IMPORTANT PRINCIPLE IN THE CHEMISTRY OF HETEROCYCLES: ELECTROPHILIC REACTIONS OF COMPOUNDS OF THE PENTADIENYL ANION TYPE* (REVIEW)

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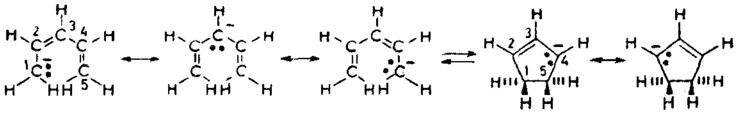
Data on the electrocyclic reactions of heteroanalogs of the pentadienyl anion that contain heteroatoms in various positions of the five-membered system are correlated.

Introduction and General Principle

Young scientists and experienced specialists in organic chemistry suffer equally from the abundance of factual material. The flow of facts should be manageable and reach those to whom it is addressed. The development of principles for the systemization of facts is also precisely one of the great missions of science.

The cyclization of anions of the pentadienyl anion type is not a new concept in the chemistry of heterocycles. In 1970 Reimlinger [1] described "1,5-dipolar cyclization" as one of the aspects of the behavior of conjugated 1,3-dipoles. A year later Elguero [2] noted the related characteristics in some of the cationic cyclizations that he carried out in the synthesis of pyrazolines and detected similar reactions in the literature.

Scheme 1



Electrocyclic reactions [3] are characterized by cyclic transfer of electrons, the end result of which is conversion of one π bond to a σ bond or vice versa. Polyenyl systems are structures with π bonds and an odd number of component atoms, and pentadienyl is the second member of the series of vinylogs. The resonance concept of the 6π-electron system of the pentadienyl anion indicates distribution of the negative charge in the 1, 3, and 5 positions. Ring formation consists of concerted deformations and bending — 90° rotation about the axis of the terminal bonds is necessary for the 1 and 5 carbon atoms to be able to approach one another and form a new σ bond from the former π orbitals. The remaining four π electrons form an allyl anion, which is the lower vinylog of the pentadienyl anion. Migration of negative charge is a characteristic element of cyclization. The 2 and 4 carbon atoms, which do not have negative charge in the starting anion, participate in its distribution in the new anion. The MO theory confirms these concepts but not so graphically as the resonance structures. In addition, the advantages of the MO model are manifested during an examination of orbital control of the stereospecificity of the process.

Orbital Control and Stereochemistry

Electrons of the upper π MO are used in the electrocyclic reaction for the formation of a new σ bond. Consequently, according to Woodward and Hoffmann [3], the simplest approach in this case is an examination of the symmetry of the upper occupied molecular orbital (UOMO) (Scheme 2). Two 90° rotations in opposite directions are necessary for overlapping that ensures a bonding interaction during the formation of a new σ bond. This concerted movement is called disrotation.

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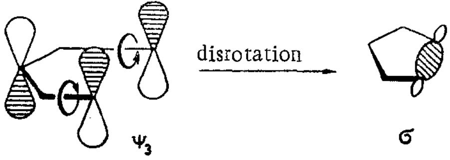
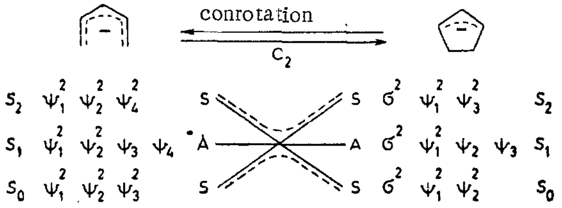
Scheme 2



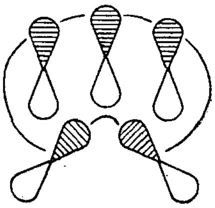
The correlation diagram [4, 5] presented in Scheme 3 for thermally forbidden conrotation illustrates a more complex approach. Ground state S_0 of the pentadienyl anion correlates with the second excited state S_2 of the cyclopentadienyl anion, which is inaccessibly high in energy. The S_0 and S_2 electron states are identical with respect to symmetry, and the transformation along the dashed line corresponds to the requirements of the electron configuration, but thermal conrotation is forbidden by the high energy barrier between the ground states of the starting and final substances.

Scheme 3



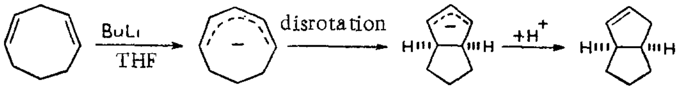
In conformity with the Evans—Zimmerman—Dewar model [6, 7], the topology of the basis set does not display dislocation of the phases for the transition state of the disrotatory process (Scheme 4). The 6π electrons oriented in this manner form an aromatic system of the Hückel type.

Scheme 4



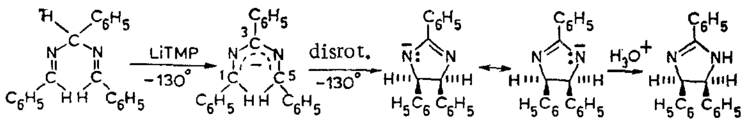
What do we know about the stereospecificity of the reaction? The 6π system that is a part of the cyclooctadienyl anion is shown in Scheme 5. Disrotatory cyclization of this anion takes place with a half-reaction period of 80 min at 35°C and leads to cis fusion of the two five-membered rings. However, the cis configuration is also determined by thermodynamic considerations, and this reduces the importance of orbital control.

Scheme 5



Laurent discovered the cyclization of hydrobenzamide to amarine in 1844 [9]. Recently Hunter and co-workers [10] observed the base-catalyzed generation of an anion at —130°C under the influence of lithium tetramethylpiperidide (LiTMP). The resulting anion (a purple solution) undergoes rapid cyclization (Scheme 6). The electrocyclic reaction proceeds in the case of a U configuration of the diazapentadienyl anion. In the most favorable U configuration the phenyl groups in the 1 and 5 positions are turned outwards. The symmetry-allowed disrotatory process directs ring formation with exclusive stereospecificity (>99.7%) to favor the amarine anion with an unfavorable cis orientation of the phenyl groups. Upon

Scheme 6



Amarine

prolonged contact with a base, amarine undergoes isomerization to isoamarine with a more stable trans orientation of the phenyl substituents.

The elegance and persuasiveness of this fine experiment are diminished somewhat upon comparison with the results of a study by Hunter and Steiner [11], who also studied the monoaza analog of the triphenylpentadienyl anion and found that its cyclization is not stereoselective. We will not discuss the possible reasons for this.

Thermodynamics and Configuration

The solvation of ions and the formation of ion pairs hinder the drawing of unambiguous thermodynamic conclusions. The small difference in the energies of the bonds for the intramolecular cyclization shown in Scheme 7 makes it possible to give an estimate only a *posteriori*. The decrease in the delocalization energy on passing from the pentadienyl to the cyclopentenyl anion should not exceed 14 kcal·mole^{-1}.

Scheme 7

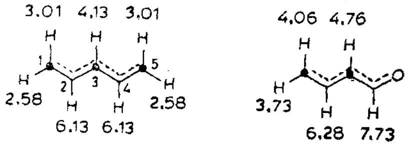
$-\Delta G \geq 2$ kcal·mole^{-1}

$\pi \longrightarrow \sigma$ bond	-20
increase in ring strain (calc.)	+ 4
decrease in delocalization energy	$\leq$ +14

The tragic fate of the parental systems is a subject worthy of a separate book. The pentadienyl anion, which is the forefather of the series (Scheme 1), is well known, but, as we have shown, it does not undergo cyclization; it is not even clear whether this is due to kinetic or thermodynamic reasons.

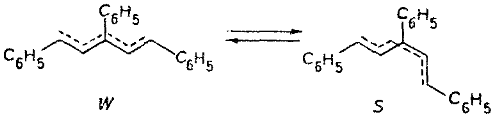
The ^{1}H NMR spectra of the potassium salt of the pentadienyl anion in liquid ammonia provide evidence for the preferableness of the W form [12]. The shift of the signals of the protons attached to the 1, 3, and 5 atoms (the black points in Scheme 8) to strong field indicates the presence of negative charge in these positions. The shifts of the 2- and 4-H protons are typical for olefins (Scheme 8). Replacement of the terminal CH_2 group by an oxygen atom gives rise to a shift of the bulk of the negative charge to oxygen; this is manifested in a decrease in the shielding.

Scheme 8



The PMR spectrum of 1,3,5-triphenylpentadienyllithium in tetrahydrofuran (THF) [13] indicates the existence of an equilibrium between the W and S configurations in comparable amounts (Scheme 9). The U form necessary for cyclization is not observed; however, it may be present in a low equilibrium concentration.

Scheme 9



$\Delta G^{\ddagger} = 12$ kcal·mole^{-1}

Introduction of Heteroatoms

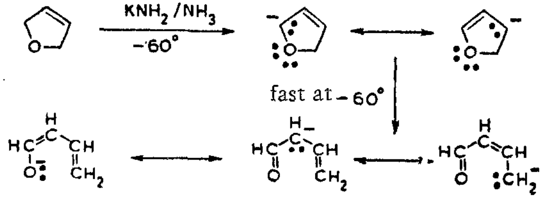
Systems that contain heteroatoms are much more important than purely hydrocarbon systems. When a heteroatom is introduced, the substitution may have isoionic and isoelectronic character. In the case of isoionic substitution (Scheme 10) the negative charge of the carbanion is retained in the amide or oxide anion, whereas the neutral imine nitrogen atom or the carbonyl oxygen atom replaces the olefinic carbon in the resonance structures. It is apparent that the terminal carbon atom in the pentadienyl anion can be replaced by an NR group or an oxygen atom. The inner 2 and 4 positions do not make any choice possible other than a nitrogen atom in place of a monosubstituted carbon atom (CR). The same holds true for the heteroatoms of higher periods.

Scheme 10

Systems with Isoionic Substitution

Potassium amide deprotonates 2,5-dihydrofuran to give the oxacyclopentenyl anion, which cannot be detected in the NMR spectrum, since even at −60°C electrocyclic ring opening to give an oxapentadienyl system occurs extremely rapidly (Scheme 11) [14]. The first of the three resonance structures makes the chief contribution to the distribution of the electrons of the ground state. The basicity of the oxapentadienyl anion is 20 pK units lower than that of the pure carbon system. The conversion of the cyclic allyl anion to a butadiene oxide anion shifts the thermodynamic equilibrium markedly to favor the open form.

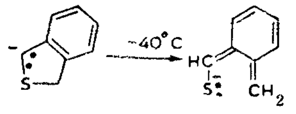
Scheme 11



The kinetic effect of oxa substitution is also impressive. The unshared pair of electrons of the oxygen atom is conjugated with the allyl anion of the cyclic form. In the case of electrocyclic ring opening there is no need for two 90° rotations; one rotation about the C—C bond is sufficient. Precisely the difference in the stereospecificity of the orbitals evidently lowers the activation barrier between the cyclic and noncyclic forms.

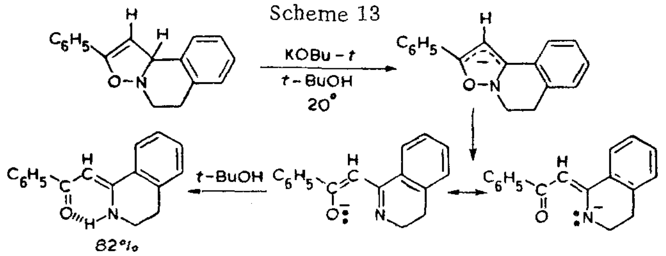
Benzo-condensed systems in pericyclic reactions can be regarded as unsaturated. This phenomenon, which seemed surprising in the development of the Woodward—Hoffmann rules in the sixties, is now well understood. Thus in the 1,3-dihydrobenzo[c]thiophene anion the thiacyclopentenyl anion, the open form of which was proved by Kloosterziel [15] from the NMR spectrum, which is characteristic for an unfavorable o-quinoid structure, is "latent."

Scheme 12



Under the influence of bases 4-isoxazolines form β-enamino ketones with ring cleavage [16, 17] (Scheme 13). The weakness of the N—O single bond in the hypothetical intermediate anion and the migration of the negative charge to the terminal N and O atoms promote electrocyclic ring opening. The heteroatoms located at both ends of the pentadienyl system exclude the necessity for rotations about the bonds during the transformation.

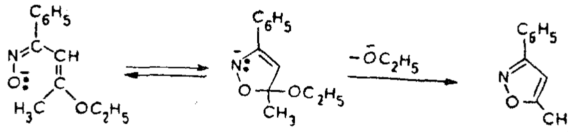
Scheme 13



How substantially this differs from isoionic substitution by the heteroatoms in the 2 and 4 positions! In the previously examined hydrobenzamide ion (Scheme 6) the nitrogen atoms do not participate in stabilization of the negative charge. However, cyclization leads precisely to the appearance of this charge on nitrogen. Amide ions are more favorable than carbanions, and ring formation acquires an additional thermodynamic stimulus, so that the process takes place rapidly even at −130°C [10].

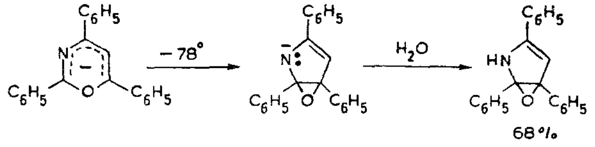
Other (in addition to protonation) final steps in the cyclization process are also conceivable. The Claisen synthesis of isoxazoles [18] in a basic medium evidently includes electrocyclization of the anion of the α,β-unsaturated oxime (Scheme 14). It is possible that ring formation is slightly endothermic or thermally neutral, but the aromatic isoazole system develops during subsequent splitting out of an ethoxide anion. This cyclization can also be conceived of as nucleophilic addition of the oxime anion to the electrophilic azabutadiene fragment. The differences here are most likely in the designation rather than in the mechanism.

Scheme 14



The pentadienyl anion is represented as a fragment of the structure in the 2,4,6-triphenyl-1,3-oxazine anion (Scheme 15); neither heteroatom participates in the charge distribution. The electrocyclic formation of the ring of this dark-blue 8π anion proceeds as intramolecular annealation. The driving force for the reaction is the concentration of the negative charge on the nitrogen atom, as well as the loss of antiaromatic character [19]. The resulting gain in energy substantially exceeds the losses due to the strain of the resulting ring.

Scheme 15



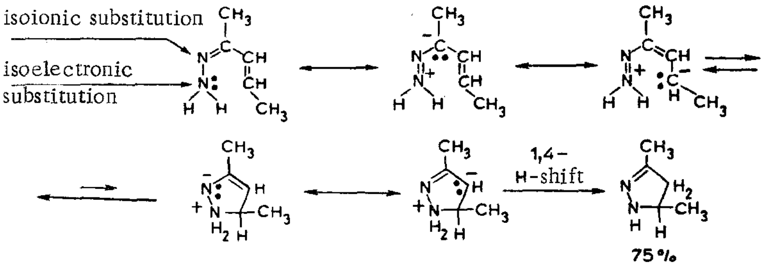
Isoelectronic Substitution in the 1 Position

More numerous variants arise in the case of isoelectronic substitution than in the case of isoionic substitution. In this case (Scheme 16) the carbanion center is replaced by the available (to the free ion pair) trivalent but uncharged nitrogen atom of the amino group or by the neutral oxygen atom of the ether. The neutral ethylene carbon atom is compared with the isoelectronic (with respect to it) iminium nitrogen atom and the oxonium oxygen atom in the second series of Scheme 16.

Scheme 16

All of these substitutions are conceivable in any position. As an example, the result of such substitution is shown.

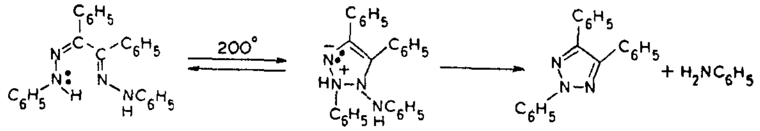
Scheme 17



von Auwers and Heimke [20] were unable to isolate ethylideneacetone hydrazone but instead obtained immediately 3,5-dimethyl-2-pyrazoline (the reaction was carried out at room temperature). Having compared the hydrazone in Scheme 17 with the pentadienyl anion, one can identify isoelectronic substitution in the 1 position and isoionic substitution in the 2 position. It is logical to conceive of this compound not only as a structure without formal charges but also as two zwitterions. If one decides on a neutral structure, the migration of charges necessary for cyclization should lead to the formation of a zwitterion. The ammonium group and the azaallyl anion of the cyclic form undergo successive acid–base reactions. The entire process is undoubtedly exothermic, since the 2-pyrazoline contains one more σ bond.

In Scheme 18 the oxazone of benzil is depicted in such a way as to reveal the pentadienyl system. Cyclization by heating may be entirely endothermic, but splitting out of aniline gives a derivative of the aromatic 1,2,3-triazole. Meyer [21] discovered this osotriazole synthesis in 1888.

Scheme 18

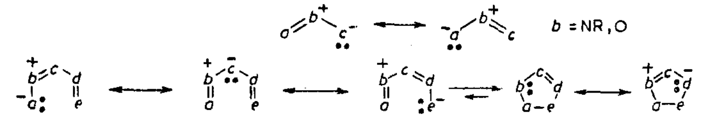


Isoelectronic Substitution in the 2 Position:

Cyclization of Conjugated 1,3-Dipoles of the Allyl Type

1,3 Dipoles are 4π reagents in concerted 1,3-dipolar cycloaddition [22, 23]. Dipoles of the allyl type are allyl anions in which the uncharged middle carbon atom is replaced by an iminium or oxonium fragment. Conjugation of the 1,3 dipole with the C=C bond or various multiple bonds between heteroatoms (d=e) leads to a pentadienyl system with the usual delocalization of negative charge (Scheme 19). However, the onium charge is localized on the b atom as a result of isoelectronic substitution in the 2 position. During cyclization the anionic charge migrates to the 2 and 4 positions, thus neutralizing the positive charge on the b atom. The five-membered ring does not have formal charges, and the contributions of a zwitterion structure is insignificant.

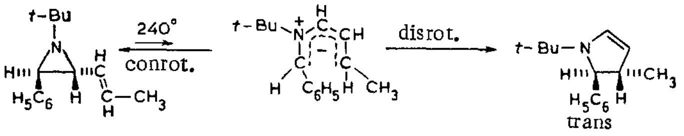
Scheme 19



The case examined above unites the largest number of known pentadienyl cyclizations that were designated as 1,5-dipolar cyclizations by Reimlinger [1]. Taylor and Turchi [26] recently reported 280 references to the cyclization of this series. The examples selected will help to shed light on the character and scope of this reaction.

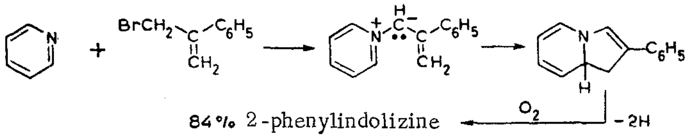
As shown in Scheme 20, a vinylaziridine derivative undergoes electrocyclic ring opening at 240°C. The very small amount of vinyl azomethine ylid that exists in equilibrium undergoes 1,5 cyclization with the loss of its formal charge. Both electrocyclic reactions are permitted with respect to orbital symmetry; the first such reaction proceeds with conrotation, while the second takes place with disrotation [25].

Scheme 20



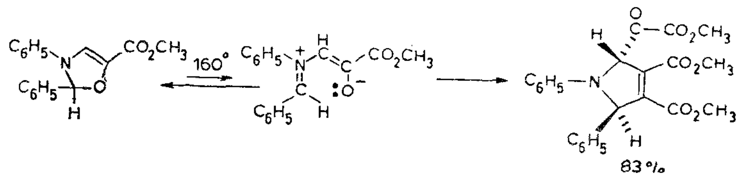
When α-bromomethylstyrene is refluxed in pyridine, one observes the formation of a pyridinium betaine (Scheme 21), which can be regarded as a vinyl azomethine ylid with a C=N bond that is latent in the pyridine ring. Disruption of the aromatic character of the pyridine ring in the case of cyclization does not prevent the conversion to phenyldihydroindolizine [26].

Scheme 21



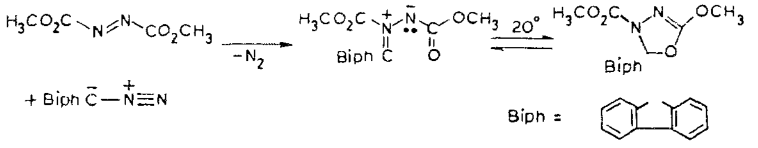
Thermal opening of the 4-oxazoline ring, as shown in Scheme 22, gives a small equilibrium amount of a colored acylazomethine ylid. The open form is a 1,3-dipole and can be recorded by cycloaddition to dimethyl acetylenedicarboxylate [16, 17, 27].

Scheme 22



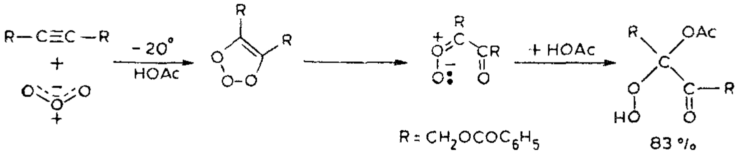
The electrophilic dimethyl azidodicarboxylate attacks diazofluorene with nitrogen evolution. The crystalline reaction product is 1,3,4-oxadiazoline (Scheme 23). Fahr and co-workers [28] have established that in solution at room temperature it exists in equilibrium with the open form, viz., acylazomethineimine. Thus, this electrocyclic system is energically well balanced.

Scheme 23



Thermodynamic principles require opening of the 1,2,3-trioxole ring formed as a result of the cycloaddition of ozone to a disubstituted acetylene [29] (Scheme 24). The instability of the O—O single bond in the trioxole and the excellent stabilization of the negative charge in the acylcarbonyl oxide ensure that the electrocyclic process takes place. The pentadienyl system with one isoelectronic and two isoionic substitutions is a conjugated 1,3-dipole. The reaction product is recorded in the form of an adduct with acetic acid.

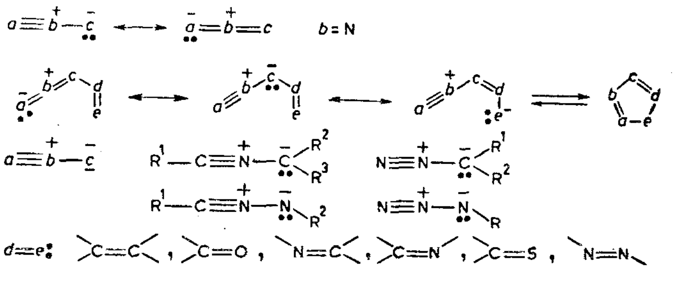
Scheme 24



Cyclization of Conjugated 1,3-Dipoles of the Propargyl-Allyl Type

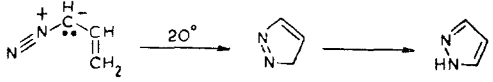
All 1,3-dipoles of the propargyl-allenyl type [22, 23] have an additional double bond between the a and b atoms; the π orbitals of this bond are perpendicular to the orbitals of the allyl anion. Only the nitrogen atom can serve as the onium center in such linear 1,3-dipoles. Conjugation with the d=c bond (Scheme 25) leads to the same charge distribution as in conjugated 1,3-dipoles of the allyl type. Their essential difference consists in the fact that the cyclization product is not an allyl anion but rather a 1,3-diene.

Scheme 25



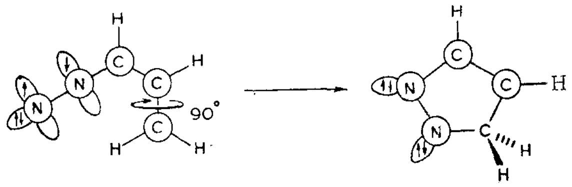
Nitrilium and diazonium betaines, the anionic center of which is the ylid carbon atom or the imine nitrogen atom, may act as a—b—c 1,3-dipoles. The choice of elements for the added d=c bond is unlimited. The cyclization of vinyldiazomethane [30-32] (Scheme 26) can be taken as an example for discussion of the possible stereoelectronic reaction pathways. The resulting nonaromatic 3H-pyrazole is converted to an aromatic pyrazole as a result of a prototropic shift.

Scheme 26



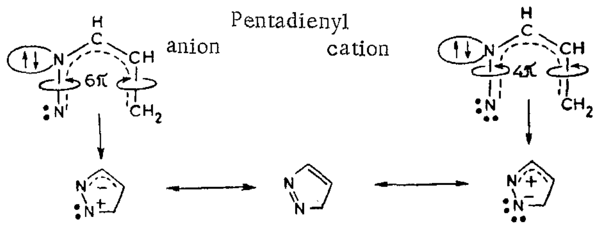
The additional π bond of the diazonium group is electrophilic. Two electrons are shifted to the central nitrogen atom, thereby undergoing conversion to its unshared pair, when a nucleophile is added to the terminal nitrogen atom. In Scheme 27 it is apparent that only one 90° rotation is necessary for cyclization; not all of the N,N part of the pentadienyl system but only the additional π bond participates in the formation of a new σ bond. Thus, four atomic orbitals of the five that make up the pentadienyl system are retained in the new diene system.

Scheme 27



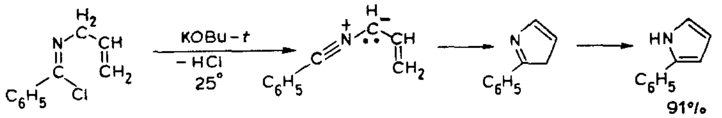
Two rotations are necessary for the other transformations (Scheme 28). In a formal analysis of the reaction sequence the first act is bending of the linear diazomethane structure, in the course of which the electrons of the π bond become the unshared pair of the nitrogen atom in the 2 position. The terminal nitrogen atom has a sextet of electrons, and the pentadienyl system, depending on whether a filled or vacant orbital of the nitrogen atom in the 1 position is included in it, during cyclization may behave either as a 6π or a 4π system. Structures of the cyclopentenyl anion or cation type make a minimal resonance contribution to the structure of the resulting 1,3-diene. The contradictory character of these two mechanisms is only apparent and is essentially semantic.

Scheme 28



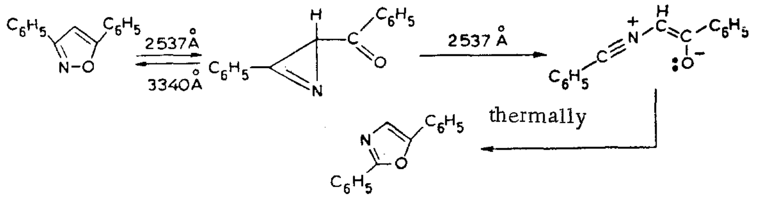
The first ylids of nitriles were obtained in Munich as a result of the splitting out of HCl from imidoyl chlorides [33, 34]. Using this method Engel and Steglich [35] obtained benzonitrile allyl ylid, which, being a vinyl nitrile ylid, undergoes cyclization to 2-phenylpyrrole through the nonaromatic 3-H isomer (Scheme 29).

Scheme 29



The isoxazoles undergo photoisomerization to oxazoles. Singh and Ullman [36, 37] observed an interesting sequence of transformations (Scheme 30). Contraction of the 3,5-diphenylisoxazole ring to a 2H-azirine derivative is reversible, and the photostatic equilibrium depends on the wavelength. After irradiation with a mercury lamp, one can isolate 2H-azirine. This is followed by its slow photochemical conversion to a benzoylated nitrile ylid, which undergoes rapid thermal cyclization to an oxazole. The energy of the oxazole bonds is ∿20 kcal·mole^{-1} higher than in the case of the isoxazole.

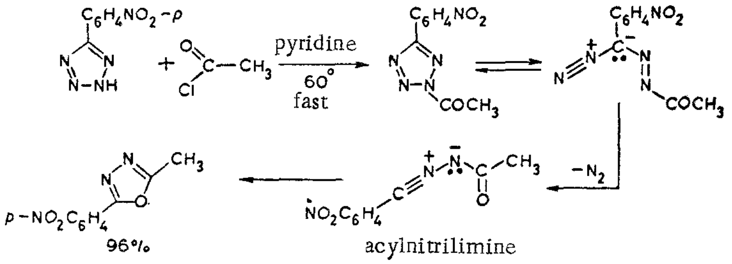
Scheme 30



1,3,4-Oxadiazoles are formed in high yields in the reaction of 5-substituted tetrazoles with aliphatic and aromatic acid chlorides [38]. The sequence of reactions shown in

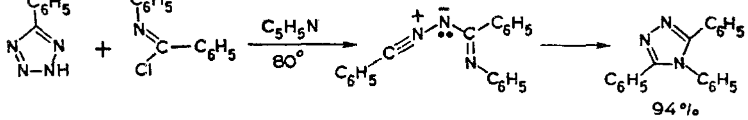
Scheme 31 includes two electrocyclic reactions of the pentadienyl type. Equilibrium electrocyclic opening of the ring in the azodiazoalkane possibly precedes acylation in the 2 position. It is thought that the slow step is the elimination of nitrogen [39, 40], which leads to an N-acylnitrilimine, which, as a pentadienyl derivative, undergoes cyclization to an aromatic oxadiazole.

Scheme 31



The synthesis of 1,2,4-triazoles from tetrazoles and imidoyl chlorides [41] is the same general reaction (Scheme 32). In this case iminonitrilimines are formed as intermediates, and electrocyclization of the ticklike [sic] intermediate connects the ends of the pentadienyl fragment.

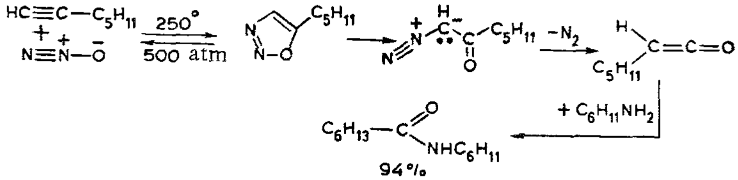
Scheme 32



The cyclization of vinyldiazomethanes to 3H-pyrazoles has already been mentioned [30-32]. Acyldiazoalkanes (diazo ketones), on the other hand, are stable and do not undergo cyclization.

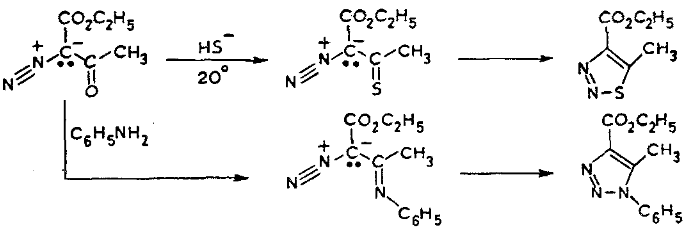
Buckley and Levy have studied the reactions of nitrous oxide with acetylenes under pressure and with heating (Scheme 33). It is extremely likely that the first step is 1,3-dipolar cycloaddition, after which the 1,2,3-oxadiazole ring undergoes electrocyclic opening. The resulting diazo ketone is unstable at 250°C and, as usual, after ejection of nitrogen gives a ketene, as in the Wolff rearrangement. When the reaction is carried out in cyclohexylamine, the pentylketene is fixed in the N-cyclohexylheptanoylamide form.

Scheme 33



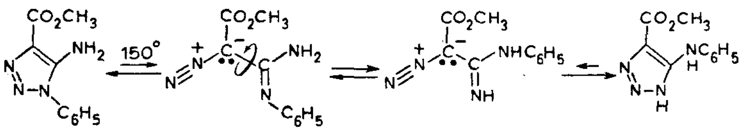
Whereas acyldiazoalkanes are stable, the corresponding thioacyl- or iminodiazoalkanes undergo cyclization to 1,2,3-thiadiazoles and 1,2,3-triazoles, respectively [43, 44] (Scheme 34). Thus the equilibrium in electrocyclic reactions is controlled by the delicate balance between the bond energies and resonance.

Scheme 34



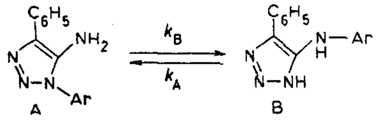
A thoroughly investigated example of cyclization of iminodiazoalkanes was presented by O. Dimroth — one of the founders of physical organic chemistry. 1-Substituted 5-amino-1,2,3-triazoles undergo thermal rearrangement to aminotriazoles that are substituted in the side chain [45, 46] (Scheme 35). Dimroth excluded direct migration of the substituent and proved the participation in the reaction of guanyldiazoalkane, which exists in equilibrium with the amidine tautomer, which undergoes cyclization to a triazole. Neither ring opening nor reformation of the ring requires rotation about the terminal bonds of the pentadienyl system.

Scheme 35



Lieber and co-workers [47] investigated the effect of substituents on the kinetics and thermodynamics of the Dimroth rearrangement. The equilibrium and rate constants of the reaction correspond to the Hammett substituent constants. The competitive resonance effects in compounds of the A type (Scheme 36) are such that electron-acceptor substituents in A favor the conversion to B.

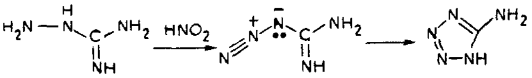
Scheme 36



Ar	$t_{1/2}(k_B)$	k_B/k_A (133°)
$C_6H_4NO_2$-*p*	5,6 min	88
C_6H_5	55	4.8
$C_6H_4OCH_3$-*p*	133	1.8

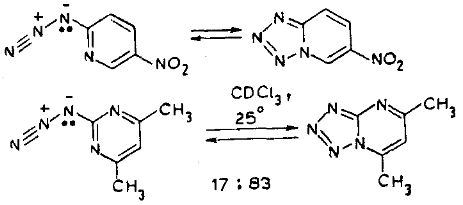
Another classical example, viz., the cyclization of guanyl azide to "5-aminotetrazoic acid," obtained by Thiele in 1892 [48], is presented in Scheme 37. Protonated guanyl azide is stable in acidic solution, but the base, which is liberated at pH 9, undergoes cyclization with a reaction half-period of 2.2 min [47].

Scheme 37



6-Nitrotetrazolopyridine (Scheme 38) is stable in the crystalline state, whereas an electrocyclic equilibrium with azidopyridine is established in solution [49]. Similarly, 2-azido-4,6-dimethylpyridine exists in equilibrium with a two-ring aromatic compound at room temperature [50]. After these first observations, there were reports regarding hundreds of variants of the imidazide ⇄ tetrazole equilibrium [51, 52], and this reaction became the most widely described electrocyclic reaction of compounds of the pentadienyl anion.

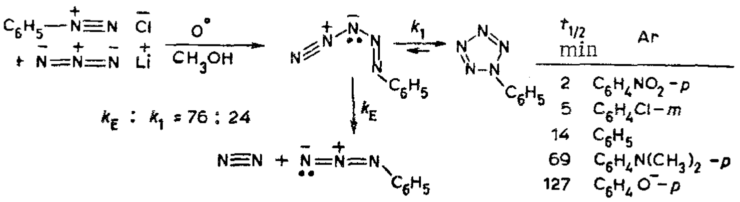
Scheme 38



The iminoazide can be regarded as a pentadienyl anion with one isoelectronic substitution in the 2 position and three additional isoionic substitutions. The cyclization of benzodiazoazide to phenylpentazole [53] is the limiting case in which no carbon atoms remain at all in the ring. The benzodiazoazide formed as a result of diazo coupling reacts via two pathways. Nitrogen evolution with the formation of phenyl azide competes with electrocyclization to give a ring that is not yet a heteroring, since all of the ring atoms are identical. Pentazoles can be called organic compounds only *honoris causa,* since they are the culmination of the azole series.

Phenylpentazole decomposes in methanol at 0°C with a decomposition half-period of 14 min, probably via electrocyclic opening of the ring. The existence of arylpentazoles was proved by ^{15}N labeling and the UV spectra of crystalline samples. The dependence of the rate of decomposition on the character of the substituent in the aryl ring [54] is the same as in the case of 1-aryl-5-aminotriazoles (see Scheme 36).

Scheme 39

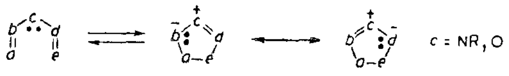


$t_{1/2}$ min	Ar
2	$C_6H_4NO_2$-*p*
5	C_6H_4Cl-*m*
14	C_6H_5
69	$C_6H_4N(CH_3)_2$-*p*
127	$C_6H_4O^-$-*p*

Isoelectronic Substitution in the 3 Position

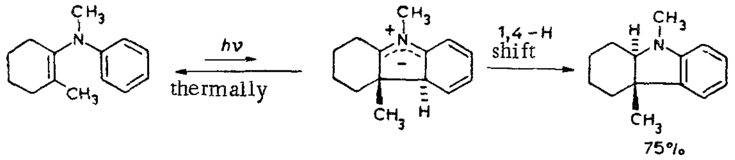
Isoelectronic substitution in the 3 position opens up a new section. An acyclic formally uncharged system undergoes cyclization to a 1,3-dipole of the allyl type, which is described by two resonance structures (Scheme 40). Central link c in the 3 position may be a nitrogen-containing function or an oxygen atom. The open form without charge separation is thermodynamically more favorable.

Scheme 40



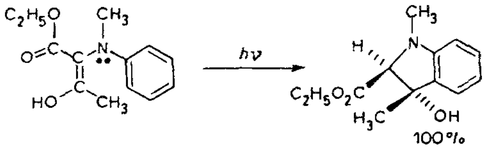
A quantum of light gives rise to conversion of this structure to the energy level of a cyclic 1,3-dipole. Photocyclization of an N-cyclohexenylaniline derivative (Scheme 41) leads to a dimethylhexahydrocarbazole [55]. The hypothetical intermediate is a cyclic azomethine ylid, which either undergoes thermal decyclization or undergoes a 1,4-shift of a hydrogen atom. The aromatic character of the benzene ring is restored in both cases.

Scheme 41



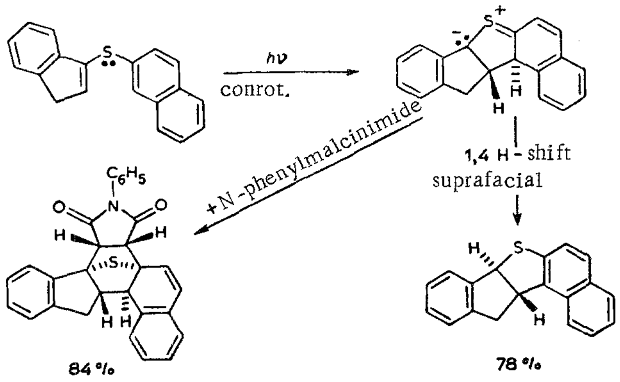
Irradiation of N-methylanilinoacetoacetic ester similarly leads to a dihydroindole [56] (Scheme 42). Aromatic indoles are formed in the presence of acid.

Scheme 42



The sophisticated experiment of Schultz and De Tar [57] makes it possible to draw a conclusion regarding the stereochemistry of the photocyclization of a divinyl sulfide derivative (Scheme 43). The cyclic thiocarbonyl ylid, in which one benzene ring has lost its aromatic character, is stabilized as a result of a suprafacial 1,4-shift of hydrogen — a thermally allowed sigmatropic process. The fact that conrotatory formation of a ring occurs initially follows from the established structure of the pentacyclic dihydrothiophene

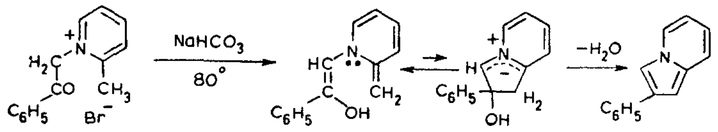
Scheme 43



derivative (the lower right-hand part of the scheme). In fact, conrotation is a symmetry-allowed egress from the first excited singlet state. Irradiation of the starting sulfide in the presence of N-phenylmaleinimide confirms the intermediate formation of a thiocarbonyl ylid. 1,3-Dipolar cycloaddition proceeds more rapidly than the 1,4-shift of hydrogen. The data from an x-ray diffraction analysis of the adduct indicate a trans orientation of the two hydrogen atoms in the new σ bond formed as a result of an electrocyclic reaction.

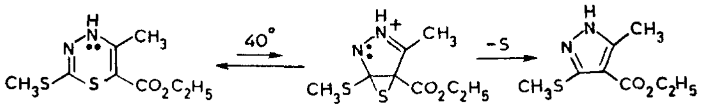
The transformations of N-phenacyl-α-picolinium bromide in Scheme 44 illustrate the synthesis of an indolizine via the Chichibabin reaction [58]. Its deprotonation by such a weak base as bicarbonate leads to a pentadienyl system with isoelectronic substitution by an amine function in the 3 position. The presumable endothermic character of the cyclization step is more than compensated by the subsequent splitting out of water.

Scheme 44



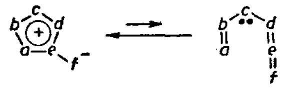
4H-Thiadiazines form pyrazoles via ring contraction. The transformation (Scheme 45) observed by Beyer and co-workers [59] takes place upon gentle heating in an organic solvent. The assumption of an electrocyclic equilibrium with a bicyclic azomethineimine, which readily splits out sulfur as a result of a cheletropic reactions, seems tempting although it is speculative.

Scheme 45



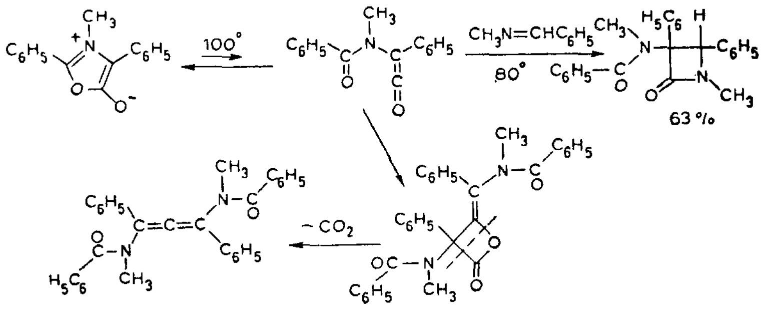
Ollis and Ramsden [60] regard electrocyclic ring opening as a general reaction of mesoionic compounds (Scheme 46), although there is not much direct evidence for the existence of a noncyclic tautomer with a cumulated system of bonds.

Scheme 46



When a mesoionic oxazolone was heated (Scheme 47) to 100°C in toluene, an allene derivative with a rigorously proved structure was obtained [61]. The reaction probably proceeds with participation of the benzamidoketene tautomer. Decarboxylation of its dimer with a β-lactone structure leads to the final allene.

Scheme 47

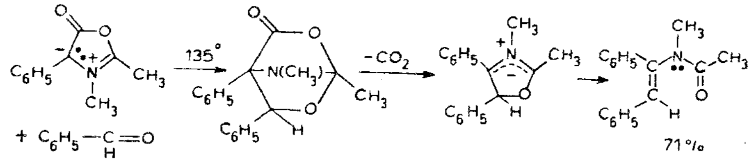


The ketene, which exists in tautomeric thermal equilibrium with the oxazolone, cannot be detected spectroscopically. However, its cycloaddition to azomethines (Scheme 47) serves as additional evidence for its existence. The oxazolone in the form of the noncyclic tautomer adds to the N=C bond to give β-lactams [62]. This reaction of ketenes was known from the time of Staudinger.

Why is the cyclic form the preferred form in the electrocyclic equilibrium in this case? A possible reason for this is the good delocalization of the charges and the aromatic character of the mesoionic ring.

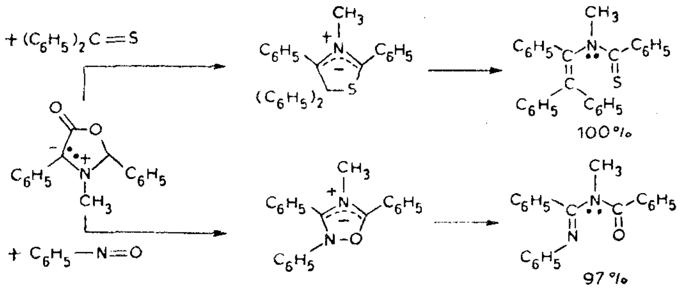
Cyclic 1,3-dipoles are often formed as short-lived intermediates in ring opening processes. Mesoionic oxazolones are active 1,3-dipoles and react like azomethine ylids with, for example, the carbonyl group [63, 64] (Scheme 48). The bicyclic adduct of 2,3-dimethyl-4-phenyl-oxazolia-5-olate and benzaldehyde splits out CO_2 during 1,3-dipolar recyclization. The new cyclic azomethine ylid, in contrast to the starting compound, does not have aromatic character and is therefore not stabilized. The rapid electrocyclic opening of the ring to give N-methylacetamidostilbene is undoubtedly exothermic.

Scheme 48



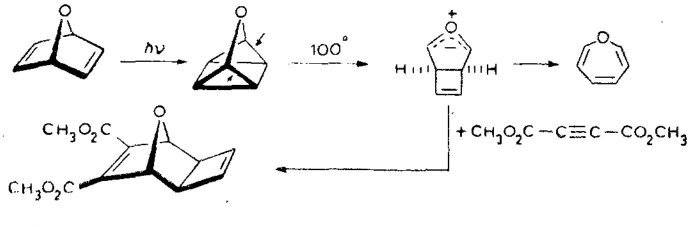
Similar processes involving the addition of a mesoionic oxazolone (Scheme 49) to thiobenzophenone or nitrosobenzene also take place with CO_2 evolution [65-67]. Heterocyclic 1,3-dipoles lose their formal charges during electrocyclic ring opening.

Scheme 49



Prinzbach and co-workers [68, 69] present a persuasive example of such a reaction (Scheme 50). The first step is intramolecular photochemical [2+2]-cycloaddition of oxanornadiene. The resulting oxaquadricyclane undergoes 1,3-dipolar recyclization, once again via an intramolecular pathway. Electrocyclic opening of the carbonyl ylid ring gives a divinyl ether grouping, which is included in an oxepin ring. Elimination of the strain of the cyclobutene ring promotes the process. Despite this, ring opening in the carbonyl ylid does not take place at an immeasurably rapid rate. Approximately half of the intermediate can be trapped by 1,3-cycloaddition to dimethyl acetylenedicarboxylate.

Scheme 50



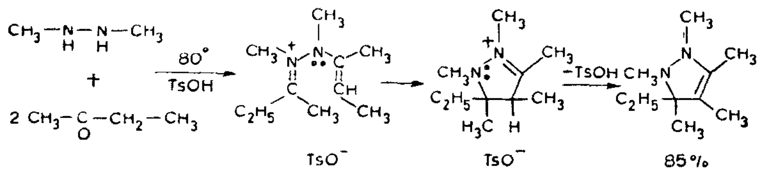
Systems with Double Isoelectronic Substitution

One isoelectronic substitution introduces a positive charge in the system of the pentadienyl anion, so that the resulting cyclic or open system can be depicted without formal charges. A second isoelectronic substitution imparts cationic character to the molecule. The reactions that are typical for the pentadienyl anion but are also observed for the cations do not contradict the general definition.

Elguero, Jacquier, and co-workers [70] investigated the synthesis of pyrazolines from disubstituted hydrazines and methylethyl ketone in the presence of p-toluenesulfonic acid (Scheme 51). The resulting hydrazonium ion has two trigonal nitrogen atoms in the 2 and 3 positions corresponding to a double isoelectronic substitution. The positive charge during

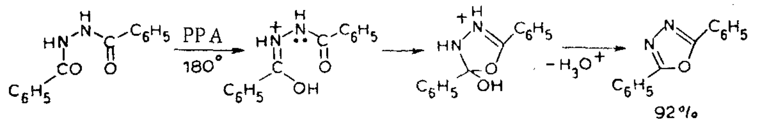
ring formation migrates from the 2 position to the adjacent nitrogen atom. The detachment of a proton from the 4 position leads to a 3-pyrazoline.

Scheme 51



Many acid-catalyzed processes belong in this group of reactions. The formation of 1,3,4-oxadiazoles from N,N'-diacylhydrazines under the influence of electrophilic catalysts is examined in Scheme 52 [71, 72]. In all likelihood, dibenzoylhydrazine is protonated at the oxygen atom. A pentadienyl system with two isoelectronic and one iosionic substitutions is obtained. Ring formation with subsequent dehydration leads to an aromatic system.

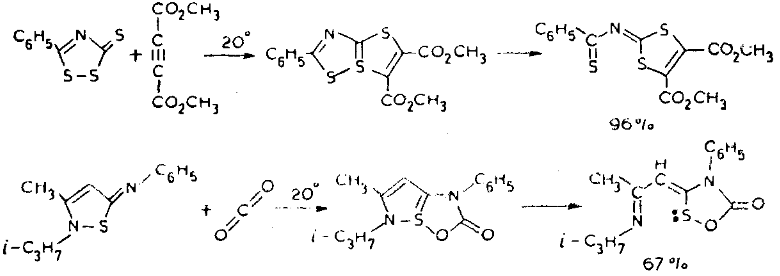
Scheme 52



Special Cases

The brilliant diversity of special cases is illustrated below by several examples. Sulfur can be both di- and tetravalent, and changes in the valence may neutralize the effect of charge migration in electrocyclic processes. The 1,3-adduct of 5-phenyl-1,2,4-dithiazole-3-thione and dimethyl acetylenedicarboxylate, which was obtained by Behringer and co-workers [73], is best described by a structure with tetravalent sulfur (Scheme 53). After electrocyclic ring opening, one can again write an uncharged structure owing to conversion of sulfur to the divalent state.

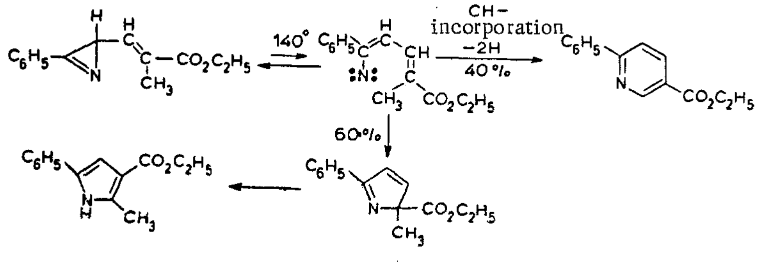
Scheme 53



The second example in Scheme 53 convinces one that only one sulfur atom in the terminal position of the pentadienyl system is sufficient. 5-Imino-3-isothiazoline is capable of reacting with the inert CO_2 molecule. The five-membered ring of the cycloadduct opens up, but the reaction product does not have the character of a zwitterion [74].

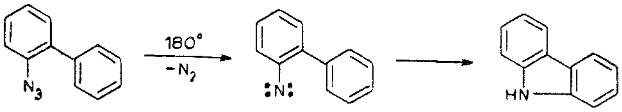
The cyclization of dienylnitrenes is a special case. A 2-vinyl-2H-azirine derivative (Scheme 54) upon thermolysis [75] forms a dienylnitrene, which is partially incorporated in the C-H bond of the methyl group and, after dehydrogenation, is converted to a pyridine derivative. On the other hand, ring closure to give a five-membered ring can be regarded as a 6π-electrocyclic reaction. The final step in this process is a sigmatropic 1,5-shift of the ester group.

Scheme 54



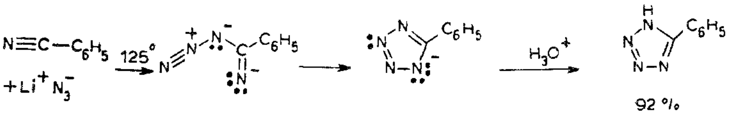
This sort of cyclization has many variants. The synthesis of carbazoles by thermolysis of 2-azidodiphenyls is typical [76] (Scheme 55). There are sufficient reasons to not regard this process as the simple incorporation of the nitrene in the C–H bond.

Scheme 55



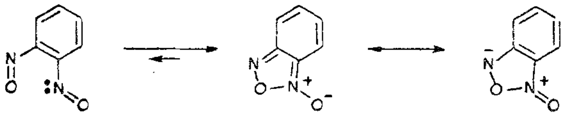
Another special case is shown in Scheme 56. Benzonitrile reacts with lithium azide to give the 5-phenyltetrazole anion, the protonation of which culminates in the simple synthesis of 5-aryltetrazoles [77]. The primary adduct is an iminoazide with an additional negative charge on the terminal nitrogen atom. In order for this reaction to be regarded as an electrocyclic process it is necessary that there be agreement with a rather arbitrary expansion of the definition of the process.

Scheme 56



o-Dinitrosobenzene exists in the form of a cyclic tautomer, viz., benzofuroxan [78, 79]. If one takes into account the unshared electron pair of the nitrogen atom of the nitroso group, the cyclization can be regarded as a transformation of the pentadienyl anion (Scheme 57). On the other hand, the existence of a heterohexa-1,3,5-triene system indicates the possibility of an electrocyclic reaction of the polyene rather than the polyenyl.

Scheme 57



Closing Remarks

Unfortunately, there have as yet been too few thorough studies of the kinetics and mechanism of 1,5-electrocyclic reactions. One may with a certain probability assume that not all the reactions discussed above have the same mechanism. However, there is no doubt that the cyclization of the pentadienyl anion is the prototype of an extremely large number of reactions. The identification and classification of the hundreds of examples scattered throughout the literature is a fascinating task. We hope that familiarization with the principle of systemization set forth here will promote the further study of this rich division of heterocyclic chemistry.

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MACROHETEROCYCLES.

7.* SYNTHESIS AND EXTRACTION CAPACITY OF SOME DIBENZO-18-CROWN-6-DERIVATIVES

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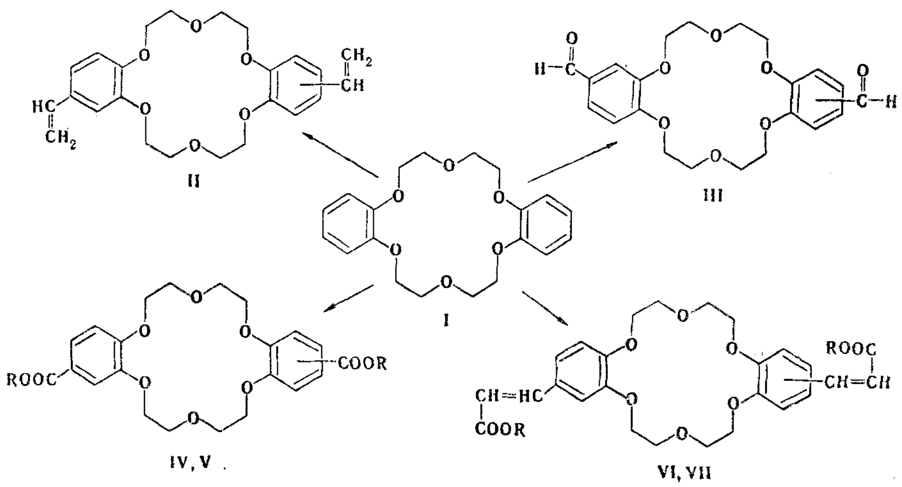
Derivatives that contain vinyl, formyl, acetyl, carboxy, carbethoxy, β-carboxyvinyl, or β-carbethoxyvinyl groups in the benzene rings were synthesized from dibenzo-18-crown-6. The ability of the synthesized crown ethers to extract picrates of alkali metals from the aqueous phase to the chloroform phase was investigated.

The unique ability of macrocyclic polyethers (crown ethers) to form stable complexes with ions of alkali and alkaline earth metals and to solubilize inorganic salts in nonpolar solvents has led to their wide use as catalysts for interphase transfer, extractants, materials for ion-selective detectors, analytical reagents, and model systems for the study of the transport of ions through biological membranes [2, 3]. One of the most accessible and effective complexones with a broad spectrum of activity is dibenzo-18-crown-6 (I). In order to study the effect of various substituents on the complexing ability of dibenzo-18-crown-6 we obtained a number of its new derivatives (II-VII).



IV, VI $R = H$; V, VII $R = C_2H_5$

4,4'(5')-Divinylbenzo-18-crown-6 (II) was synthesized by acylation of crown ether I with acetic acid in polyphosphoric acid (PPA) [4] with subsequent reduction of 4,4'(5')-diacetyldibenzo-18-crown-6 (VIII) with sodium borohydride and dehydration of the resulting 4,4'(5')-bis(α-hydroxyethyl)dibenzo-18-crown-6 (IX) via the following scheme:

See [1] for Communication 6.

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