Translated from *Uspekhi Khimii*, **56**, 814-843 (1987) U.D.C. 547.759.2'.3'556.8'594:541.124'127:543.422.6

The Cope Aza-rearrangement in Organic Synthesis

N.M.Przheval'skii and I.I.Grandberg

The latest advances in the application of the Cope aza-rearrangement in organic synthesis are examined and the results of studies on the mechanism of the reaction and of its use in syntheses are surveyed.
The bibliography includes 147 references.

CONTENTS

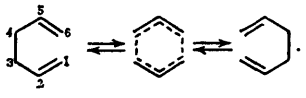
I. Introduction 477
II. The Cope 3-aza-rearrangement 478
III. The Cope 2-aza-rearrangement 481
IV. The Cope 3,4-diaza-rearrangement 484
V. The Cope 2,5-, 2,3-, and 1,3-diaza-rearrangements 485
VI. The Cope polyhetero-rearrangements 486

I. INTRODUCTION

Pericyclic reactions, including sigmatropic rearrangements, have attracted much attention by chemists in recent years.[1-3] In the first place this is because the [3, 3]sigmatropic shift, which embraces also the Cope rearrangement,[4] gives rise to a predictable regiostereoselectivity in the formation of new bonds.[5,6] No less important is also the fact that new approaches to the synthesis of a wide variety of heterocyclic and acyclic structures have been demonstrated and interesting stereochemical features of the rearrangement have been observed with the aid of this reaction.

In the present review we shall consider studies devoted to the theoretical and synthetic aspects of the Cope aza-rearrangement. Mainly studies carried out in 1978–1984, published after the review of Heimgartner et al.[7] which quotes the literature up to 1977 inclusive, are discussed. In certain instances earlier communications are invoked in order to preserve the integrity of the exposition.

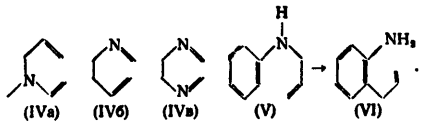
The thermal rearrangement of hexa-1,5-dienes (I), called the Cope rearrangement,[4] belongs to the class of [3, 3]sigmatropic processes[8] which proceed via the six-membered transition state (II):



(I) (II) (III)

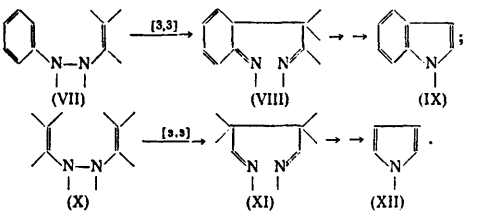
The replacement of one or several carbon atoms in the diene (I) by nitrogen leads to the corresponding aza-hexadiene systems (IVa–c), for the rearrangement of which the term the Cope aza-rearrangement has been proposed.[9]

When 3-azahexa-1,5-diene (V), in which one double bond is incorporated in an aromatic nucleus, undergoes the Cope rearrangement, then reactions of this type are frequently referred to as the Claisen (V) → (VI) amino-rearrangement.[10]



(IVa) (IVб) (IVв) (V) (VI)

On passing to 3,4-diazahexa-1,5-diene, systems of the type of the enehydrazine (VII) or dienehydrazine (X) are produced, whose rearrangement is a stage in the formation of the carbon–carbon bond in the Fischer indole synthesis[11,12] and the Piloty pyrrole synthesis:[13]



(VII) (VIII) (IX)

(X) (XI) (XII)

The transformations (V) → (VI) and (VII) → (IX) can be regarded as the Cope 3-aza- and 3,4-diaza-rearrangements. A general classification of sigmatropic "Cope hetero-rearrangements" has been published.[14]

Apart from the reactions indicated, those involving systems of type (IV), containing heteroatoms (O, S) other than the nitrogen atom, i.e. the Cope oxaza- and thiaza-rearrangements, have been discussed.

The general postulates of the theory of sigmatropic rearrangements developed by Woodward and Hoffmann,[8] mainly for thermal non-catalytic reactions of hydrocarbons, were subsequently extended to both thermal and catalytic reactions of aliphatic and aromatic heterosystems.[15]

The following criteria were mainly used to assign these reactions to the concerted [3, 3]shift type: the first order of the reaction; the large negative activation entropies; comparatively small (by a factor of 20–30) changes in the rate after the introduction of electron-donating or electron-accepting substituents; the inversion of allyl groups; the retention of optical activity in the products when the initial molecule was optically active. The mechanism of the Cope 3-oxa-rearrangement of a series of allyl vinyl[17] and allyl aryl ethers[17] (the aliphatic and aromatic Claisen rearrangements), their thioanalogues,[18] (the Claisen thia-rearrangement), and the allyl esters of carboxylic acids,[19] for example, has been established with the aid of these criteria.

Numerous experimental data obtained in the course of these investigations demonstrated that the Cope rearrangements and the Cope hetero-rearrangements are much faster for charged or highly polarised systems.[1-3,7] Reactions of this type have been called charge-induced[20,21] and charge-accelerated[22] [3, 3 sigmatropic rearrangements.

The charge-induced reactions are in fact of greatest interest for the Cope aza-rearrangements, because they facilitate significantly the conditions under which they can be carried out and increase the yield of products.

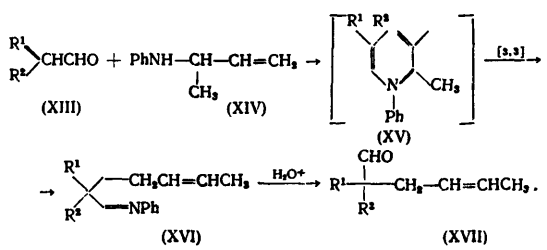
At the same time, as stated in a review,[7] the available information about the mechanism of these reactions is limited. Definite progress has been achieved in this respect only recently (see Sections II–VI).

II. THE COPE 3-AZA-REARRANGEMENT

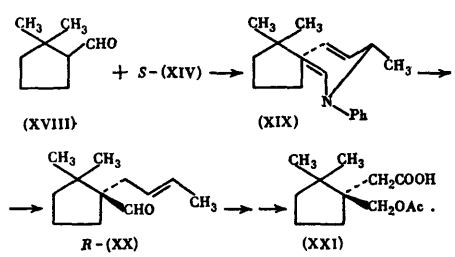
1. The Aliphatic Cope 3-Aza-rearrangement

One of the first examples of the aliphatic Cope 3-aza-rearrangement was described in a study[10] where it was shown that it proceeds via a transition state in the chair conformation. Since the thermal Cope 3-aza-rearrangement usually requires high temperatures, attempts have been made to achieve the reaction under mild conditions using Lewis acids,[23,24] sulphuric acid,[25] and $TiCl_4$ [26] as catalysts.

Thus the reaction of the aldehydes (XIII) with *N*-(1'methylallyl)-aniline (XIV) (benzene, $TiCl_4$) leads to the formation of the intermediate (XV) which rearranges to the imine (XVI), whose hydrolysis affords the aldehyde (XVII):



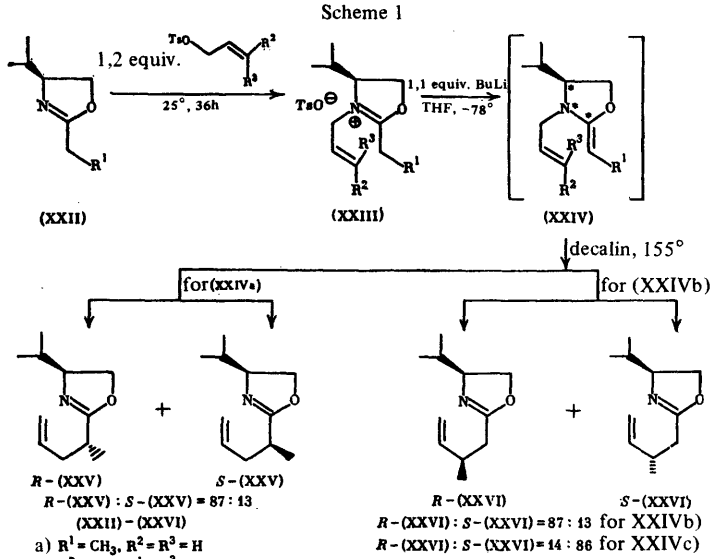
If the optically active amine *S*-(XIV) with $[\alpha]_D^{27} = 1.47°$ is introduced into the reaction with 2,2-dimethylcyclopentanaldehyde (XVIII), then the *trans*-aldehyde (XX) with $[\alpha]_D^{27} = -2.53°$ and having the *R*-configuration is formed via the intermediate *S*-(XIX):[26]



By reduction with sodium tetrahydroborate, acetylation, and oxidation with permanganate, compound (XX) was converted into the acid (XXI), which is an important intermediate in the synthesis of an optically active pheromone.[27]

One of the disadvantages of the above transformation (XV) → (XVII) is the necessity to employ optically pure allyl substrates in order to obtain optically pure products. Furthermore, the chirality in the initial optical centre is lost during the reaction. An attempt to overcome these difficulties has been made in a theoretically and synthetically important study[28] in which asymmetric induction was achieved in the Cope 3-aza-rearrangement by means of an auxiliary reagent. The authors began with the hypothesis that an auxiliary chiral centre bound covalently to the nitrogen atom would create a transition state bias in the Cope aza-rearrangement. In order to enhance to the maximum possible extent the topological influence of the auxiliary chiral reagent, this centre, the nitrogen atom, and the C(1) atom of the vinyl fragment (denoted by an asterisk) were incorporated in the five-membered oxazoline ring:

Scheme 1

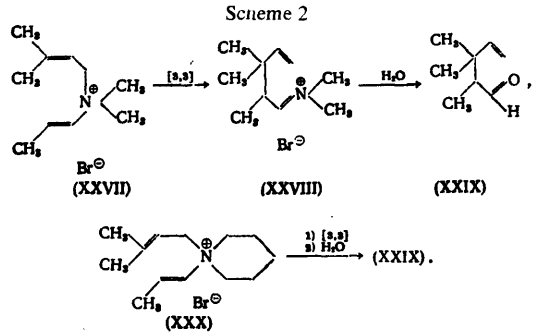


The salts (XXIIIa–c) were obtained from the oxazolines (XXIIa–c) with the aid of allyl toluene-*p*-sulphonates. The neutralisation of the salts (XXIIIa–c) leads to the *NO*-acetals (XXIVa–c) which rearrange in decalin, without isolation, to the oxazolines (XXV) and (XXVI) in yields exceeding 85% (Scheme 1).

The diastereoselectivity of this Cope 3-aza-rearrangement was determined in the following manner. The oxazoline (XXV) was hydrolysed (3 *N* HCl 90 °C, 1.5 h) and the subsequent optical measurement showed that *R*-(−)-2-methylpent-4-enoic acid is formed in excess so that compound (XXIVa) rearranges predominantly to the oxazoline *R*-(XXV). The ratios of the diastereoisomeric oxazolines *R*-(XXV)/*S*-(XXV) and *R*-(XXVI)/*S*-(XXVI) were established by means of high-pressure liquid chromatography. Analysis of the high-resolution ^1H NMR spectra (500 MHz) of the *N*-methyl-oxazolinium salts obtained from compounds (XXV) and (XXVI) by methylation with dimethyl sulphate demonstrated that one of the diastereoisomers is present in 72–74% excess in the rearrangements (XXIVa) → *R*-(XXV), (XXIVb) → *R*-(XXVI), and (XXIVc) → *S*-(XXVI).

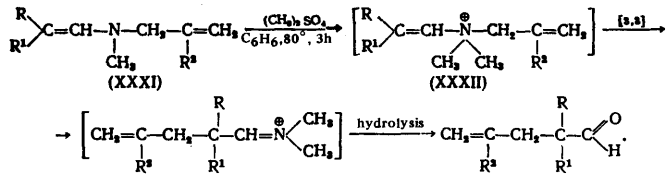
The rearrangement of the enammonium salt (XXVII) under mild conditions (20 °C) under the influence of bases has been described.[29] The hydrolysis of the resulting amine (XXVIII) leads to the aldehyde (XXIX):

Scheme 2



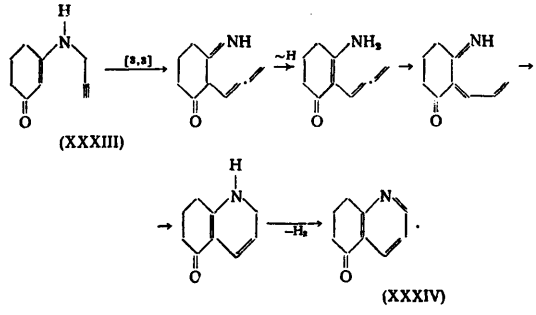
The aldehyde (XXIX) also arises as a result of the Cope 3-aza-rearrangement when a benzene solution of the bromo-derivative (XXX) is maintained at room temperature[29] (Scheme 2).

A promising method for the generation of the quaternary carbon centre under mild conditions with the aid of the Cope 3-aza-rearrangement of the enammonium salts (XXXII) has been proposed:[30]

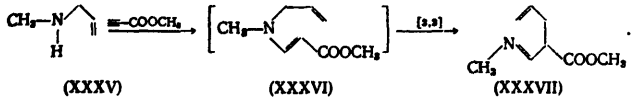


The advantage of this method over that proposed previously[31] is because the allylenamines (XXXI) were obtained by the selective *N*-alkylation of the corresponding allylamines, which made it possible to avoid the difficulties quoted by Opitz et al.[31] associated with the fact that, when vinylamines were used as the initial compounds for the synthesis of structures of type (XXXII), the formation of a mixture of isomers was observed as a result of the simultaneous occurrence of the *C*- and *N*-allylation reactions.

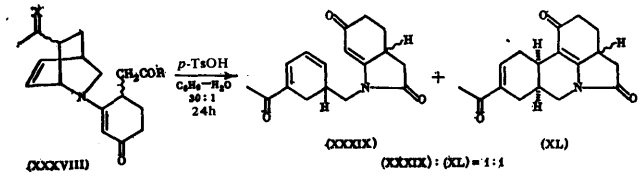
The Cope 3-aza-rearrangement has been used successfully to synthesise the pyridines (XXXIV) from the propargyl-vinylamines (XXXIII):[32]



The addition of the allylamine (XXXV) to methyl propionate with the subsequent Cope 3-aza-rearrangement of the intermediate (XXXVI) leads to the imine (XXXVII):[33]

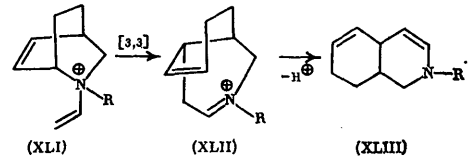


The acid-catalysed reaction of *N*-(β-cyclohexenoyl)isoquinuclidines (XXXVIII), leading to the tetracyclic skeleton of the type of lycorane (XL), has been described in a recently published study[34] in which the investigation[35–39] of the Cope aza-rearrangement initiated previously was continued.



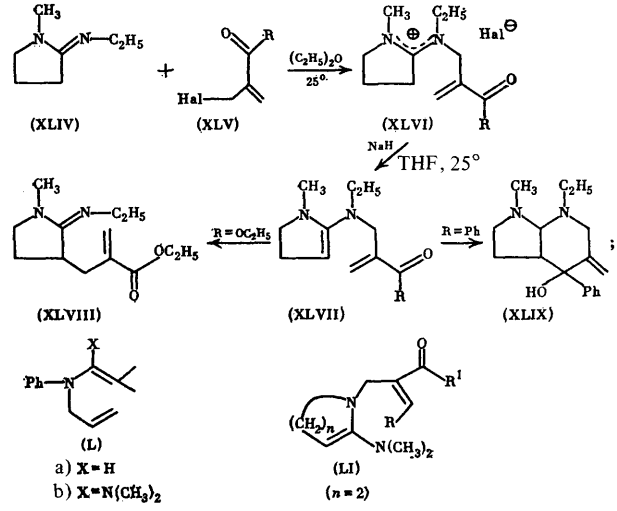
The lactam (XXXIX) is a precursor of the lactam (XL), since only compound (XL) is formed in 40% yield when the reaction is carried out over a period of 48 h.

It is assumed that the hexahydroisoquinoline ring (XLIII) is formed via the elimination of a proton from the intermediate (XLII), which arises from vinylisoquinuclidine (XLI) as a result of the Cope 3-aza-rearrangement:[35]



In certain cases the Cope aza-rearrangement may be accompanied by side reactions (see also Section III). Thus the rearrangement of the amidinium salt (XLVI) via the base (XLVII) leads both to the [3, 3]sigmatropic rearrangement product (XLVIII) and to the product (XLIX) of the intramolecular aldol addition[38] (Scheme 3).

Scheme 3



Systems of type (XLVII) merit attention from the standpoint of the elucidation of the influence of electronic factors on the Cope 3-aza-rearrangement, because they contain both electron-donating (>N–CH_3) and electron-accepting (–C(=O)R) substituents. The dialkylamino-group is known to accelerate the Cope oxa-rearrangement.[2] On the other hand, the rearrangement of the amine (La) take place at 170 °C,[26] while that of the diamine (Lb) occurs at 280 °C.[39]

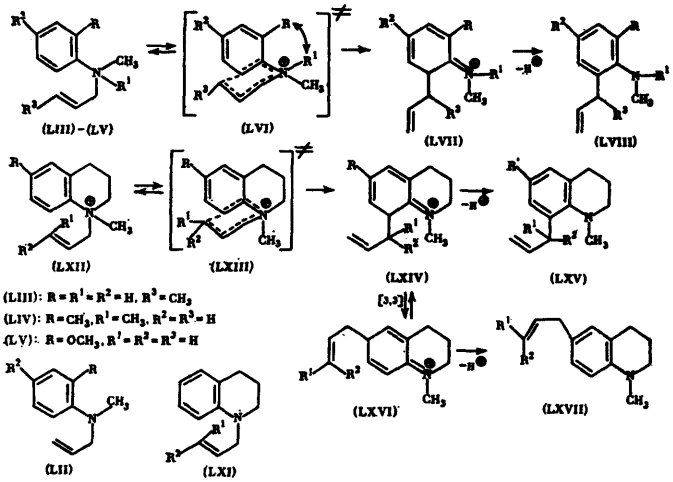
It might have been expected that the simultaneous presence of electron-donating and electron-accepting substituents in a system of type (L) would facilitate the Cope aza-rearrangement. However, it has been found that the rearrangement of the diene (LI), formed from the corresponding amidinium salt on treatment with sodium hydride, takes place even at room temperature and is 10^6–10^8 times faster than the rearrangement of the amine (Lb).[38]

2. Aromatic Cope 3-Aza-rearrangement

The influence of electronic and steric factors on the course of the aromatic Cope 3-aza-rearrangement of *N*-allylanilines [the base (LII) and the salts (LIII)–(LV)][40–42] and the corresponding tetrahydroquinolines (LXI) and (LXII)[42,43] has

been investigated in a series of studies by Japanese workers[40–43] (Scheme 4):

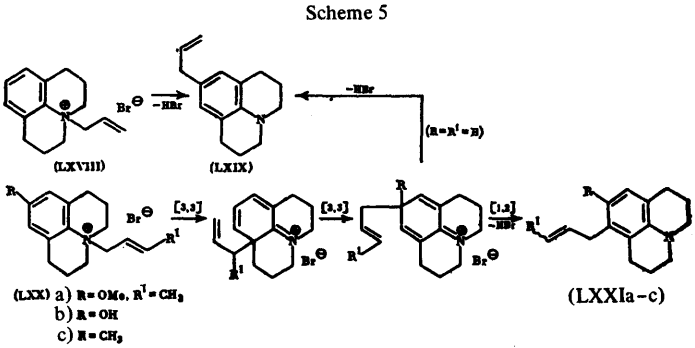
Scheme 4



The concerted reaction mechanism was confirmed in relation to the rearrangement of the *N*-crotyl salt (LIII) (2:1 glycerol–water mixture, 140 °C, 4 h). The reaction proceeds via the transition state (LVI) and the aniline (LVIII) with an inverted allyl group is formed. The rearrangement of the quinolines (LXII) takes place via the transition state (LXIII) in the chair conformation, leading to the intermediate (LXIV), from which the quinolines (LXV) and (LXVII) are formed. The intermediate (LXIV) may undergo the usual Cope rearrangement (LXIV) → (LXVI) → (LXVII), which leads to the formation of 6-substituted quinolines (LXVII) with a high stereoisomeric purity. In contrast to anilines with R=H and the quinolines (LXI) and (LXII), the *ortho*-substituted allylanilines (LIV), (LV) afford mainly deallylation and not rearrangement products, which can be accounted for by the steric interaction between the groups R and R^1 in the transition state (LVI).[42] The decrease in the yield of 8-allylquinolines (LXV) on passing from the unsubstituted to the mono- and di-methylallyl groups is associated with increase in the steric interaction of the alkyl groups with the proton in the 8-position in the quinoline ring in the transition state (LXIII).

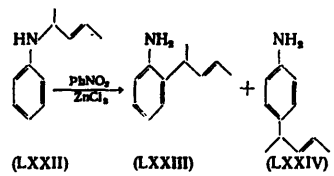
An interesting result has been obtained in the study of the Cope 3-aza-rearrangement of bromo-derivatives of the 4-allyljulolidines (LXVIII) and their 9-substituted analogues (LXXa to c)[41] (Scheme 5). The products (LXXIa–c), involving the rearrangement to the *meta*-position, were discovered first (the analogous Claisen *meta*-rearrangement is known for the reaction of allyl 2,4,6-trimethylphenyl ether in the presence of BCl_3 [44]):

Scheme 5



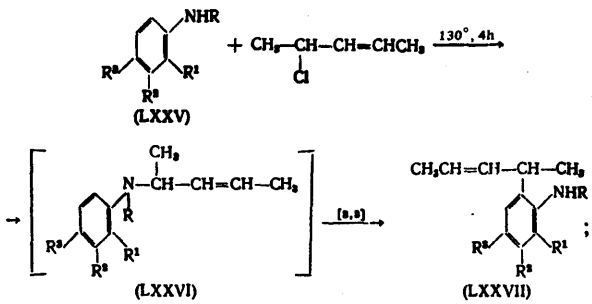
A mechanism involving two consecutive [3, 3]sigmatropic shifts [the transformation (LXVIII) → (LXIX) takes place analogously] and a [1, 2]shift with elimination of a hydrogen bromide molecule has been proposed for the rearrangement (LXX) → (LXXI) (Scheme 5).

The aromatic[45–51] Cope 3-aza-rearrangement of various N-alkenylanilines has been investigated. It has been shown that the rearrangement of *N*-(1-methyl-2-butenyl) aniline (LXXII) is catalysed by the hydrochlorides of aromatic amines and Lewis acids and that the best yield of the corresponding *ortho*- and *para*-alkenylanilines is attained in the presence of $ZnCl_2$ [the yield of (LXXIII) + (LXXIV) is 97%]:[45,50]



An analogous reaction has been achieved for octa,2,7-dienylaniline[46] and *N*-(1-methyl-2-butenyl)-2,5-xylidine.[51]

The rearrangement of *N*-alkenylanilines proved to be an effective method for the synthesis of various *C*-substituted anilines:[47,48]

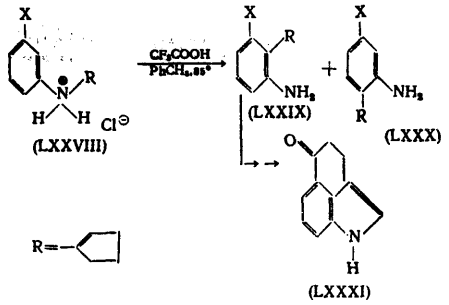


$R^1 - R^3$ = alkyl, halogen, OCH_3,
R = alkyl.

N-Alkenylanilines (LXXVI), formed in the reaction of substituted anilines (LXXV) with 4-chloro-*trans*-pent-2-ene, are immediately converted into the corresponding product (LXXVII) under the reaction conditions.

The kinetics of the acid-catalysed Cope 3-aza-rearrangement of various *N*-allylanilines of type (LXXV) in nitrobenzene have been investigated[49] and it has been shown that in all cases the rearrangement is accompanied by elimination, but that the contribution of the latter is different for different substituents. For equal initial concentrations of aniline and hydrochloric acid, the reaction is described by a first-order equation. The results have been explained from the standpoint of the formation of a contact ion pair from PhNHR.HCl, which can either undergo a rearrangement to 2-allylaniline in the solvent cage or elimination.

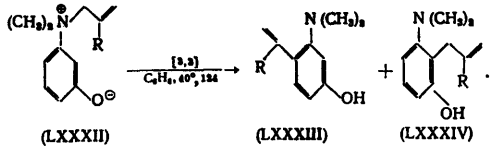
The influence of electron-accepting groups on the regioselectivity of the aromatic Cope 3-aza-rearrangement of *meta*-substituted anilinium salts, (LXXVIII) → (LXXIX) → (LXXX), has been studied:[52]



	a	b	c	d	e
X	—C≡N	CO_2CH_3	NO_2	F	CF_3
(LXXIX):(LXXX)	2.9:1	(LXXIX) not detected	1:10	1:3.7	1:2

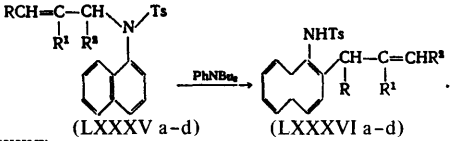
In all cases [with the exception of *m*-cyanoaniline (LXXVIIIa)], the preferential formation of products in the rearrangement to the *p*-position relative to the substituent X was observed. These data have been explained[52] by the steric influence of the group X, because the activation energy for the transition to the isomer (LXXIX) is lower than that for the transition to the isomer (LXXX).[53] The transformation (LXXVIIIa) → (LXXIXa) is of undoubted interest, since it permits the synthesis of the Uhle's ketone (LXXXI), which is a key intermediate on the way to ergot alkaloids.[54]

The [3, 3]sigmatropic rearrangement of the betaine (LXXXII) leads to a mixture of the phenols (LXXXIII) and (LXXXIV), the main product being the isomer (LXXXIII) [(LXXXIII):(LXXXIV) = 4:1].[55]



The exceptionally mild reaction conditions are associated with the possibility of the delocalisation of the charge in the course of the rearrangement.[55]

Japanese workers[56] investigated the influence of substituents in the allyl group on the thermal aromatic Cope 3-aza-rearrangement of *N*-allyl-*N*-tosyl-α-naphthylamines (LXXXV) → (LXXXVI):

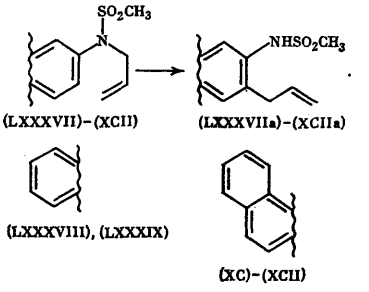


a) R=R¹=H, R²=CH_3
b) R=R²=H, R¹=CH_3
c) R¹=R²=H, R=CH_3
d) R¹=R²=H, R=Ph

The formation of the naphthylamines (LXXXVIa, c, d) from the amines (LXXXVa, c, d) indicates the concerted character of the rearrangement.

In the rearrangement of compounds (LXXXVb), (LXXXVc), and (LXXXVd), the corresponding 4-substituted naphthylamines are formed in addition. The *para*/*ortho* product ratio increases in the series of amines (LXXXVb) < (LXXXVc) < (LXXXVd), which supports the occurrence of consecutive [3, 3]sigmatropic shifts, whose driving force is the steric interaction between the tosylamino-group and the 1-substituted allyl group.

The influence of the aromatic ring on the rate of the thermal Cope 3-aza-rearrangement of *N*-allyl-*N*-methanesulphonylamines [the aniline (LXXXVII), the 1- and 2-naphthylamines (LXXXVIII) and (LXXXIX), and the 2-, 3-, and 9-phenanthrylamines (XC), (XCI), and (XCII)] in *NN*-dibutyl-aniline containing a small amount of triphenylphosphine has been studied:[57]



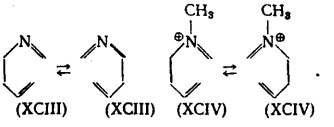
In all cases the rearrangement (LXXXVII) → (XCII) → (LXXXVIIa) → (XCIIa) obeys a first-order kinetic equation and has negative activation entropies, which suggested a concerted process mechanism.[57]

The highest rate of rearrangement has been observed for *N*-allyl-*N*-methanesulphonyl-1-naphthylamine (LXXXVIII) and *N*-allyl-*N*-methanesulphonyl-9-phenanthrylamine (XCII). The data ($\ln k$) obtained are satisfactorily correlated ($r = 0.991$; $s = 0.290$) with the corresponding delocalisation energies.

An analogous correlation of the logarithms of the rate constants with the localisation energies has been observed also for the Claisen rearrangement of the corresponding o-allyl ethers of phenol, naphthol, and phenanthrol ($r = 0.999$; $s = 0.110$).[57]

III. THE COPE 2-AZA-REARRANGEMENT

The Cope 2-aza-rearrangement of 3-butenylimines (XCIII) is degenerate:

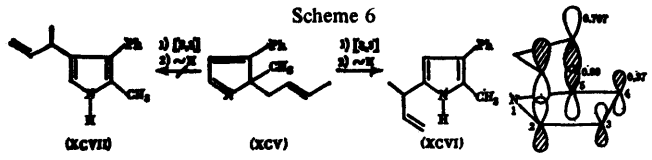


The equilibrium position in substituted systems of type (XCIII) can be established on the basis of "secondary" structural factors such as, for example, steric interactions or the conjugation effect in the reactants and products.[7] A number of instances of rearrangements of systems (XCIII) and (XCIV) have been quoted in a review.[7] It has been established that, as a rule, iminium salts of type (XCIV) rearrange under much milder conditions than the isoelectronic type (I) Cope systems and the rearrangement is faster than the reaction of the uncharged imine (XCIII).[7]

One of the latest studies devoted to the comparative investigations of the Cope rearrangement and its 2-aza-analogue has been carried out by French investigators.[58] The thermolysis of the model 2*H*-pyrrole (XCV), which has no substituents in the 4- and 5- positions (170 °C, 3.5 h), led to the isolation in 90% yield of one product (XCVI), whose formation has been explained by the Cope 2-aza-rearrangement with

subsequent migration of hydrogen:

Scheme 6

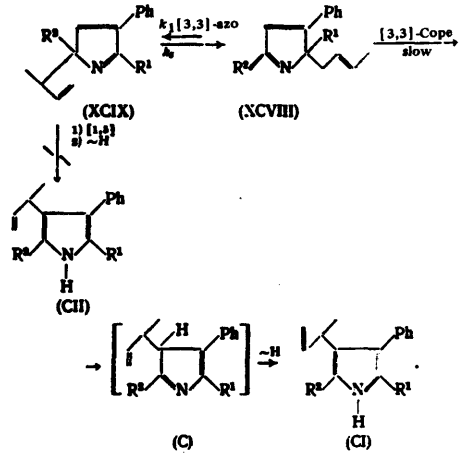


(XCVII) (XCV) (XCVI)

The following conclusions have been reached concerning the possibility of the migration of the *trans*-crotyl group.[58] If the 2*H*-pyrrole is unsubstituted in the 3- and 4-positions, then the [1, 5]shift to the 3-position takes place; when the 4-position is the only one remaining free, the Cope rearrangement [migration to C(4)] is observed; finally, when the 4- and 5-positions are free, only the Cope 2-aza-rearrangement [migration to C(5)] takes place. The absence of the Cope rearrangement (XCV) → (XCVII) has been explained by the difference in the interaction of the frontier orbitals of pyrrole and the allyl group in the two transition states leading respectively to the Cope reaction and the Cope 2-aza-reaction. The difference between the amplitudes of the atomic orbitals of the carbon atoms in the 4- and 5-positions demonstrates the possibility of the migration to the C(4) atom[58] (Scheme 6). The data obtained in the above study made it possible to account for earlier experimental observations.[59,60]

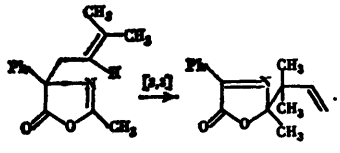
The finding that the thermolysis of the pyrrole (XCVIII) does not lead to the product (XCIX) of the Cope aza-rearrangement[60] can be logically explained by the following factors: firstly, the rate constant k_2 for the reversible isomerisation (XCVIII) ⇄ (XCIX) is higher than k_1; secondly, the slower Cope reaction converts the pyrole (XCVIII) into the 3*H*-pyrrole (C), which isomerises irreversibly to the pyrrole (CI); thirdly the 1,5-migration with formation of the pyrrole (CII) is not observed when the 3-position is substituted[58] (Scheme 7):

Scheme 7



(XCIX) (XCVIII) (CII) (C) (CI)

The Cope 2-aza-rearrangement has been observed in the series of oxazoles.[61] Thus the thermolysis (162 °C, benzene) of allyl-substituted Δ²-oxazolinones leads to the Δ³-oxazolinone system:

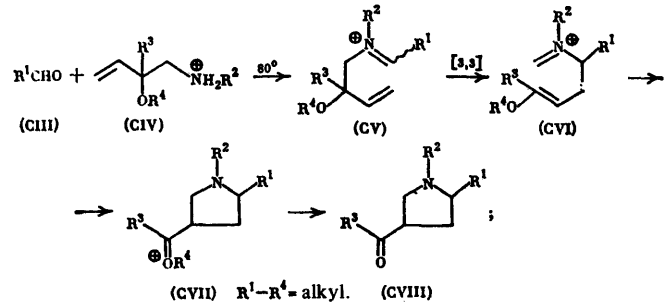


The formation of 2-(1,1-dimethyl-2-propenyl)-Δ³-oxazolinone shows that the reaction proceeds via the [3, 3]sigmatropic and not the [1, 3]sigmatropic shift.[61]

In recent years the Cope 2-aza-rearrangement has been widely used by several groups of investigators for the synthesis of various heterocyclic systems.

A series of studies[62–71] have been devoted to the "directed" Cope 2-aza-rearrangement of charged systems of type (XCIV). The condensation of the aldehyde (CIII) with salts of secondary amines (CIV) leads to the iminium salts (CV), which undergo the [3, 3]sigmatropic rearrangement to the intermediates (CVI), which are further transformed via the oxonium cation (CVII) into the acylpyrrolidines (CVIII) in 80 to 95% yield[62] (Scheme 8):

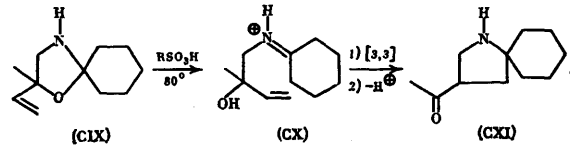
Scheme 8



(CIII) (CIV) (CV) (CVI) (CVII) R^1–R^4 = alkyl. (CVIII)

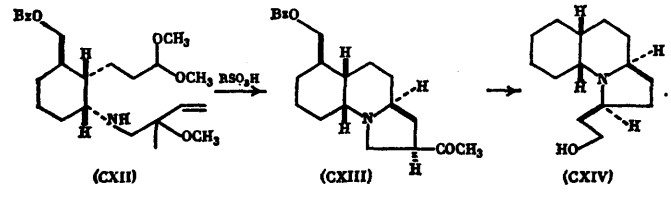
The reaction described constitutes a new method of synthesis of the pyrrolidine ring. The cationic Cope aza-rearrangement and the Mannich reaction have been used consecutively to synthesise poly-substituted pyrrolidines of type (CVIII) (isoprene) derivatives were used as the initial compounds).[69]

It has been shown[63] that the imminium ion (CX) [an analogue of the ion (CV)] can be generated from the oxazolidine precursor (CIX), which permitted the synthesis of substituted 1-aza-spiro-[4, 5]decanes (CXI):



(CIX) (CX) (CXI)

A reaction in which the iminium ion is formed intramolecularly has been used for the single-stage synthesis of the indolizine (CXIII) [(CXII) → (CXIII)],[70] which is a key compound on the way to the alkaloid DL-perhydrogenphyrotoxin (CXIV):

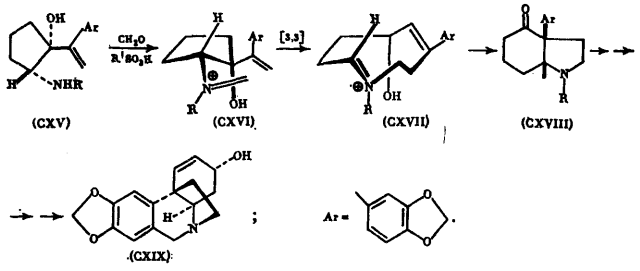


(CXII) (CXIII) (CXIV)

A novel method of synthesis of the pyrrolidine ring, involving the consecutive occurrence of two processes, namely ring expansion and contraction, has been demonstrated in the

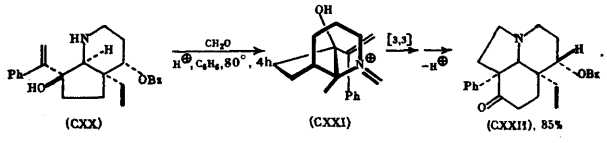
synthesis of *cis* 3a-aryl-octahydroindolones [Scheme 8, (CXV) → (CXVIII), R = $CHPh_2$].[64,66] This reaction makes it possible to achieve a new stereoselective synthesis of the alkaloid crinin (CXIX).

Scheme 8a



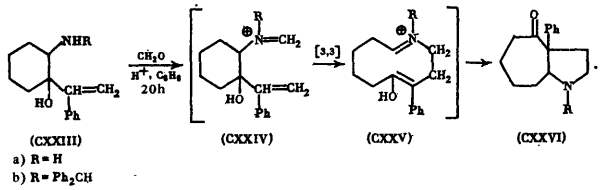
The formation of the *cis*-product (CXVIII) follows from the *trans*-orientation of the amino- and vinyl groups in the amine (CXV). As a result of such *trans*-disposition, the iminium ion undergoes the Cope 2-aza-rearrangement via the only possible transition state in the chair conformation, affording *trans*, *trans*-azacyclonona-1,6-diene (CXVII). The latter is converted stereospecifically into the *cis*-intermediate (CXVIII) after the intramolecular Mannich ring closure.

The above method of ring expansion with the subsequent formation of the pyrrolidine ring has been used successfully for the synthesis of the complex 9a-arylhydrolilodine system [(CXX) → (CXXII)], which is the basis of the *Aspidosperma* alkaloids:[65]



The synthetic possibilities of the cationic Cope 2-aza-rearrangement have also been demonstrated in relation to the stereospecific synthesis of *cis*- and *trans*-3a-aryl-4-oxodecahydrocyclohepta[*b*]pyrroles (CXXVI):[67,68,71]

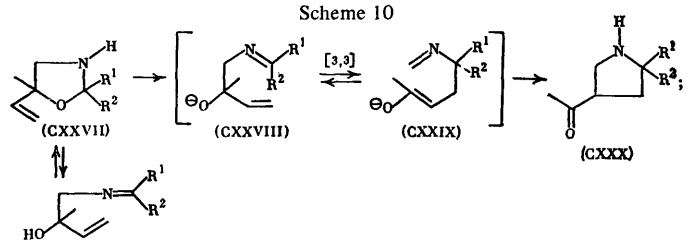
Scheme 9



In the case of the cyclohexanols (CXXIIIa, b), with the *trans*-disposition of the vinyl and amino-groups, the rearrangement leads to the *cis*-pyrrolidine (CXXVI) via the iminium cation (CXXIV) and the intermediate *trans*, *trans*-azacyclodeca-1,7-diene (CXXV) (cf. with Scheme 8a).

Instances of the Cope 2-aza-rearrangement enumerated above (see, for example, Overman and co-workers[62,63]) are either thermal or acid-catalysed processes. However, it has been shown[65] that the above rearrangement can be achieved under exceptionally mild conditions in the presence of a base (Scheme 10):

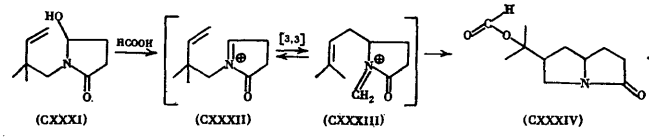
Scheme 10



R^1, R^2 = alkyl, cycloalkyl, aryl.

On heating in THF (at 25 °C) for 24 h in the presence of 1.5 equivalents of KH and 0.1 of an equivalent of 18-crown-6 ether, 5-vinyl-oxazolidines (CXXVII) give rise to the pyrrolidines (CXXX) in 50–90% yield. Potassium hydride converts the oxazolidine (CXXVII) into the intermediate (CXXVIII), which undergoes the [3, 3]sigmatropic rearrangement to the enolate anion (CXXIX), which effects ring closure to 3-acetylpyrrolidine (CXXX) via the intramolecular endocyclic attack on the imino-group. The transformation (CXXVII) → (CXXX) constitutes the first example of the base catalysis of the Cope hydroxy-2-aza-rearrangement (the acceleration of the usual Cope hydroxy-rearrangement by bases is well-known[73–76]).

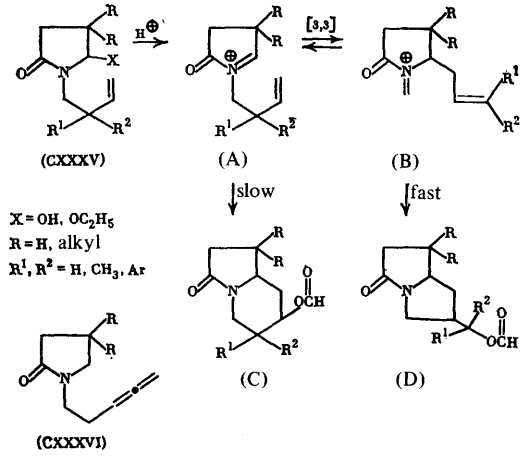
The Cope 2-aza-rearrangement of *N*-acyliminium salts has been used in a number of studies to synthesise heterocyclic systems.[77–81] A rearrangement of this kind was described for the first time in a study[77] where it was shown that treatment of the carbinolamide (CXXXI) with formic acid leads to the pyrrolizidinone (CXXXIV):



A key stage is the Cope 2-aza-rearrangement of the *N*-acyliminium ion (CXXXII) with the subsequent cyclisation of the intermediate (CXXXIII) to the formate (CXXXIV). Later this method was used to synthesise a series of pyrrolizidine bases.[78]

The mechanism of the Cope 2-aza-rearrangement of *N*-acyliminium salts has been investigated[79–81] and it has been established that the pyrrolidinones (CXXXV)–(CXXXVI) can react via two pathways in an acid medium.[79–81] One of them leads to the pyrrolizidine system (P)[80,81] and the other leads to the indolizidines (C) (Scheme 11).

Scheme 11



Both processes proceed via a stage involving the formation of the "secondary" iminium ion (A), which either undergoes the reversible Cope 2-aza-rearrangement to the "primary" iminium ion (B) and then rapidly cyclises (the relevant kinetic data have been published[81]) to the pyrrolizidine (D) or is immediately converted into the indolizidine (C) in a slow stage. The lactams (CXXXVI) containing an allene residue react analogously. The pathway followed in the reactions of the lactams (CXXXV) and (CXXXVI) and the ratio of the products (C) and (D) depend on the nature of the groups R, R^1, and R^2 in the pyrrole ring and in the allyl component of the molecule.[79-81]

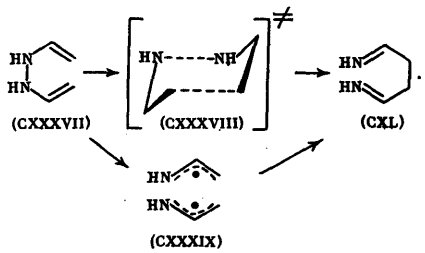
IV. THE COPE 3,4-DIAZA-REARRANGEMENT

As stated in the introduction, the Cope 3,4-diaza-rearrangement of the enehydrazines (VII) and (X) is in essence a stage in the formation of the C–C bond in the Fischer indole synthesis and in the Piloty pyrrole synthesis.

The idea that these reactions be considered from the standpoint of [3,3]sigmatropic rearrangements was first put forward in two reviews.[11,13] A number of studies devoted to the elucidation of the mechanism of the thermal and acid-catalysed Cope 3,4-diaza-rearrangements have been discussed in a monograph.[7] New results demonstrating the validity of the approach to the mechanism of the rearrangement of enehydrazines from the standpoint of the theory of concerted processes have been obtained in recent years.

The rearrangement of the model divinylhydrazine (CXXXVII) has been investigated[82] by the MINDO/3 method (Scheme 12).

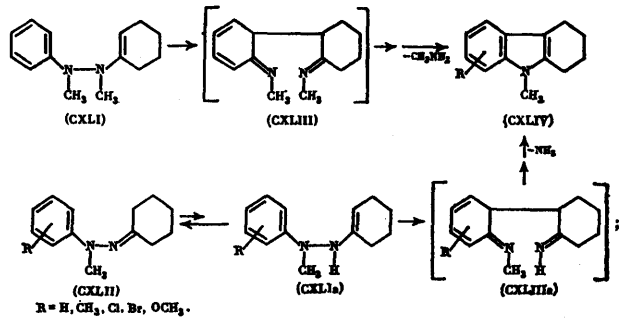
Scheme 12



The MINDO/3 calculation showed that the transition state (CXXXVIII) in the [3,3]sigmatropic migration (CXXXVII) → (CXL) has the chair structure (C_2 symmetry), which indicated an analogy with the rearrangement of hexa-1,5-diene.[8] The multistage mechanism involving the formation of the radical pair (CXXXIX) is energetically less favourable (by 8.2 kcal mol^{-1}) than the concerted mechanism, but such a small difference between the energies of the two migration mechanisms does not allow the complete exclusion of homolysis from the general scheme of the rearrangement[82] (the concerted mechanism of the Cope rearrangement involving hexa-1,5-diene is more favourable to the extent of 33.4 kcal mol^{-1} than the multi-stage mechanism[83]).

Experimental confirmation of the concerted mechanism in the stage involving the formation of the carbon–carbon bond in the Fischer reaction, (CXLI) → (CXLIII) and (CXLIa) to (CXLIIIa), has been obtained on the basis of kinetic data for the rearrangement of *NN'*-dimethyl-*N*-phenyl-*N'*-(1-cyclohexenyl)hydrazine (CXLI) and substituted cyclohexanone *N*-methyl-phenylhydrazones (CXLII) to the tetrahydrocarbazoles (CXLIV)[82,84] (Scheme 13).

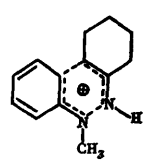
Scheme 13



It has been established that both the thermal and acid-catalysed rearrangements of the enehydrazine (CXLI) are faster than the corresponding reactions of the hydrazones (CXLII), which indicates a significant contribution by the stage (CXLII) → (CXLIa) to the overall rate of the process.[82] Substituents of different types and solvent polarity have little influence on the rate of conversion of the hydrazones (CXLII) into indoles, which proceeds in accordance with a first-order equation and in addition this reaction has fairly high negative activation entropies in all cases.[82,84]

The acidity of the medium has an appreciable influence on the rate of the transformations (CXLI) → (CXLIV) and (CXLII) → (CXLIV). Thus the factor by which the sulphuric acid-catalysed (two moles of acid per mole of reactant) rearrangement of the enehydrazine (CXLI) is accelerated compared with the thermal rearrangement at 60 °C is ~400,[82] which agrees with other data.[85,86]

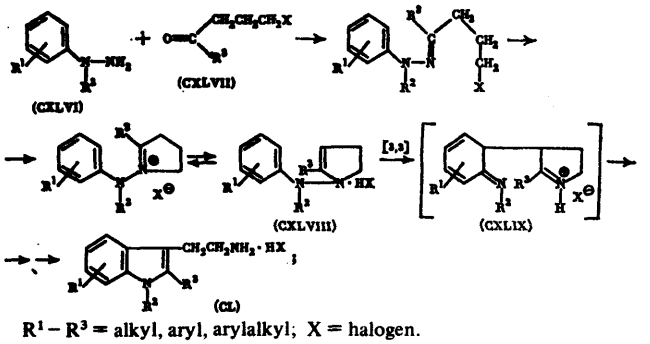
This finding supports the charge-induced pericyclic reaction.[20] This reaction takes place so rapidly because the positive charge in the six-membered transition state (CXLV) is delocalised between the six atoms of the reacting system. An analogous acceleration has been observed in the aromatic Cope 3-aza-rearrangement (Section II).


(CXLV)

The main stage in the synthesis of the tryptamines (CL) and related structures from γ-halogenocarbonyl compounds (CXLVII) (or their δ-analogues) and the arylhydrazines (CXLVI), namely the formation of the C–C bond via the reaction (CXLVIII) → (CXLIX), is also a type of the Cope 3,4-diaza-rearrangement and proceeds via the mechanism of the

[3,3]sigmatropic rearrangement (Scheme 14) (see the relevant review[87] and the literature quoted therein).

Scheme 14



(CXLVI) (CXLVII) (CXLVIII) (CXLIX) (CL)

$R^1 - R^3$ = alkyl, aryl, arylalkyl; X = halogen.

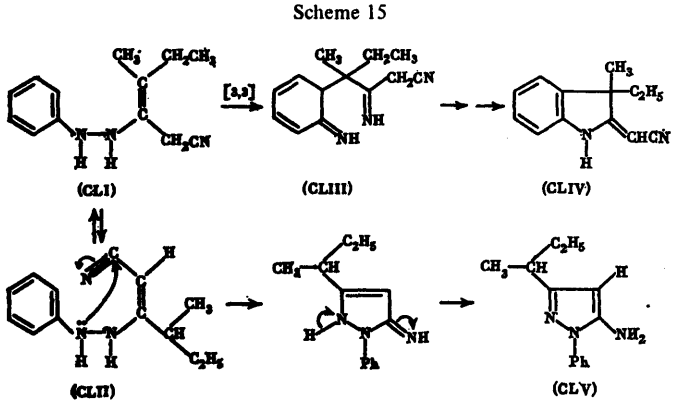
This reaction is a special case of the Fischer indole synthesis without the evolution of ammonia.

Numerous studies of various aspects of the mechanism of the Fischer reaction have been published in recent years. Thus the possibility of the formation of intermediates and their structures has been investigated by ^{13}C NMR,[88] ^{15}N NMR,[89] and mass spectrometry.[90] The influence of the electronic and steric factors on the direction of the indole formation reaction, its mechanism, and the ratio of the isomeric products has been studied.[91-100] The results of the comparative investigation of the Fischer indole synthesis and of the "anomalous" [3,5]- and [5,5]-sigmatropic rearrangement of various o-substituted arylhydrazones and also the migration of the substituents in these systems have been discussed in detail in a review[103] and recent communications.[102,103]

The authors of the above studies[91-103] adhere to the concept of the concerted character of the carbon–carbon bond formation stage in the Fischer reaction.

An interesting example of the Cope 3,4-diaza-rearrangement, namely (CLI) → (CLIII) has been observed for the adduct (CLI) formed in the reaction of phenylhydrazine with an allene nitrile[104] (Scheme 15):

Scheme 15

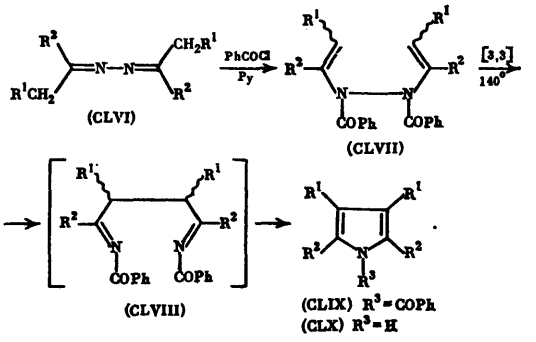


(CLI) (CLIII) (CLIV) (CLII) (CLV)

Since the enehydrazine (CLII) (isolated in a pure state) does not undergo the [3,3]sigmatropic rearrangement and gives rise to the pyrazole (CLV), the formation of the indoline (CLIV) from this enehydrazine can be explained by the prototropic isomerisation (CLII) → (CLI) with the subsequent Cope 3,4-diaza-rearrangement.[104]

The latest advances in the chemistry of the enehydrazines of type (VIII), including their ability to undergo the Cope 3,4-diaza-rearrangement with formation of pyrrole systems, have been analysed in detail in a review.[105]

We shall mention only the study[106] in which a general method has been proposed for the synthesis of the pyrroles (CLIX) and (CLX) from the azines of the enolysable aldehydes and ketones (CLVI) via the concerted thermal rearrangement (CLVII) → (CLVIII) of the benzoyl derivatives (CLVII):

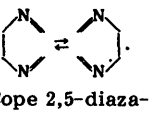


(CLVI) (CLVII) (CLVIII) (CLIX) R^3=COPh (CLX) R^3=H

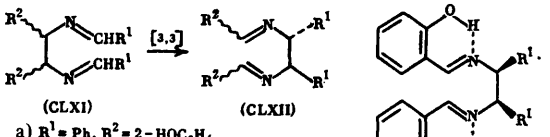
The dienehydrazines (CLVII), which are fairly stable compounds (characterised by ^1H NMR), have been used in the synthesis of the pyrroles (CLIX) without isolation. The hydrazinolysis of the latter made it possible to obtain readily the pyrroles (CLX).

V. THE COPE 2,5-, 2,3-, AND 1,3-DIAZA-REARRANGEMENTS

The Cope 2,5-diaza-rearrangement is in the general case a reversible process and in the absence of substituents is a degenerate process:



However, the directed Cope 2,5-diaza-rearrangement (CLXI) → (CLXII)[107] has been achieved for the double Schiff base (CLXI) containing the 2-hydroxyphenyl group (see also Heimgartner et al.[7]). The subsequent hydrolysis of the diimine (CLXII) leads to a carbonyl compound and *meso*-1,2-diaryl-1,2-ethylenediamine:



(CLXI) (CLXII)

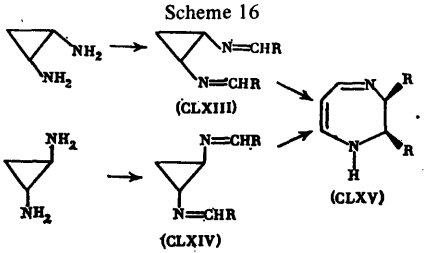
a) R^1 = Ph, R^2 = 2-HOC_6H_4

b) R^1 = 2-C_5H_4N, R^2 = 2-HOC_6H_4

In the given instance the relative stability of the diimines (CLXIIa) and (CLXIIb) is due to the presence of the intramolecular hydrogen bond between the imine nitrogen atom and the phenolic hydroxyl.

The possibility of the thermal Cope 2,5-diaza-rearrangement was first demonstrated in 1965 for *trans*-1,2-bis(benzylideneamino)cyclopropane (CLXIV, R = Ph); the reaction yielded 2,3-diphenyl-2,3-dihydro-1*H*,1,4-diazepine (CLXV)[108] (Scheme 16). However, the stereochemistry of the process remained unelucidated.

Scheme 16

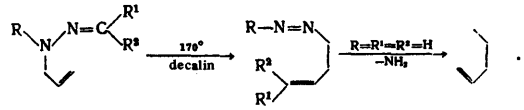


(CLXIII) (CLXIV) (CLXV)

The thermal rearrangement of the *cis*- and *trans*-bisimines (CLXIII) and (CLXIV) (R = t-butyl, phenyl, *p*-tolyl, or mesityl), formed from the corresponding diaminocyclopropanes, has been investigated.[109] It was found that in all cases the only reaction product is a *cis*-substituted dihydrodiazepine (CLXV). This result demonstrates that the Cope 2,5-diaza-rearrangement involves one structure with the same configuration at both C=N bonds [for the imine (CLXIII) this is the *EE*-configuration]. A strong influence of the t-butyl groups on the rearrangement of the bis-imines (CLXIII) and (CLXIV) has been observed. Thus the *cis*-imine (CLXIII, R = t-Bu) is only slowly converted into the diazepine (CLXV) at 100 °C (93 h, yield 49%), while the reaction of *cis*-diaminocyclopropane with benzaldehyde at 0 °C leads to a 90% yield of the diazepine (CLXV, R = Ph). This effect can be explained by the fact that, in the formation of the C(2)–C(3) bond in 2,3-dihydro-1,4-diazepine, the substituents must have an eclipsed disposition, and in the case of two t-butyl groups this destabilises the molecule to the extent of 63 kJ mol^{-1}.[109]

We may note that the Cope 2,5-diaza-rearrangement, illustrated in Scheme 16, constitutes one of the important preparative methods whereby it is possible to achieve ring expansion by four units at once with formation of a heterocyclic system (the Claisen rearrangement and the Cope hydroxy-rearrangement have also been studied for this purpose, but these processes involve the formation of carbocyclic compounds[110]).

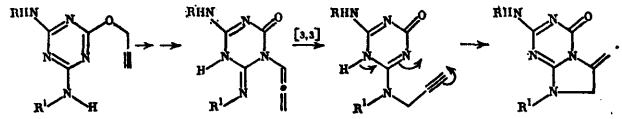
The Cope 2,3-diaza-rearrangement of *N*-alkyl-*N*-allylhydrazones (CLXVI) has been proposed for the preparative synthesis of the γδ-unsaturated azo-compounds (CLXVIII)[111] [the thermolysis of the hydrazone (CLXVII) led to the alkene (CLXIX)[112]]:



(CLXVI), (CLXVII) (CLXVIII) (CLXIX)
(CLXVII): R=R¹=R²=H

The Cope 2,3-diaza-rearrangement has also been observed in the vacuum pyrolysis of *N*-allyloxadiazolinones.[113] For charged systems, this reaction has not been described in the literature.

One of the stages in the thermal[114] and catalytic [$(CF_3COO)_2$][115] transformations of the propargyl ethers of hydroxytriazine (CLXX) into imidazo[1,2-*a*]-1,3,5-triazines (CLXXIII) can be regarded as the Cope 1,3-diaza-rearrangement (CLXXI) → (CLXXII):



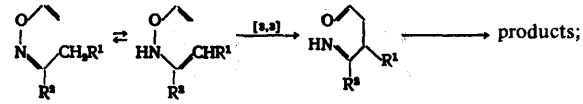
(CLXX) (CLXXI) (CLXXII) (CLXXIII)

VI. THE COPE POLYHETERO-REARRANGEMENTS

The rearrangements of systems containing oxygen and sulphur atoms in addition to nitrogen atoms, i.e. the Cope oxaza- and thiaza-rearrangements are considered in this section.

1. The Cope Oxaza-rearrangement

The [3,3]sigmatropic rearrangement in which the nitrogen–oxygen bond dissociates (thermal rearrangement or rearrangement in the presence of acids) was described in 1971 in relation to *O*-aryl- and *O*-vinyl-oximes:[116]

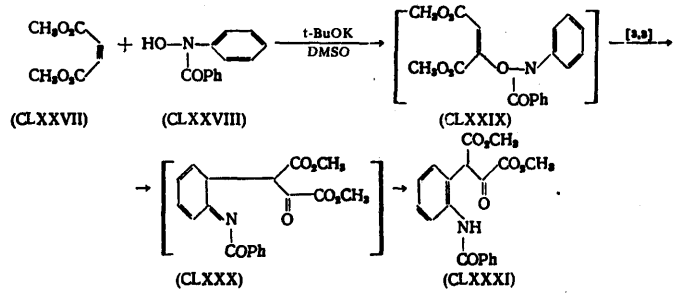


(CLXXIV) (CLXXV) (CLXXVI)
R^1, R^2 = H, alkyl, aryl.

Presumably the fairly severe reaction conditions are necessary only for the isomerisation of the oxime (CLXXIV) → (CLXXV), while the stage involving the rearrangement proper (CLXXV) → (CLXXVI) should occur spontaneously under mild conditions by virtue of the relatively weak and highly polar N–C bond.

Indeed it has been found that if the Cope hetero-system of type (CLXXIX) is produced directly by the addition of *N*-phenylbenzohydroxamic acid (CLXXVIII) to dimethyl acetylenedicarboxylate (CLXXVII), then the rearrangement (CLXXIX) → (CLXXX) takes place readily (20 °C, 1 h) and leads to the ester (CLXXXI) in a high yield[117] (Scheme 17):

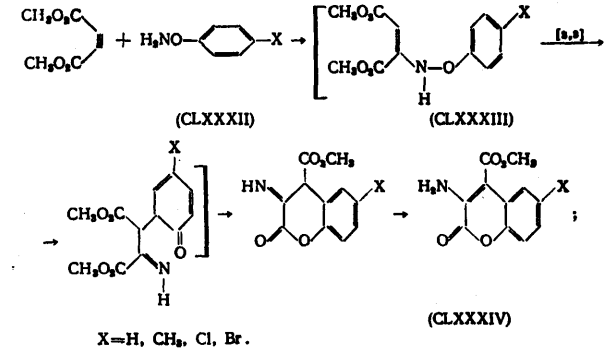
Scheme 17



(CLXXVII) (CLXXVIII) (CLXXIX) (CLXXX) (CLXXXI)

The addition of *p*-substituted *O*-arylhydroxylamines (CLXXXII) to)CLXXVII) (ethanol, 20 °C, 2 h) takes place in the absence of alkaline catalysts and the adduct (CLXXXIII) formed is converted via a stage involving the [3,3]sigmatropic shift into 3-aminocoumarins (CLXXXIV)[117] (Scheme 18):

Scheme 18



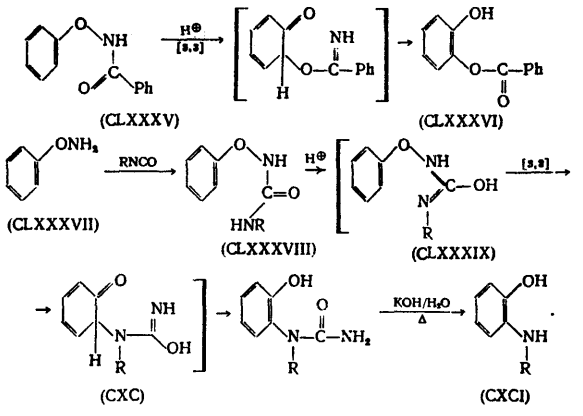
(CLXXXII) (CLXXXIII)

X=H, CH_3, Cl, Br. (CLXXXIV)

The acid-catalysed Cope oxaza-rearrangement is the principal stage in the reactions of derivatives of *O*-arylhydroxylamines described by a group of Japanese investigators[118,119]

(Scheme 19). It is of interest that the hetero-hexa-1,5-diene systems (CLXXXV) and (CLXXXIX) contain three hetero-atoms, which increases their reactivity:

Scheme 19

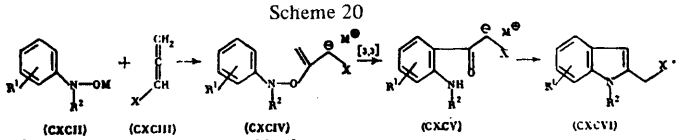


(CLXXXV) (CLXXXVI) (CLXXXVII) (CLXXXVIII) (CLXXXIX) (CXC) (CXCI)

Thus treatment of *N*-benzoyl-O-phenylhydroxylamine (CLXXXV) with a 5:1 mixture of trifluoroacetic and trifluoromethanesulphonic acids for 24 h at 20 °C leads to a high yield of *o*-hydroxyphenyl benzoate (CLXXXVI),[118] while the urea derivative (CLXXXVIII) readily gives rise to 2-alkylaminophenols (CXCI) in dichloromethane at room temperature.[119]

The Cope oxaza-rearrangement has been used in a number of instances for the synthesis of the indole ring.[120–123] 2-Substituted indoles (CXCVI) are readily formed from derivatives of *N*-phenylhydroxylamine (CXCII) and allenes with electron-accepting substituents (CXCIII).[120] The key stage in this synthesis is the formation of *o*-substituted anilines (CXCV) via the [3,3]sigmatropic rearrangement (CXCIV) → (CXCV) (Scheme 20):

Scheme 20



(CXCII) (CXCIII) (CXCIV) (CXCV) (CXCVI)

R^1 = H, 4-CH_3, 3-OH, 4-Cl; X = SO_2Ph

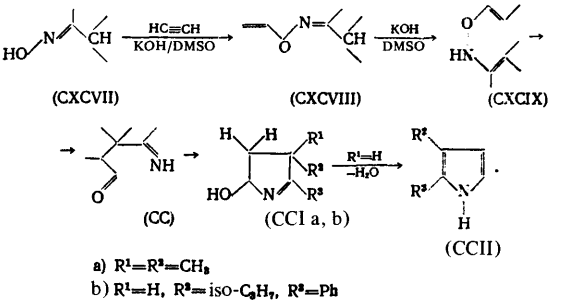
R^2 = $COCH_3$, $COCH_2Ph$, C_2H_5; M = Li, Na, K

The anilide (CXCV, R^1 = 4-CH_3, R^2 = $COCH_3$, X = So_2Ph) has been obtained in 90% yield from the corresponding salt of the hydroxamic acid (CXCII) at room temperature in the course of 10 min while in the reaction involving the use of *N*-alkylphenylhydroxylamines (R^1 = H, R^2 = C_2H_5) spontaneous conversion into the indole (CXCVI) was observed.

An additional cause of the extremely great ease of the Cope oxaza-rearrangement (CXCIV) → (CXCV) (apart from the lability of the N–O bond) is the presence in the molecule of compound (CXCIV) of a carbanionic centre, which is known to accelerate the Cope rearrangement[124] and the Cope hydroxy-rearrangement.[125] Derivatives of *N*-phenylhydroxylamine have also been used to synthesise 2,3-unsubstituted indoles,[121] pyrrolo[1,2-*a*]indole,[122,123] and 2-substituted *N*-acylindoles.[126,127] All the reactions indicated proceed via a stage involving the [3,3]sigmatropic shift, analogous to that illustrated in Scheme 20.

The Cope oxaza-rearrangement of derivatives of *N*-aryl-hydroxylamine has also been used for the regioselective acyl-amination of the benzene ring[128] and the synthesis of *o*-acyl-oxyanilides.[129]

Data confirming the concerted variant of the mechanism of the reaction involving the formation of pyrroles from ketoximes and acetylene[132] proposed previously[131] have been published:[130]



(CXCVII) (CXCVIII) (CXCIX) (CC) (CCI a, b) (CCII)

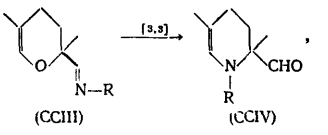
a) R^1=R^3=CH_3

b) R^1=H, R^3=iso-C_5H_7, R^2=Ph

The vinyloxyimine (CXCVIII), obtained from the ketoxime (CXCVII) and acetylene in the superbasic catalytic system KOH–dimethyl sulphoxide system, isomerises to the *ON*-divinylhydroxylamine (CXCIX), which undergoes the Cope oxaza-rearrangement to the intermediate (CC), which has been isolated in the form of the dihydropyrrole (CCI). On heating, the latter is readily converted into the pyrrole (CCII).[130]

Apart from the examples of the Cope oxaza-rearrangement, occurring with dissociation of the N–O bond, which has been described above, reactions are known for the hexa-1,5-diene system in which the nitrogen and oxygen atoms are not linked directly to one another.

Thus dihydropyranimines (CCIII) have been made to undergo a thermal (200–250 °C) rearrangement to the aldehydes (CCIV) via the mechanism of the Cope oxaza-rearrangement:[133]

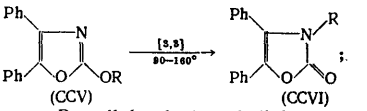


(CCIII) (CCIV)

where R = s-butyl, benzyl, phenyl, or cyclohexyl.

An analogous scheme has been proposed for the rearrangement of *O*-cyclohexynyl carbimidates.[134]

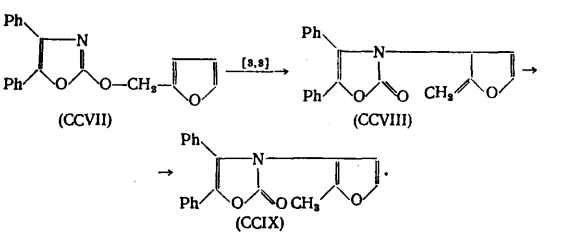
The thermal rearrangement of 2-allyloxyoxazoles (CCV) to 2-oxazolinones (CCVI) has been described:[135,136]



(CCV) (CCVI)

R = allyl, substituted allyl.

The hypothesis that the reaction (CCV) → (CCVI) proceeds via the stage of the [3,3]sigmatropic rearrangement has been confirmed by the isolation of the intermediate (CCVIII) on heating the oxazole (CCVII) in a benzene–pyridine mixture:[136]

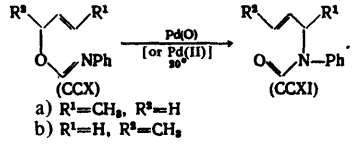


(CCVII) (CCVIII) (CCIX)

On heating or in the presence of acids, the adduct (CCVIII) is converted into the oxazolinone (CCIX).

The use of the complex palladium catalysts $Pd(PPh_3)_4$ and $Pd(PhCN)_2Cl_2$ makes it possible to carry out the Cope oxaza-rearrangement under mild conditions.[137] *O*-allyl *N*-phenyl-formimidates (CCX) readily rearrange at room temperature

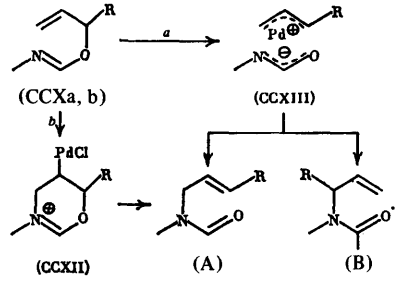
to the corresponding *N*-allyl-*N*-phenylformamides (CCXI):



It has been shown that the regioselectivity of the rearrangement (CCX) → (CCXI) depends on the nature of the palladium complex. Thus catalysis by the palladium(II) complex of the rearrangement of the imidates (CCXa) and (CCXb) leads solely to the corresponding formamides (CCXIa) or (CCXIb), while a zerovalent palladium complex affords in both cases a 2:1 mixture of the products (CCXIa) and (CCXIb) (it is noteworthy that the stereochemistry of the process has not been rigorously established.

These results can be explained by two possible mechanisms of the interaction of the palladium complex with the hexadiene system (CCX)[137] (Scheme 21):

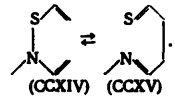
Scheme 21



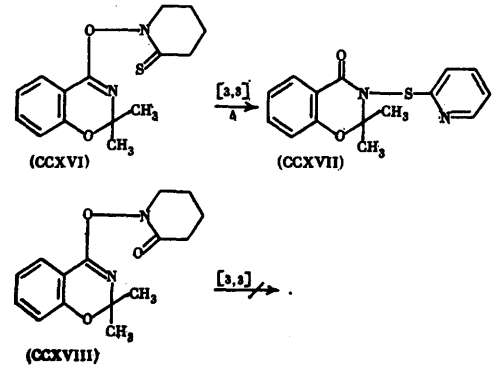
The zerovalent palladium complex catalyses the rearrangement proceeding via the formation of the allyl π-complex (CCXIII) by its oxidative addition to the C–O bond of the formimidate (pathway *a*). There is then a possibility of the formation of two isomers (A) and (B). On the other hand, the palladium(II) complex tends to form the six-membered intermediate (CCXII) (pathway *b*), which leads to only one product (A) [an analogous mechanism has been proposed for the Cope rearrangement catalysed by palladium(II)[138] and mercury(II)[139] complexes].

2. The Cope Thiaza-rearrangement

The Cope thiaza-rearrangement has a number of features which distinguish it from the oxaza-analogue. Firstly, systems of type (CCXIV), for which the transformation (CCXIV)→ (CCXV) would be possible (see, for example, Padwa and Cohen[136]), are unknown:

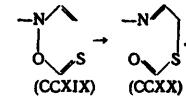


On the other hand, the formation of the S–N bond [i.e. the transition (CCXV) → (CCXIV), which has not been observed for the *ON*-system] via the thermal [3,3]sigmatropic rearrangement of the benzoxazine (CCXVI) to the benzoxazinone (CCXVII) has been described:[140]

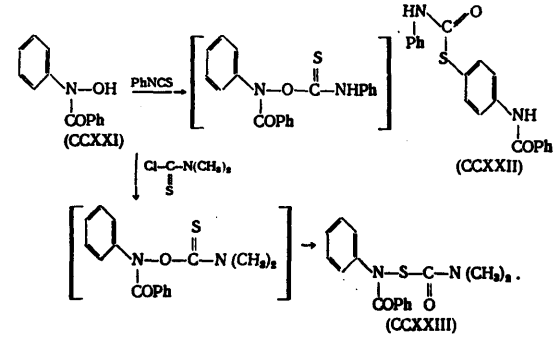


The possibility of the reaction (CCXVI) → (CCXVII) evidently arises not only from the presence of four heteroatoms and the labile N–O bond in the reacting system (CCXVI) but also from the adequate stability of the N–S bond formed, because the benzoxazine (CCXVIII) is not involved in a similar rearrangement.[140]

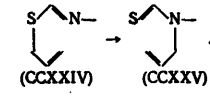
At the same time the attempts to achieve a concerted reaction of the type (CCXIX) → (CCXX) were unsuccessful:



Thus the interaction of *N*-benzoyl-*N*-phenylhydroxylamine (CCXXI) with phenyl isothiocyanate[141] and dimethylthiocarbamoyl chloride[142] led to the formation of the products of the *n*-rearrangement [compound (CCXVII)] and 1,3-migration [compound (CCXXIII)] respectively, which virtually rules out a concerted mechanism:



The rearrangement of *S* allyl thiomidates (CCXXIV) → (CCXXV) has been investigated in a number of studies:[143–147]



It has been shown[143] that the rearrangement of allylthiocaprolactam proceeds via a zwitter-ionic intermediate and not via a concerted mechanism.

Palladium(II) salts [$PdCl_2$ or $PdCl_2(PhCN)_2$ [144]] **proved to be effective catalysts of the Cope thiaza-rearrangement of *S*-allyl thioimidates:**

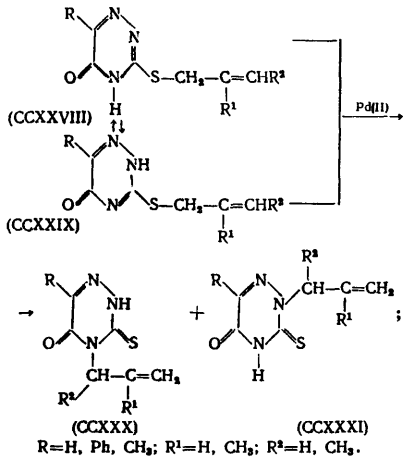


(CCXXVI) (CCXXVII)

Thus the *S*-allyl thioimidate (CCXXVI) is converted quantitatively into the *N*-allylthioamide (CCXXVII) in the presence of a bivalent palladium salt, while the usual thermal reaction (150 °C, decalin) leads only to the product of the isomerisation with respect to the double bond in the allyl group. The reaction mechanism proposed by the authors[147] includes the formation of a six-membered intermediate analogous to that presented in Scheme 21.

The Cope thiaza-rearrangement of 3-allylthio-4*H*-1,2,4-triazin-5-one (CCXXVIII) and 3-allylthio-2*H*-1,2,4-triazin-5-one (CCXXIX), catalysed by palladium(II) complexes, leads to a mixture of the thiones (CCXXX) and (CCXXXI) as a result of the tautomeric equilibrium (CCXXVIII) ⇄ (CCXXIX)[146,147] (Scheme 22).

Scheme 22



R=H, Ph, CH_3; R^1=H, CH_3; R^2=H, CH_3.

During the preparation of the manuscript, a number of studies of the mechanism and synthetic use of the aliphatic[148–151] and aromatic[152–155] Cope 3-aza-rearrangements have been published. The Cope 2-aza-rearrangement has been investigated in relation to the cyclisation of *N*-acyliminium salts[156,157] and a series of oxazoline derivatives.[158] The fairly rare Cope 1-aza-rearrangement, achieved under the conditions of flash vacuum thermolysis, has been described.[159] The Cope oxaza-rearrangement has been investigated[160–162] and the thiaza-rearrangement has been used to synthesise condensed thiazole systems[163–164] and also for the synthesis of the indole ring.[165,166]

REFERENCES

1. S.J.Rhoads and N.R.Raulins, Organic Reactions, 1975, **22**, 61.
2. P.E.Ziegler, Acc.Chem.Res., 1977, **10**, 227.
3. C.B.Bennett, Synthesis, 1977, 589.
4. A.C.Cope and E.M.Hardy, J.Amer.Chem.Soc., 1940, **62**, 441.
5. H.-J.Hansen and H.Schmid, Tetrahedron, 1974, **30**, 1959.
6. P.A.Barlett, Tetrahedron, 1980, **36**, 3.
7. H.Heimgartner, H.-J.Hansen, and H.Schmid, in "Iminium Salts in Organic Chemistry (Edited by H. Böhme and H.G.Viehe), Wiley Intersci., New York, 1979, p.655.
8. R.B.Woodward and R.Hoffmann, "Conservation of Orbital Symmetry" (Translated into Russian), Izd. Mir, Moscow, 1971.
9. K.Winterfeldt, Fortschr.Chem.Forsch., 1970, **16**, 75.
10. R.K.Hill and N.W.Gilman, Tetrahedron Lett., 1967, 1421.
11. B.Robinson, "The Fischer Indole Synthesis", Wiley-Intersci., New York, 1982.
12. Yu.P.Kitaev and T.V.Troepol'skaya, Khim.Geterotsikl. Soed., 1978, 1011.
13. I.I.Grandberg, Izv.Timiryazev, Sel'skokhoz.Akad., 1972(5), 188.
14. F.Vögtle and E.Goldschmitt, Chem.Ber., 1976, **109**, 1.
15. T.Gilchrist and R.C.Storr, "Organic Reactions and Orbital Symmetry" (Translated into Russian), Izd. Mir, Moscow, 1976, p.297.
16. C.J.Burrow and B.K.Carpenter, J.Amer.Chem.Soc., 1981, **103**, 6983.
17. M.D.Kirk and G.Korver, J.Amer.Chem.Soc., 1979, **101**, 2746.
18. A.P.Anisimov and E.A.Viktorova, Khim.Geterotsikl. Soed., 1980, 435.
19. E.S.Lewis, J.T.Hill, and E.R.Newman, J.Amer. Chem.Soc., 1968, **90**, 662.
20. U.Widmer, J.Zsindely, H.-J.Hansen, and H.Schmid, Helv.Chim.Acta, 1973, **56**, 75.
21. U.Widmer, H.-J.Hansen, and H.Schmid, Helv.Chim. Acta, 1973, **56**, 1895.
22. U.Widmer, H.-J.Hansen, and H.Schmid, Helv.Chim. Acta, 1973, **56**, 2644.
23. J.Borgulya, R.Madeja, P.Fahrni, H.-J.Hansen, H. Schmid, and R.Barner, Helv.Chim.Acta, 1973, **56**, 14.
24. M.Schmid, H.-J.Hansen, and H.Schmid, Helv.Chim. Acta, 1973, **56**, 105.
25. S.Jolidon and H.-J.Hansen, Helv.Chim.Acta, 1977, **60**, 978.
26. R.K.Hill and H.N.Khatri, Tetrahedron Lett., 1978, **19**, 4337.
27. J.Smolanoff, A.F.Klugl, J.Meinwald, A.McPhail, R.W. Miller, K.Hicks, and T.Eisner, Science, 1975, **188**, 734.
28. M.J.Kurth and O.H.W.Decker, Tetrahedron Lett., 1983, **24**, 4535.
29. T.Laird, W.D.Ollis, and I.O.Sutherland, J.Chem. Soc., Perkin Trans.I, 1981, 1477.
30. J.C.Gilbert and K.P.A.Senaratne, Tetrahedron Lett., 1984, **25**, 2303.
31. C.Opitz, H.Hellmann, H.Mildenberger, and M.Suhr, Annalen, 1961, **649**, 36.
32. K.Berg-Nielsen and L.Skattebol, Acta Chem.Scand., 1978, **32**, 553.
33. K.Hayakawa and S.Motohiro, J.Amer.Chem.Soc., 1981, **103**, 4605.
34. Y.Chen, P.L.Huesmann, and P.S.Mariano, Tetrahedron Lett., 1983, **24**, 1021.
35. P.S.Mariano, D.Dunaway-Mariano, P.L.Huesmann, and R.Beamer, Tetrahedron Lett., 1977, **18**, 4299.
36. P.S.Mariano, D.Dunaway-Mariano, and P.L.Huesmann, J.Org.Chem., 1979, **44**, 124.
37. Y.Chen, P.S.Mariano, G.M.Little, D.O'Brien, and P.L.Huesmann, J.Org.Chem., 1981, **46**, 4643.
38. R.Gompper and B.Kohl, Angew.Chem., 1982, **94**, 202.
39. J.Ficini and C.Barbara, Tetrahedron Lett., 1966, **7**, 6425.

40. H.Katayama, Chem.Pharm.Bull., 1978, **26**, 2027.
41. H.Katayama, Chem.Comm., 1980, 1009.
42. H.Katayama and N.Takatsu, Chem.Pharm.Bull., 1981, **29**, 2465.
43. H.Katayama, Y.Tachikawa, N.Takatsu, and A.Kato, Chem.Pharm.Bull., 1983, **31**, 2220.
44. P.Fuhrni, A.Habich, and H.Schmid, Helv.Chim. Acta, 1960, **43**, 448.
45. I.B.Abdrakhmanov, V.M.Sharafutdinov, I.A.Sagitdinov, and G.A.Tolstikov, Zhur.Org.Khim., 1979, **15**, 2601.
46. I.B.Abdrakhmanov, R.N.Fakhretdinov, R.I.Khusnutdinov, and U.M.Dzhemilev, Zhur.Org.Khim., 1981, **17**, 2604.
47. I.B.Abdrakhmanov, V.M.Sharafutdinov, N.G.Nigmatullin, I.A.Sagitdinov, and G.A.Tolstikov, Zhur. Org.Khim., 1982, **18**, 1466.
48. I.B.Abdrakhmanov, V.M.Sharafutdinov, and G.A. Tolstikov, Izv.Akad.Nauk SSSR, Ser.Khim., 1982, 2160.
49. I.B.Abdrakhmanov, V.M.Sharafutdinov, N.G.Nigmatullin, A.G.Mustafin, Z.N.Saraeva, and G.A.Tolstikov, Izv.Akad.Nauk SSSR, Ser.Khim., 1983, 1273.
50. I.B.Abdrakhmanov, V.M.Sharafutdinov, and G.A. Tolstikov, Zhur.Org.Khim., 1984, **20**, 620.
51. I.B.Abdrakhmanov, T.B.Shabaeva, A.G.Mustafin, and G.A.Tolstikov, Zhur.Org.Khim., 1984, **20**, 663.
52. S.J.Danishefsky and G.B.Phillips, Tetrahedron Lett., 1984, **25**, 3159.
53. L.M.Harwood, Chem.Comm., 1983, 530.
54. J.Rebec, D.F.Tai, and Y.-K.Shue, J.Amer.Chem. Soc., 1984, **106**, 1813.
55. W.D.Ollis, R.Somanathan, and I.O.Sutherland, J. Chem.Soc., Perkin Trans.I, 1982, 893.
56. S.Inada, R.Kurata, T.Ishida, T.Uda, and M.Okazaki, J.Chem.Soc.Japan, Chem.Ind.Chem., 1978, 723.
57. S.Inada and Y.Sodeyama, J.Chem.Soc.Japan, Chem. Ind.Chem., 1978, 571.
58. A.Laurent, F.Mison, A.Nafti, and N.Pellissier, Tetrahedron Lett., 1982, **23**, 655.
59. J.M.Patterson, J.D.Ferry, J.W.de Haan, and M.R. Boyd, J.Amer.Chem.Soc., 1975, **97**, 360.
60. A.Padwa, P.Mison, A.Nafti, and N.Pellissier, Tetrahedron Lett., 1979, **20**, 1587.
61. A.Padwa, M.Akiba, L.A.Cohen, and J.G.MacDonald, Tetrahedron Lett., 1981, **22**(26), 2435.
62. L.E.Overman and M.Kakimoto, J.Amer.Chem.Soc., 1979, **101**, 1310.
63. L.E.Overman, M.Kakimoto, and M.Okawara, Tetrahedron Lett., 1979, 4041.
64. L.E.Overman and L.T.Mendelson, J.Amer.Chem.Soc., 1981, **103**, 5579.
65. L.E.Overman, M.Sworin, L.S.Bass, and J.Clardy, Tetrahedron, 1981, **37**, 4041.
66. L.E.Overman, L.T.Mendelson, and L.A.Flippin, Tetrahedron Lett., 1982, **23**, 2733.
67. L.E.Overman and E.J.Jacobsen, Tetrahedron Lett., 1982, **23**, 2737.
68. L.E.Overman and E.J.Jacobsen, Tetrahedron Lett., 1982, **23**, 2741.
69. L.E.Overman, M.Kakimoto, M.E.Okuzaki, and P.Meier, J.Amer.Chem.Soc., 1983, **105**, 6222.
70. L.E.Overman and C.Fukaya, J.Amer.Chem.Soc., 1980, **102**, 1454.
71. L.E.Overman, E.J.Jacobsen, and K.J.Doedens, J.Org. Chem., 1983, **48**, 3393.
72. M.Kakimoto and M.Okawara, Chem.Letters, 1979, 1171.
73. D.A.Evans and A.M.Golob, J.Amer.Chem.Soc., 1975, **47**, 4765.
74. D.Seebach, K.H.Geiss, and M.Pohmakotr, Angew. Chem.Int.Ed., 1976, **15**, 437.
75. W.C.Still, J.Amer.Chem.Soc., 1977, **99**, 4186.
76. D.A.Evans, D.J.Baillargeon, and J.V.Nelson, J. Amer.Chem.Soc., 1978, **100**, 2242.
77. D.J.Hart and Y.M.Tsai, Tetrahedron Lett., 1981, **22**, 1567.
78. D.J.Hart and T.K.Yang, Tetrahedron Lett., 1982, **23**, 2761.
79. P.M.M.Nossin and W.N.Speckamp, Tetrahedron Lett., 1981, **22**, 3289.
80. P.M.M.Nossin, J.A.M.Hamersma, and W.N.Speckamp, Tetrahedron Lett., 1982, **23**, 3807.
81. H.Ent, H.de Koning, and W.N.Speckamp, Tetrahedron Lett., 1983, **24**, 2109.
82. N.M.Przheval'skii, M.E.Kletskii, I.I.Grandberg, and L.Yu.Kostromina, Khim.Geterotsikl.Soed., 1985, 779.
83. M.J.S.Dewar, G.P.Ford, M.L.McKee, H.Rzepa, and L.A.Wade, J.Amer.Chem.Soc., 1977, **99**, 5069.
84. N.M.Przheval'skii, L.Yu.Kostromina, and I.I.Grandberg, Khim.Geterotsikl.Soed., 1985, 1207.
85. P.Schiess and A.Greeder, Helv.Chim.Acta, 1974, **57**, 2643.
86. P.Schiess and E.Sendi, Helv.Chim.Acta, 1978, **61**, 1364.
87. I.I.Grandberg, Zhur.Org.Khim., 1983, **19**, 2439.
88. A.W.Douglas, J.Amer.Chem.Soc., 1978, **100**, 6463.
89. A.W.Douglas, J.Amer.Chem.Soc., 1979, **101**, 5676.
90. G.L.Glich and R.G.Cooks, J.Amer.Chem.Soc., 1978, **100**, 6720.
91. F.M.Miller and W.N.Schinske, J.Org.Chem., 1978, **43**, 3384.
92. G.W.B.Reed, P.T.W.Cheng, and S.McLean, Canad. J.Chem., 1982, 419.
93. I.I.Grandberg and V.I.Sorokin, Uspekhi.Khim., 1974, **43**, 266 [Russ.Chem.Rev., 1974(2)].
94. N.N.Suvorov, V.I.Shkil'kova, and M.Ya.Podkhalyuzina, Zhur.Org.Khim., 1981, **17**, 745.
95. D.Binder, B.C.Prager, and C.R.Noe, J.Chem.Res. Synop., 1981(5), 140.
96. G.Baccolini, G.Bartoli, E.Marotta, and P.E.Todesco, J.Chem.Soc., Perkin Trans.I., 1983, 2695.
97. N.M.Przheval'skii, I.I.Grandberg, and N.A.Klyuev, Khim.Geterotsikl.Soed., 1976, 1065.
98. N.M.Przheval'skii, I.I.Grandberg, N.A.Klyuev, and A.B.Belikov, Khim.Geterotsikl.Soed., 1978, 1349.
99. N.M.Przheval'skii and I.I.Grandberg, Khim.Geterotsikl.Soed., 1982, 940.
100. A.N.Kost, G.A.Golubeva, and Yu.N.Portnov, Dokl. Akad.Nauk SSSR, 1971, **200**, 342.
101. R.Fusco and F.Sannicolo, Tetrahedron, 1980(72), **36**, 161.
102. R.Fusco and F.Sannicolo, J.Org.Chem., 1982, **47**, 1691.
103. F.Sannicolo, Tetrahedron Lett., 1984, **25**, 3101.
104. S.R.Landor, P.D.Landor, and Z.T.Fomum, Tetrahedron Lett., 1977, 3743.
105. W.Sucrow, Org.Prep. and Proced.Intern., 1982, **14**, 91.
106. J.E.Baldwin and J.C.Bottaro, Chem.Comm., 1982, 624.
107. F.Vögtle and E.Goldschmitt, Chem.Ind.(London), 1973, 1072.
108. H.A.Staab and F.Vögtle, Chem.Ber., 1965, **98**, 2701.
109. H.Quast and J.Stawitz, Tetrahedron Lett., 1977, 2709.

110. H.Heimgartner, Chimia, 1980, **34**, 334.
111. V.A.Isidorov, V.A.Moloshnikov, and I.K.Zenkevich, Zhur.Org.Khim., 1978, **14**, 1832.
112. R.V.Stevens, E.E.McEntire, W.E.Barnett, and E. Wenkert, Chem.Comm., 1973, 662.
113. A.Padwa, T.Caruso, S.Nahm, and A.Rodriquez, J. Amer.Chem.Soc., 1982, **104**, 2865.
114. K.K.Balasubramanian, G.V.Bindumadhavan, M.R. Udups, and B.Krebs, Tetrahedron Lett., 1980, **21**, 4731.
115. C.V.B.Madhavan and K.K.Balasubramanian, Tetrahedron, 1985, **41**, 111.
116. T.Sheradsky and G.Salemnick, J.Org.Chem., 1971, **36**, 1061.
117. T.Sheradsky, E.Nov, S.Segal, and A.Frank, J. Chem., Soc.Perkin Trans.I, 1977, 1827.
118. Y.Endo, K.Shudo, and T.Okamoto, J.Amer.Chem. Soc., 1982, **104**, 6393.
119. Y.Endo, K.Shudo, and T.Okamoto, Synthesis, 1983, 471.
120. S.Blechert, Tetrahedron Lett., 1984, **25**, 1547.
121. P.Martin, Helv.Chim.Acta, 1984, **67**, 1647.
122. R.M.Coates and I.M.Said, J.Amer.Chem.Soc., 1977, **99**, 2355.
123. R.M.Coates and C.W.Hutchings, J.Org.Chem., 1979, **44**, 4742.
124. S.E.Denmark and M.A.Harmata, J.Amer.Chem.Soc., 1982, **104**, 4972.
125. D.H.Evans and J.V.Nelson, J.Amer.Chem.Soc., 1980, **102**, 774.
126. K.Mohri, Y.Oikawa, Ken-ichi Hirao, and O.Yonemitsu, Chem.Pharm.Bull., 1982, **30**, 3097.
127. K.Mohri, Y.Oikawa, Ken-ichi Hirao, and O.Yonemetsu, Heterocycles, 1982, **19**, 515.
128. R.Höfelmeier and S.Blechert, Angew.Chem., 1982, **94**, 375.
129. S.Oae and T.Sakurai, Tetrahedron, 1976, **32**, 2289.
130. B.A.Trofimov, S.E.Korostova, A.I.Mikhaleva, L.I. Sobenina, V.V.Shcherbakov, and M.V.Sigalov, Khim. Geterotsikl.Soed., 1983, 276.
131. B.A.Trofimov, Uspekhi Khim., 1981, **50**, 248 [Russ. Chem.Rev., 1981(3)].
132. B.A.Trofimov, A.S.Atavin, A.I.Mikhaleva, G.A. Kalabin, and E.G.Chebotareva, Zhur.Org.Khim., 1973, 2205.
133. K.B.Lipkowitz, S.Scarpone, D.McCullough, and C. Barney, Tetrahedron Lett., 1979, **20**, 2241.
134. S.Knapp and D.V.Patel, Tetrahedron Lett., 1982, **23**, 3539.
135. A.Padwa and L.A.Cohen, Tetrahedron Lett., 1982, **23**, 915.
136. A.Padwa and L.A.Cohen, J.Org.Chem., 1984, **49**, 399.
137. T.Ikariya, Y.Ishikawa, K.Hirai, and S.Yoshikawa, Chem.Lett., 1982, 1815.
138. L.E.Overman and F.M.Knoll, J.Amer.Chem.Soc., 1980, **102**, 865.
139. L.E.Overman, C.B.Campbell, and F.M.Knoll, J.Amer. Chem.Soc., 1978, **100**, 4822.
140. R.Tachikawa, K.Wachi, S.Sato, and A.Teroda, Chem., Pharm.Bull., 1981, **29**, 3529.
141. V.N.Drozd, Zhur.Org.Khim., 1983, **19**, 2626.
142. V.N.Drozd, Zhur.Org.Khim., 1984, **20**, 656.
143. R.Gompper and B.Kohl, Tetrahedron Lett., 1980, **21**, 907.
144. Y.Tamaru, M.Kagotani, and Yoshida Zen-ichi, J.Org. Chem., 1980, **45**, 5221.
145. M.Mizutani, Y.Sanemitsu, and Y.Tamaru, J.Org. Chem., 1983, **48**, 4585.
146. M.Mizutani, Y.Sanemitsu, and Y.Tamaru, Heterocycles, 1984, **21**, 515.
147. T.Sasaki and I.Shimizu, Heterocycles, 1984, **21**, 1044.
148. M.J.Kurth, O.H.W.Decker, H.Hope, and M.D.Januck, J.Amer.Chem.Soc., 1985, **107**, 443.
149. M.J.Kurth and O.H.W.Decker, J.Org.Chem., 1985, **50**, 5769.
150. S.-I.Murahashi and Y.Makabe, Tetrahedron Lett., 1985, **26**, 5563.
151. P.W.Hickmott, Md.G.Ahmed, S.A.Ahmed, and S. Wood, J.Chem.Soc.Perkin Trans., I, 1985, 2559.
152. I.B.Abdrakhmanov, G.B.Shabaeva, A.A.Kalimullin, and G.A.Tolstikov, Zhur.Org.Khim., 1985, **21**, 1183.
153. I.B.Abdrakhmanov, G.B.Shabaeva, E.V.Tal'vinskii, L.A.Biktimirova, A.A.Fatykhov, and G.A.Tolstikov, Zhur.Org.Khim., 1985, **21**, 829.
154. I.B.Abdrakhmanov, Z.N.Saraeva, N.G.Nigmatullin, and G.A.Tolstikov, Izv.Akad.Nauk SSSR, Ser.Khim., 1986(2), 383.
155. I.B.Abdrakhmanov, A.G.Mustafin, G.A.Tolstikov, R.N.Fakhretdinov, and U.Dzhemilev, Khim.Geterotsikl.Soed, 1986(3), 325.
156. H.Ent, H.de Koning, and W.N.Speckamp, Tetrahedron Lett., 1985, **26**, 5105.
157. H.Ent, H.de Koning, and W.N.Speckamp, J.Org. Chem., 1986, **51**, 1687.
158. J.Fischer, C.Kilpert, U.Klein, and W.Steglich, Tetrahedron, 1986, **42**, 2063.
159. Chu Min, Wu Pei Lin, S.Givre, and F.W.Fowler, Tetrahedron Lett., 1986, **27**, 46.
160. R.Höfelmeier and S.Blechert, 1985, **26**, 5281.
161. S.Blechert, Helv.Chim.Acta, 1985, **68**, 1835.
162. Y.Endo, K.Manikawa, T.Terashima, and K.Shudo, Heterocycles, 1986, **24**, 229.
163. M.Mizutani, Y.Sanemitsu, Y.Tamaru, and Z.Yoshida, Tetrahedron Lett., 1985, **26**, 1237.
164. M.Mizutani, Y.Sanemitsu, Y.Tamaru, and Z.Yoshida, Tetrahedron, 1986, **42**, 305.
165. J.-B.Baudin, M.Bekhazi, S.A.Julia, O.Ruel, R.L.P. de Jong, and L.Brandsma, Synthesis, 1985, 956.
166. J.-B.Baudin and S.A.Julia, Tetrahedron Lett., 1986, **27**, 837.

Timiryazev Moscow
Agricultural Academy