zefirov, Khim. Geterotsikl. Soedin., No. 12, 1633 (1977).
64. V. Gomez Aranda, J. Barluenga, G. Asensio, and M. Yus, Tetrahedron Lett., No. 35, 3621 (1972).

65. V. Gomez Aranda, J. Barluenga, M. Yus, and G. Asensio, Synthesis, No. 11, 806 (1974).
66. J. Barluenga, C. Najera, and M. Yus, Synthesis, No. 11, 2559 (1979).
67. R. O. Klaus and C. Ganter, Helv. Chim. Acta, 63, 2559 (1980).
68. J. Barluenga, C. Jiminez, C. Najera, and M. Yus, Chem. Commun., No. 22, 1178 (1981).
69. U. Kashman and A. Rudi, Tetrahedron Lett., No. 32, 2819 (1976).
70. M. Rotem and U. Kashman, Tetrahedron Lett., No. 1, 63 (1978).
71. A. Rudi and U. Kashman, Tetrahedron Lett., No. 25, 2209 (1978).
72. A. Rudi and U. Kashman, Tetrahedron, 37, 4269 (1981).
73. L. D. Quin and E. D. Middlemas, J. Am. Chem. Soc., 99, 8370 (1977).
74. L. D. Quin, E. D. Middlemas, N. S. Rao, R. W. Miller, and A. T. McPhail, J. Am. Chem. Soc., 104, 1893 (1982).
75. R. K. Summerbell and G. Lestina, J. Am. Chem. Soc., 79, 3878 (1957).
76. M. Mühlstädt, P. Schneider, and D. Martinetz, J. Prakt. Chem., 315, 929 (1973).
77. Yu. V. Migalina, V. G. Lendel, A. S. Koz'min, and N. S. Zefirov, Khim. Geterotsikl. Soedin., No. 5, 708 (1978).
78. J. Barluenga, C. Jiminez, C. Najera, and M. Yus, Synthesis, No. 5, 417 (1982).
79. J. Barluenga, C. Najera, and M. Yus, Synthesis, No. 12, 911 (1978).
80. J. Barluenga, C. Najera, and M. Yus, J. Heterocycl. Chem., 17, 917 (1980).
81. J. Barluenga, C. Jiminez, C. Najera, and M. Yus, Synthesis, No. 5, 414 (1982).
82. A. J. Bloodworth and M. F. Loveitt, Chem. Commun., No. 3, 94 (1976).
83. A. J. Bloodworth and M. F. Loveitt, J. Chem. Soc., Perkin Trans. I, No. 6, 522 (1978).
84. A. J. Bloodworth and J. A. Khan, J. Chem. Soc., Perkin Trans. I, No. 11, 2450 (1980).
85. A. J. Bloodworth and J. A. Khan, Tetrahedron Lett., No. 33, 3075 (1978).
86. A. J. Bloodworth and B. P. Leddy, Tetrahedron Lett., No. 8, 729 (1979).
87. J. R. Nixon, M. A. Cudd, and N. A. Porter, J. Org. Chem., 43, 4048 (1978).
88. W. Adam and K. Sakanishi, J. Am. Chem. Soc., 100, 3935 (1978).

SYNTHESIS AND SOME ELECTROPHILIC SUBSTITUTION REACTIONS OF 2-PHENYLOXAZOLE

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A new synthesis of 2-phenyloxazole that includes the preparation of 2-phenyloxazoline and aromatization of the latter by the action of nickel peroxide was developed. It was established that under conditions that exclude protonation electrophilic substitution reactions are directed to the oxazole ring of 2-phenyloxazole; the 5 position is considerably more active than the 4 position.

Relatively little study has been devoted to the investigation of electrophilic substitution reactions in the oxazole series, and the studies that have been made have dealt almost exclusively with disubstituted compounds that bear orientators of the I type (see [1-4]). This creates the idea of the low tendency of oxazoles to undergo electrophilic substitution and also hinders an evaluation of the relative activities of the individual positions of the oxazole ring. However, an examination of even the limited literature data provides evidence that the low activity of oxazoles in electrophilic substitution reactions is due not so much to the nature of the oxazole ring, which includes a "pyridine" nitrogen atom, as to deactivation of the heteroring as a consequence of protonation under the reaction conditions. This is confirmed particularly graphically in the case of nitration, attempts to carry out which were either unsuccessful or led, in the case of aryloxazoles, to the introduction of a nitro group into the benzene ring [5]. Nitration of both rings occurs only in the case of activated 2-dimethylamino-4-phenyloxazole, and 2-dimethylamino-5-nitro-4-(p-nitrophenyl)oxazole is formed [6]. At the same time, 2-aryl-4-substituted oxazoles are brominated quite smoothly by bromine in neutral solvents (benzene, carbon disulfide) [7, 8] and acetic acid [9]; bromine enters the 5 position of the oxazole ring. It must be noted that the yields of bromo-substi-

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