

The Effect of Pressure on Organic Reactions

Frank-Gerrit Klärner* and Frank Wurche

Essen, Institut für Organische Chemie der Universität

Received July 20th, 2000

Dedicated to Professor Paul Rademacher on the Occasion of his 60th Birthday

Keywords: Cycloadditions, High-pressure chemistry, Pericyclic reactions, Radical reactions, Synthetic methods

Abstract. The utility of high pressure for the understanding of chemical reactions and its application in organic synthesis is shown for cycloadditions (inter- and intramolecular Diels–Alder reactions, 1,3-dipolar and [2+2] cycloadditions), cheletropic reactions and pericyclic rearrangements (Cope and Claisen rearrangements and electrocyclizations). The origin of the effect of pressure on chemical reactions is discussed.

Especially, the change in the packing coefficient during cyclization of chains and the effect of electrostriction on reactions, in which charged species are generated, contribute substantially to a volume contraction leading to a powerful pressure-induced acceleration of such reactions. Finally, the effect of pressure on free-radical reactions (homolytic bond dissociations and quinone oxidations) is described.

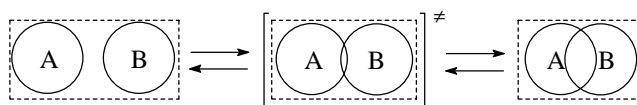
Contents

1. Introduction
2. Cycloadditions
 - 2.1 Diels–Alder Reactions, Mechanistic Aspects
 - 2.2 Synthetic Applications
 - 2.3 1,3-Dipolar [3+2] Cycloadditions
 - 2.4 [2+2] Cycloadditions
 - 2.5 Cheletropic Reactions
3. Pericyclic Rearrangements
 - 3.1 Sigmatropic [3.3] Shifts: Cope and Claisen Rearrangement
 - 3.2 Electrocyclic Rearrangements
 - 3.3 Intramolecular Diels–Alder Reactions
 - 3.4 The Relationship between Activation or Reaction Volume and Ring-Size
4. Free-Radical Reactions
 - 4.1 Homolytic Bond Dissociations
 - 4.2 Quinone Oxidations (Hydrogen Transfer Reactions)
5. Ionic Reactions
6. Concluding Remarks

1. Introduction

Pressure in the range of 1–20 kbar strongly influences the rate and equilibrium position of many chemical reactions. (Units of pressure: 1 kbar = 100 MPa = 0.1 GPa = 14503.8 psi = 986.92 atm). Processes accompanied by a decrease in volume such as a C–C bond formation, in which the distance between two carbon atoms decreases from the van der Waals distance of ca. 3.6 Å to the bonding distance of ca. 1.5 Å, are accelerated by pressure (volume of activation: $\Delta V^\ddagger < 0$) and the equilibria are shifted toward the side of products

(volume of reaction: $\Delta V < 0$). The reverse reaction, a homolytic bond cleavage, leads to an increase in volume ($\Delta V^\ddagger > 0$, $\Delta V > 0$). Pressure induces a deceleration of such a process and a shift of the equilibrium toward the side of reactants (Scheme 1). Therefore, the effect



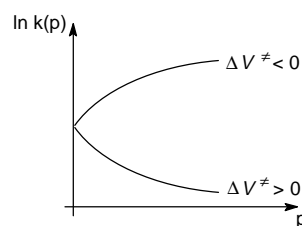
Forward reaction: decrease of volume ($\Delta V, \Delta V^\ddagger < 0$) \Rightarrow accelerated by pressure
 Reverse reaction: increase of volume ($\Delta V, \Delta V^\ddagger > 0$) \Rightarrow retarded by pressure

$$\Delta V = \left(\frac{\partial \Delta G}{\partial p} \right)_T = \left(\frac{-\partial \ln K_p}{\partial p} \right)_T \cdot RT \quad \Delta V^\ddagger = \left(\frac{\partial \Delta G^\ddagger}{\partial p} \right)_T = \left(\frac{-\partial \ln k_p}{\partial p} \right)_T \cdot RT$$

$$\Delta V = V(\text{A-B}) - [V(\text{A}) + V(\text{B})]$$

$$\Delta V^\ddagger = V([\text{A} \cdots \text{B}]^\ddagger) - [V(\text{A}) + V(\text{B})]$$

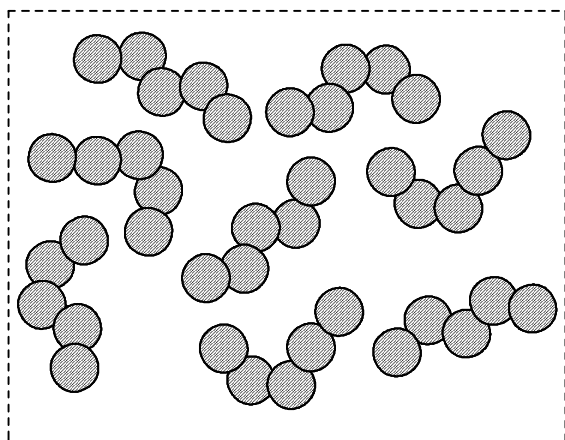
$\Delta V, \Delta V^\ddagger$: volumes of reaction and activation
 V : partial molar volume
 K_p : equilibrium constant at pressure p
 k_p : rate constant at p
 $\Delta G, \Delta G^\ddagger$: Gibbs enthalpy and Gibbs enthalpy of activation



Scheme 1 Volumes of reaction (ΔV) and activation (ΔV^\ddagger)

of pressure seems to be particularly useful in controlling the course of competitive and consecutive reactions. Provided, that the activation volumes of the single reaction steps are different from each other, the application of high pressure can lead to an improvement of chemo-, regio- and stereoselectivity.

The effect of pressure on chemical equilibria and rates of reaction can be described by the wellknown relation between pressure and the Gibbs enthalpy of reaction and activation, respectively (Scheme 1). The volume of reaction and activation can be determined from the pressure dependence of the equilibrium constant and rate constant, respectively. The volume of reaction also corresponds to the difference between the partial molar volumes of reactants and products and is usually determined from these quantities experimentally. Within the scope of transition state theory the volume of activation can be, accordingly, considered to be a measure of the partial molar volume of the transition state with respect to the partial molar volumes of reactants (Scheme 1). Volumes of activation are experimentally determined from the pressure dependence of the rate constants. The volumes of activation and reaction are themselves also pressure-dependent as shown for the volumes of acti-



V_w, V_w^\ddagger : van der Waals volume [$\text{cm}^3 \cdot \text{mol}^{-1}$]
(intrinsic molar volume of ground or transition structures related to one mole)

V : molar volume of a pure liquid [$\text{cm}^3 \cdot \text{mol}^{-1}$] or $V = \frac{M}{d}$

partial molar volume of a solute [$\text{cm}^3 \cdot \text{mol}^{-1}$] $V = \lim_{c \rightarrow 0} \Phi$

$$\Phi = \frac{M}{d_0} - \frac{1}{c} \cdot \frac{d - d_0}{d_0}$$

η, η^\ddagger : packing coefficient

$$\eta = \frac{V_w}{V} ; \eta^\ddagger = \frac{V_w^\ddagger}{V^\ddagger}$$

M [$\text{g} \cdot \text{mol}^{-1}$]: molar mass of the solute
 d [$\text{g} \cdot \text{cm}^{-3}$]: density of the solution
 d_0 [$\text{g} \cdot \text{cm}^{-3}$]: density of the pure solvent
 c [$\text{mol} \cdot \text{l}^{-1}$]: concentration of the solute

Scheme 2 Van der Waals volumes (V_w), partial molar volumes (V) and packing coefficients (η)

vation in Scheme 1. There is no theory explaining this pressure dependence which would allow the volumes of activation or reaction to be determined over a large range of pressure. Therefore, several empirical equations are employed to fit the pressure dependencies of rate and equilibrium constants [1]. The volumes of activation and reaction derived from the pressure dependence of the rate or equilibrium constants by the use of these empirical equations are generally given at $p = 0$. These values at $p = 0$ differ only by immeasurably small amounts from those at atmospheric pressure ($p \approx 1$ bar), so that the comparison with volumes of reaction, calculated from the partial molar volumes of the reactants and products determined at atmospheric pressure, is feasible.

The change in the intrinsic volumes of reacting molecules, as discussed for the homolytic bond formation and dissociation is only, to a minor extent, responsible for the overall change in molar volumes measured experimentally from the densities of reactants and products and from the activation volumes. The intrinsic volume of a ground or transition structure is defined by the space occupied by the van der Waals spheres and can be calculated from the cartesian coordinates of the molecular structure resulting from experimental data, molecular mechanics, or quantummechanical calculations and from the van der Waals radii of the different type of atoms (e.g. $R_w(\text{C}) = 1.80 \text{ \AA}$, $R_w(\text{H}) = 1.17 \text{ \AA}$) derived from crystallographic data [2]. The intrinsic volumes of ground structures can also be calculated from table of group contributions [3]. The van der Waals volume, V_w , is the intrinsic volume of a ground or transition structure multiplied by the *Avogadro's number*. The ratio, V_w/V or V_w^\ddagger/V^\ddagger , is defined as the packing coefficient, η or η^\ddagger , of a ground or transition structure. The packing coefficients calculated for simple hydrocarbons are in the range $\eta = 0.5$ to 0.6 [4]. The empty space between the single molecules can be attributed to the so-called void volume and expansion volume required for the thermally induced motions and collisions of the molecules in the liquid state [5]. The importance of the change in packing coefficients and, hence, in the void and expansion volume for the effect of pressure on chemical reactions, in particular on cyclizations, will be discussed in the following sections.

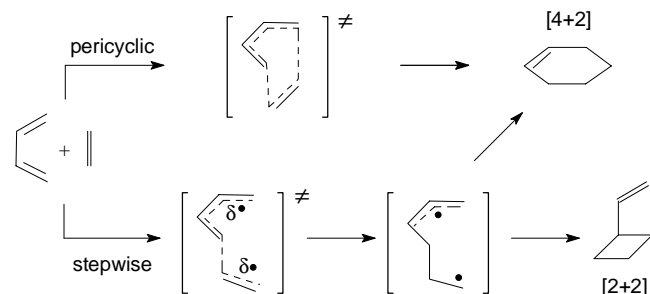
How important it is to consider the whole ensemble of molecules and not single molecules for the explanation of pressure effects can be demonstrated with the effect of electrostriction. In a heterolytic bond dissociation the attractive interaction between the newly generated ions and the solvent molecules leads to a contraction of volume that is, generally, much larger than the expansion of volume resulting from the dissociation. Thus, the overall effect, called *electrostriction*, leads to negative volumes of activation and reaction ($\Delta V^\ddagger < 0$,

$\Delta V < 0$). Neutralization of charges releases the molecules of the solvent cage, leading to positive volumes of activation and reaction ($\Delta V^\ddagger > 0$, $\Delta V > 0$). A similar but less pronounced trend due to the effect of electrostriction is observed for charge concentration and charge dispersal, respectively. An increase in steric crowding in the transition or product states results in a volume contraction ($\Delta V^\ddagger < 0$, $\Delta V < 0$), too. There are many excellent monographs [6] and reviews [7] on chemical reactions at high pressure which cover the earlier literature so that we only want to consider the literature of the past decade (from 1990 up to date). Particularly, we would like to mention the three reviews written by le Noble and Asano, the earlier one [8] and by le Noble, Asano, van Eldik *et al.* the later two, which give the most complete survey on activation and reaction volumes up to 1997 [9, 10]. In this short review we'll discuss the effect of pressure on pericyclic reactions, such as cycloadditions, electrocyclic and sigmatropic rearrangements, focussing on the work, which has been done in Essen. Furthermore, the effect of pressure on free-radical reactions and few most recent applications of high pressure in organic synthesis will be discussed.

2. Cycloadditions

2.1 Diels–Alder Reactions, Mechanistic Aspects

Many Diels–Alder reactions show a powerful pressure-induced acceleration which is often turned to good synthetic purposes [11]. Most recent applications of high pressure in Diels–Alder synthesis have been described by Jenner [12]. The activation volumes ΔV^\ddagger resulting from the pressure dependence of the rate constants are usually highly negative, sometimes even more negative than the corresponding reaction volumes ΔV so that the ratio $\Phi = \Delta V^\ddagger/\Delta V$ is close to or even larger than unity [8–10].



Pericyclic Diels–Alder reactions:
 $\Delta V^\ddagger = -25$ to $-45 \text{ cm}^3 \cdot \text{mol}^{-1}$, $\Delta V = -30$ to $-45 \text{ cm}^3 \cdot \text{mol}^{-1}$
 $\Phi = \Delta V^\ddagger/\Delta V \leq 1$ (or even > 1)
 $\Delta\Delta V^\ddagger = \Delta V^\ddagger(\text{pericyclic}) - \Delta V^\ddagger(\text{stepwise}) \approx -10 \text{ cm}^3 \cdot \text{mol}^{-1}$


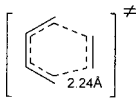
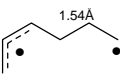

Scheme 3 Volumes of activation and reaction (ΔV^\ddagger , ΔV) of pericyclic Diels–Alder reactions. Comparison of the pericyclic processes with the corresponding stepwise processes involving diradical intermediates

Accordingly, the partial molar volumes of the pericyclic transition states, which can be derived from the activation volumes within the scope of transition-state theory, are approximately equal to or even smaller than those of the corresponding cycloadducts. This finding is surprising and seems to be contradictory to the generally accepted relation between molecular structure and its volumes. In the transition state the new bonds between diene and dienophile are only partially formed. According to quantum-mechanical calculations the lengths of the partially formed σ bonds in the pericyclic transition structures are in the range between 2.1 and 2.3 Å [13, 14]. The van der Waals volumes, V_w , calculated for the pericyclic transition structures by the use of quantum-mechanical methods are generally larger than those calculated analogously for the corresponding cycloadducts. In the case of pericyclic cycloadditions competing with stepwise cycloadditions proceeding *via* di-radical intermediates, relatively large differences in their volumes of activation ($\Delta\Delta V^\ddagger = \Delta V^\ddagger(\text{pericyclic}) - \Delta V^\ddagger(\text{stepwise}) \approx -10 \text{ cm}^3 \cdot \text{mol}^{-1}$) are observed. At high pressure this has the effect of an increased selectivity in favour of the pericyclic process. Examples are the dimerization of chloroprene [15], 1,3-cyclohexadiene [16], and 1,3-butadiene [17].

One question that needs to be addressed is: why are the activation volumes of pericyclic cycloadditions smaller (more negative) than those of the corresponding stepwise reactions? In the past it was assumed that the simultaneous formation of two new π bonds in a pericyclic [4+2] cycloaddition leads to a larger contraction of volume than the formation of one bond in the stepwise process. The interpretation presented [17] is limited by the scope of Eyring transition state theory where the activation volume is related to the transition state volume, as mentioned above, and does not incorporate dynamic effects related to pressure-induced changes in viscosity [20]. In a recent study of the pressure effect on the thermal *Z/E* isomerization of substituted azobenzenes and *N*-benzylideneanilines in viscous solvents, T. Asano *et al.* found that the pressure effect observed at lower ($p \leq 2$ kbar) were in accordance with transition state theory [21]. At higher pressure, however, the effect of further increasing viscosity becomes predominant and all reactions (also those which are first accelerated by an increase in pressure) are retarded. An extensive discussion of the viscosity dependence of reaction rate including the application of Kramer's theory considering dynamic effects can be found in Ref [9].

For the pericyclic and stepwise cycloadditions of ethene to 1,3-butadiene (the prototype of Diels–Alder reactions) the molar volumes, V , the van der Waals volumes V_w , and the packing coefficients, η , of the ground and transition structures shown in Table 1 were calculated following the method of Nakahara *et al.* [4] in

Table 1 Molar volumes, V , van der Waals Volumes, V_w , and packing coefficients, η , calculated for acyclic and cyclic ground and transition structures needed for the explanation of the pressure effect on the Diels–Alder reaction of 1,3-butadiene with ethene.

compound	d	$V = M/d^a$)	$V_w^{a) b)}$	$\eta = V_w/V$
$\text{CH}_2=\text{CH}_2$		59.9 ^{c)}	25.5	0.4257
$\text{CH}_2=\text{CH}-\text{CH}=\text{CH}_2$		83.2 ^{c)}	44.8	0.5385
$\text{CH}_2=\text{CH}-\text{CH}_2-\text{CH}_2-\text{CH}=\text{CH}_2$	0.6880	119.4	63.9	0.5354
$\text{CH}_2=\text{CH}-\text{CH}_2-\text{CH}=\text{CH}-\text{CH}_3$	0.7000	117.7	63.9	0.5443
$\text{CH}_2=\text{CH}-\text{CH}=\text{CH}-\text{CH}_2-\text{CH}_3$	0.7050	116.5	63.8	0.5475
	0.8102	101.4	59.1	0.5829
		109.1 ^{d)}	63.8	0.5829
		118.7 ^{e)}	64.4	0.5424
		120.4 ^{e)}	65.3	

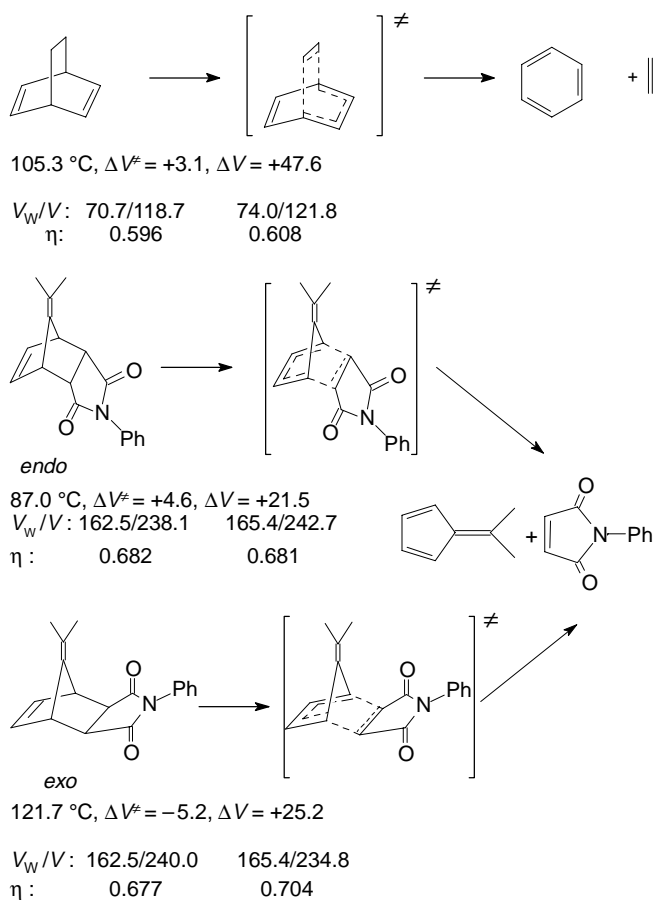
a) in $\text{cm}^3 \cdot \text{mol}^{-1}$; b) For the calculation of van der Waals volumes cartesian coordinates resulting for ground structures from molecular mechanics calculations [19] and for transition structures from *ab initio* calculations [13] and the following van der Waals radii were used: $R_w(\text{H}) = 1.17\text{\AA}$; $R_w(\text{C}) = 1.80\text{\AA}$; c) Calculated with volume increments [18]; d) with the packing coefficient of cyclohexene ($\eta = 0.5829$); e) Calculated with the average of the packing coefficients determined for the three isomeric hexadienes ($\eta = 0.5424$).

order to uncover the effect of different bonding on the transition-state volumes. The packing coefficient, η , of cyclohexene is significantly larger than those of the three isomeric hexadienes. Generally, η is found to be larger for cyclic compounds than for the corresponding acyclic ones. From the data listed in Table 1 the van der Waals volume of the Diels–Alder reaction [4, 17, 22] can be calculated to be with $\Delta V_w = (59.1 - (25.5 + 44.8)) = -11.2 \text{ cm}^3 \text{ mol}^{-1}$ only roughly one-quarter of the experimentally accessible volume of reaction ($\Delta V = 101.4 - (59.9 + 83.2) = -41.4 \text{ cm}^3 \text{ mol}^{-1}$). Consequently, a significant part of the observed ΔV results from the higher packing of the cyclic product rather than from the changes in bonding. The difference between the van der Waals volumes of activation calculated for the pericyclic and stepwise reaction ($\Delta\Delta V_w^\ddagger = \Delta V_w^\ddagger(\text{pericyclic}) - \Delta V_w^\ddagger(\text{stepwise}) = -6.7 - (-5.0) = -1.7 \text{ cm}^3 \text{ mol}^{-1}$) is small and inconsistent with the experimental value ($\Delta\Delta V^\ddagger \approx -10 \text{ cm}^3 \text{ mol}^{-1}$). In order to explain the experimental $\Delta\Delta V^\ddagger$ one has to assume [17] that the packing coefficient of the pericyclic transition state is similar to that of the cycloadduct. The difference between the activation volumes calculated for the pericyclic and step-

wise cycloaddition using the packing coefficient of cyclohexene ($\eta = 0.5829$) for the pericyclic transition structure ($\Delta V^\ddagger(\text{pericyclic}) = -109.1 - (59.9 + 83.2) = -34.0 \text{ cm}^3 \text{ mol}^{-1}$) and the average of the packing coefficients of the three hexadienes ($\eta = 0.5424$) for the acyclic transition structure of the stepwise cycloaddition ($\Delta V^\ddagger(\text{stepwise}) = -120.4 - (59.9 + 83.2) = -22.7 \text{ cm}^3 \text{ mol}^{-1}$) is with $\Delta\Delta V^\ddagger = -11.3 \text{ cm}^3 \text{ mol}^{-1}$ in good accord with the experimental findings. Therefore, the analysis of activation volumes seems to provide important information regarding whether the transition-state geometry is cyclic or acyclic.

The second question that needs to be addressed is: why are the activation volumes of some pericyclic Diels–Alder reactions smaller (more negative) than their reaction volumes so that the ratio $\Phi = \Delta V^\ddagger/\Delta V > 1$. This surprising result could be confirmed by three independent studies. In the two earlier studies G. Jenner *et al.* and N. S. Isaacs *et al.* found the ratio $\Delta V^\ddagger/\Delta V$ in the Diels–Alder reaction of furan with acrylonitrile [23] and that of *N*-benzoylpyrrole with *N*-phenylmaleic imide [24] to be larger than unity ($\Phi = 1.06$ and 1.37 , respectively). The cycloadducts isolated from both reactions

undergo smooth retro Diels–Alder reactions showing negative volume of activation ($\Delta V^\ddagger = -2.0$ and -8.3 cm³ mol⁻¹, respectively) in agreement with the value $\Phi > 1$ determined for each forward reaction. In a more recent investigation F.-G. Klärner and V. Breitkopf observed that the retro Diels–Alder reactions of dihydrobarrelene and its 2-cyanoderivative and of the *endo*-Diels–Alder adduct between dimethylfulvene and *N*-phenylmaleic imide are slightly decelerated by pressure showing positive volumes of activation whereas the retro Diels–Alder reactions of the *endo* and *exo* [4+2] cycloadducts between naphthalene and maleic anhydride and that of the *exo* adduct between dimethylfulvene and *N*-phenylmaleic imide are accelerated by pressure showing a negative volume of activation (Scheme 4) [25]. Grieger and Eckert [26] considered two explanations of the ratio $\Phi > 1$ in the Diels–Alder reaction of isoprene with maleic anhydride: a larger dipole moment of the transition state or secondary orbital interactions which can only occur in *endo* Diels–Alder reactions. The findings that the difference between the activation



all volumes (in cm³·mol⁻¹) related to the temperature of reaction.

Scheme 4 Activation and reaction volumes determined experimentally and calculated van der Waals volumes and packing coefficients of retro Diels–Alder reactions [25]

volumes of many *endo* and *exo* Diels–Alder reactions is small ($\Delta\Delta V^\ddagger < 1-2$ cm³ mol⁻¹) and that the activation volume of retro Diels–Alder reaction of the *endo* cycloadduct between dimethylfulvene and *N*-phenylmaleic imide is positive and that of the retro Diels–Alder reaction of the corresponding *exo* cycloadduct is negative (Scheme 4), rule out that secondary orbital interactions are important and induce a larger contraction of the volume of the *endo* transition state.

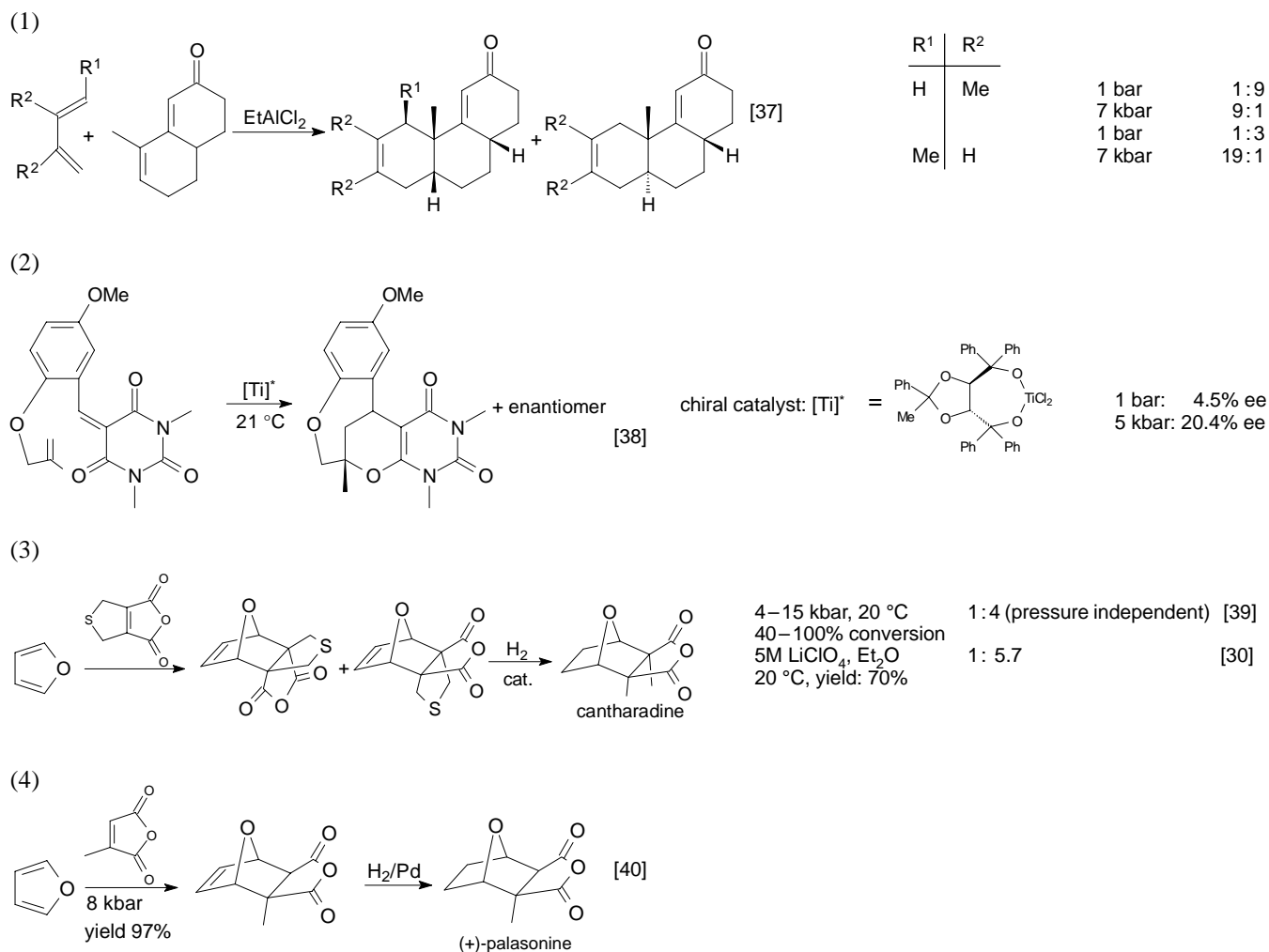
The following conclusions were drawn from the results obtained for the retro Diels–Alder reactions shown in Scheme 4. The packing of the entire ensemble consisting of solute and solvent and its reorganization during the course of reaction, and not the changes of the intrinsic molecular volumes of the reactants to the products during the course of reaction are most important for the magnitude of the activation and reaction volumes. The packing coefficients of the pericyclic transition states resemble those of the corresponding cycloadducts as already assumed for the explanation of the different activation volumes of pericyclic and stepwise cycloadditions [27]. In the retro Diels–Alder reactions showing $\Delta V^\ddagger < 0$, the packing coefficients of the transition states are calculated to be larger than those of the corresponding cycloadducts. This has been found particularly in the relatively polar systems bearing cyclic anhydride or imide functions (Scheme 4). In these cases the size of the activation volumes obviously depends not only on the effective packing probably caused by the restriction of vibrations and rotations in the transition state, but also on the transition-state polarization enhanced by the polar groups leading to a further decrease in volume which is not observed in the less polarized cycloadducts. Blake and Jorgensen [28] have assumed similar effects to explain the acceleration of Diels–Alder reactions in water which will be discussed in the following paragraph.

Breslow [29], Grieco [30] and Engberts [31] have found that the rates of cycloadditions can be strongly enhanced by conducting them in water or in saturated LiClO₄-diethyl ether solution (LPDE). These enhancements are comparable to those obtained by high pressure in conventional organic solvents. Suggested origins of these effects are high internal solvent pressure, hydrophobic association, micellar catalysis, solvent polarity, and hydrogen bonding. Jorgensen *et al.* [28] found in a Monte Carlo simulation of the solvent effect on the Diels–Alder reaction between 1,3-cyclopentadiene (CP) and methylvinylketone (MVK) that the interaction between water and the transition state leads to a substantial transition-state stabilization whereas the interaction between water and the reactants or the cycloadduct is small. Propane as solvent has accordingly no significant influence on the transition state or the ground states. The authors concluded from their calculations that the

specific aqueous acceleration of the reaction between CP and MVK is due to the hydrophobic association of the reactants in water as well as to a nonhydrophobic component stemming from the transition-state polarization that leads inter alia to a specific transition-state stabilization caused by stronger hydrogen bonds between the OH group of the water molecules and the oxygen of the polarized carbonyl group. The various methods used for acceleration and increase in selectivity of Diels–Alder reactions were reviewed by Pindur *et al.* [32].

Investigation of the pressure effect on Diels–Alder reactions in various solvents showed that also the reactions in water are strongly accelerated by pressure resulting highly negative volumes of activation which are comparable to those determined in organic solvents for example the Diels–Alder reaction between 1,3-cyclohexadiene and methylvinylketone (40 °C, $\Delta V^\ddagger = -38.0$ (CH₂Cl₂), -35.4 (CH₃OH), -32.0 cm³ mol⁻¹ (H₂O)) [33] or between 9-hydroxymethylanthracene and

N-phenylmaleic imide (45 °C, $\Delta V^\ddagger = -28.6$ (CH₂Cl₂), -31.4 (CH₃OH), -36.4 cm³ mol⁻¹ (H₂O)) [34]. Since the rates of these reactions are already enhanced by the change of the solvent from CH₂Cl₂ to H₂O by a factor between 600 to 1200 at atmospheric pressure (1 bar), the application of pressure leads to an additional acceleration of these reactions in aqueous solution. Diels–Alder reactions catalyzed by LiClO₄ in diethylether or by Lewis acids such as AlCl₃, ZnCl₂, or Yb(fod)₃ also show a powerful pressure-induced acceleration in addition to the rate enhancement caused by the catalyst. Examples are the reaction between 2,3-dimethyl-1,3-butadiene and *n*-butylacrylate (10 °C, $\Delta V^\ddagger = -28.6$ (neat), -25.7 cm³ mol⁻¹ (catalyzed by AlCl₃) [35] or acroleine as diene and ethylvinylketone as dienophile [36] (25 °C, $\Delta V^\ddagger = -29.6$ (CHCl₃), -31.7 cm³ mol⁻¹ (CHCl₃, catalyzed by Yb(fod)₃). Jenner has called this rate enhancement caused by two factors (by pressure and catalyst or solvent) as multiactivation [36].

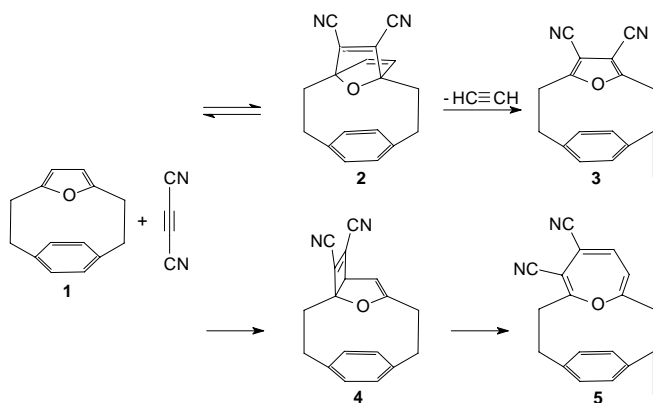


Scheme 5 Diels–Alder reactions catalyzed by Lewis acids at high pressure

2.2 Synthetic Applications

Recently reported Diels–Alder reactions illustrate that the combination of high pressure and Lewis-acid catalyst can have a synergetic effect. Some of these reactions occur only at high pressure in the presence of the catalyst. Furthermore, the stereoselectivity of the catalyzed reactions is influenced by pressure. For example the diastereoselectivity of reaction (1), (Scheme 5) is reversed at high pressure [37], and in the intramolecular Diels–Alder reaction (entry 2) catalyzed by a chiral titanium complex the enantioselectivity (enantiomeric excess - *e.e.*) is increased by pressure [38]. One of the most prominent examples for a pressure-induced reaction is the synthesis of a cantharadine precursor by the cycloaddition of furan to a substituted maleic anhydride (entry 3) which occurs only at high pressure [39] or when catalyzed by LiClO_4 at atmospheric pressure as it has been found out later [30]. (\pm)-Palasonine, however, could be synthesized by Diels–Alder reaction of furan to citraconic anhydride (entry 4) only at high pressure followed by catalytic hydrogenation. This Diels–Alder reaction does not substantially proceed at atmospheric pressure and high temperature or catalyzed by LiClO_4 [40].

The reaction of furanobenzocyclophane **1** with dicyanoacetylene (DCA) (Scheme 6) illustrates that the effect of pressure and that of a catalyst can be complementary [41]. At 160 °C and 1 bar the reaction of **1** with DCA leads to the dicyanosubstituted furan **3** (20%) and oxepin **5** (1%). In a kinetically controlled reaction of **1** with DCA at 9 kbar and 20 °C the thermally unstable Diels–Alder adduct **2**, the precursor of **3** is formed as the only product which undergoes a smooth retro Diels–Alder reaction at 1 bar and 20 °C producing the starting materials **1** and DCA. At 160 °C the retro Diels–Alder reaction of **2** leading to **3** and acetylene is obviously competitive with the non productive reaction leading to **1** and DCA. At 60 °C and 8.5 kbar or at room tempera-

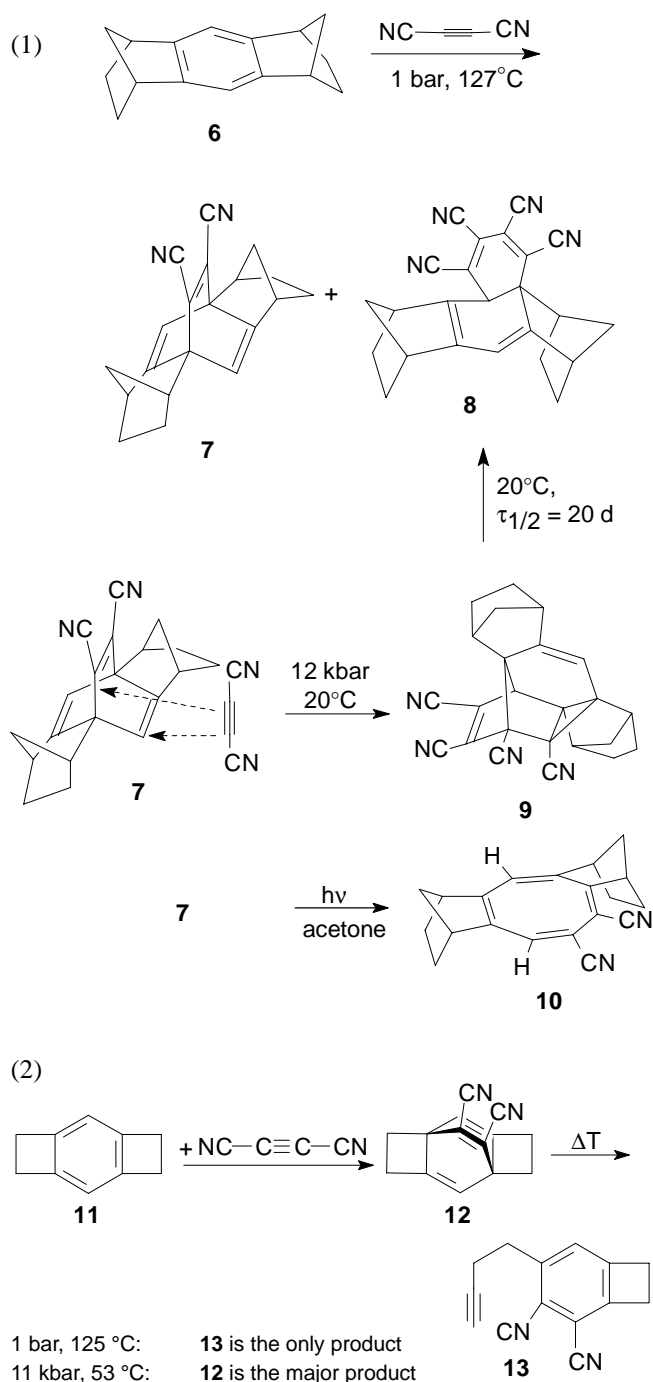


Scheme 6 Competitive and consecutive reactions of furano-benzocyclophane **1** with dicyanoacetylene (DCA)

ture in the presence of LiClO_4 as catalyst **1** reacts with DCA to produce the [2+2] cycloadduct **4** which isomerizes to the oxepin **5** at 160 °C.

The reactions of the strained benzene derivative **6** have been originally studied with the aim to synthesize planar cyclooctatetraene derivatives which are interesting compounds with respect to the question of their antiaromaticity [42]. The cyclooctatetraene derivative, **10** (Scheme 7) synthesized by photolysis of the barrelene derivative **7**, however, turned out to be nonplanar [43]. But the synthesis and the reactions of barrelene derivative **7** are interesting with respect to the utility of high pressure to control the course of reaction. The reaction of **6** with DCA at 1 bar and 127 °C produces the (1:1) Diels–Alder adduct **7** (yield: 49%) and the unexpected dark blue (2 : 1) adduct **8** (yield: 14%). At high pressure (9 kbar, 83 °C) **8** is even the major product. The observation, that the isolated (1:1) adduct **7** reacts with DCA at 1 bar and 127 °C leading to **8**, indicates that **7** is an intermediate in the reaction $\mathbf{6} + 2 \text{ DCA} \rightarrow \mathbf{8}$. At 12 kbar **7** reacts with DCA readily at room temperature producing the homo-Diels–Alder adduct **9** which smoothly undergoes a rearrangement to **8** also at room temperature so that **9** is also an intermediate in the reaction of **7** with DCA which can be detected only by the use of high pressure. The dihydronaphthalene derivative **8** is an interesting compound regarding its intense colour and intramolecular dynamics [43]. Another example, which demonstrates that pressure is a useful parameter to control consecutive reactions, is the addition of DCA to benzodicyclobutene **11** which gives benzocyclobutene **13** at 1 bar and 125 °C as the only product [43]. At 11 kbar the reaction between DCA and **11** occurs readily at 53 °C producing the primary Diels–Alder adduct **12** besides **13**. Isolated **12** rearranges to **13** slowly at 53 °C. Attempts to catalyze the reaction between **11** and DCA by means of Lewis acids such as AlCl_3 or TiCl_4 (analogously to the Diels–Alder reaction of DCA with parent benzene) failed.

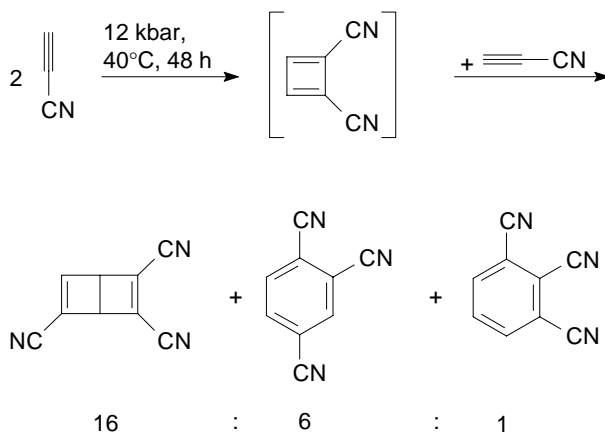
The cycloadditions of cyanoacetylene (Scheme 8, 9) are good examples for the utility of high pressure to accelerate sluggish reactions and to control the course of complex reactions. In contrast to DCA cyanoacetylene is only a moderate dienophile reacting, for example, with 1,3-cyclohexadiene at 1 bar only at a temperature of ca. 100 °C at which the primary Diels–Alder adduct (2-cyanobicyclo[2.2.2]octa-2,5-diene) is thermally not stable and undergoes a *retro* Diels–Alder reaction, producing benzonitrile and ethene [44]. The reaction is highly accelerated by pressure and occurs at 9 kbar already at 50 °C. Under these conditions the primary Diels–Alder adduct is stable and can be isolated in good yields. A similar effect of pressure was observed in the trimerization of cyanoacetylene leading to 1,2,3- and 1,2,4-tricyanobenzenes as major products at 1 bar



Scheme 7 The effect of pressure on cycloadditions of DCA to strained benzene derivatives

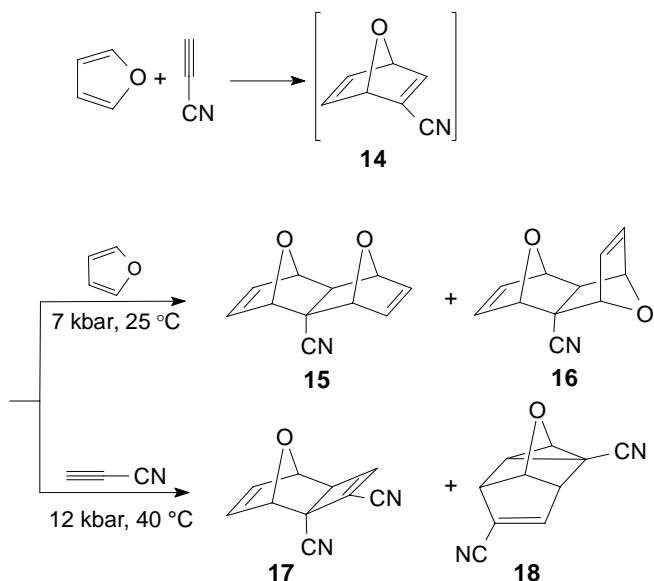
and 160 °C [44]. At 12 kbar the trimerization occurs already at 40 °C giving the thermally labile 2,3,5-tricyano-Dewar-benzene which isomerizes to 1,2,4-tricyanobenzene upon heating to a temperature ≥ 50 °C. The high-pressure results are good evidence that the thermal trimerization of cyanoacetylene occurs by a sequence of reactions consisting of the [2+2] cyclodimerization in the first step leading to the highly reactive 1,2-dicyanocyclobutadiene followed by Diels–Alder cycloaddition of cyanoacetylene to the cyclobutadiene pro-

ducing the Dewar-benzene derivatives which aromatize to the observed benzene derivatives *via* orbital-symmetry forbidden electrocyclic ring-opening.



Scheme 8 Trimerization of cyanoacetylene

The reaction of cyanoacetylene with furan leads preferentially to the (2 : 1) adduct **17** at 160 °C and 1 bar (Scheme 9). In analogy to the trimerization of cyanoacetylene and the addition of cyanoacetylene to [2+2] paracyclophane [44] the 1,2-dicyano-1,3-cyclobutadiene was assumed to be the intermediate in this reaction, too. From the investigation of the pressure effect it could be concluded, that oxanorbornadiene **14** (the Diels–Alder adduct) and not the 1,2-dicyanocyclobutadiene is an intermediate in the reaction between furan and cyanoacetylene. The investigation of the pressure effect on the reaction between the furanobenzocyclophane **1** and cyanoacetylene led to similar results [41].



Scheme 9 Addition of cyanoacetylene to furan at various pressures

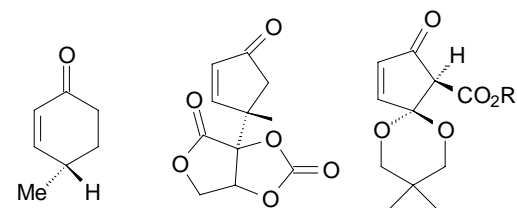
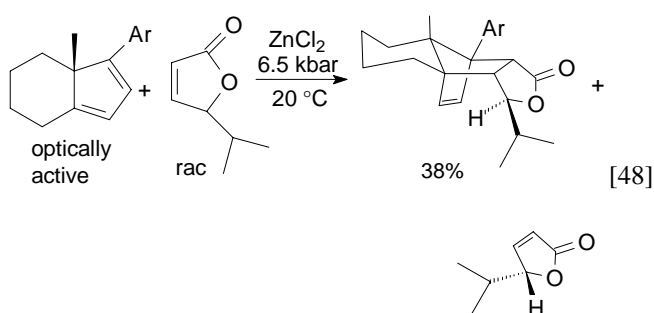
In the past decade the utility of high pressure has been demonstrated for many syntheses involving Diels–Alder reactions as key steps from which we can describe here only few selected examples.

Recently, E. Winterfeldt *et al.* found that the chiral discrimination in the Diels–Alder reactions of rigid polycyclic and bicyclic chiral dienes with various dienophiles is extraordinarily high [45]. (Scheme 10) These reactions, which occur only at high pressure, can be used either for the kinetic resolution of racemic dienophiles or for the enantioselective synthesis of optically active compounds starting from achiral dienophiles and the chiral dienes as optically active auxiliary [46]. The *endo*-selectivity of these Diels–Alder reactions and the preference for the oxygen or fluorine substituents to be placed in the inside position of the Diels–Alder adducts are most important for the observed chiral discrimination. According to quantum-mechanical calculations the *endo*-selectivity and the preference of the heteroatoms in the inside position arises from the high steric interactions between the bulky substituents such as methyl, and the π -system and hydrogen atoms of the cyclopentadiene moiety [47].

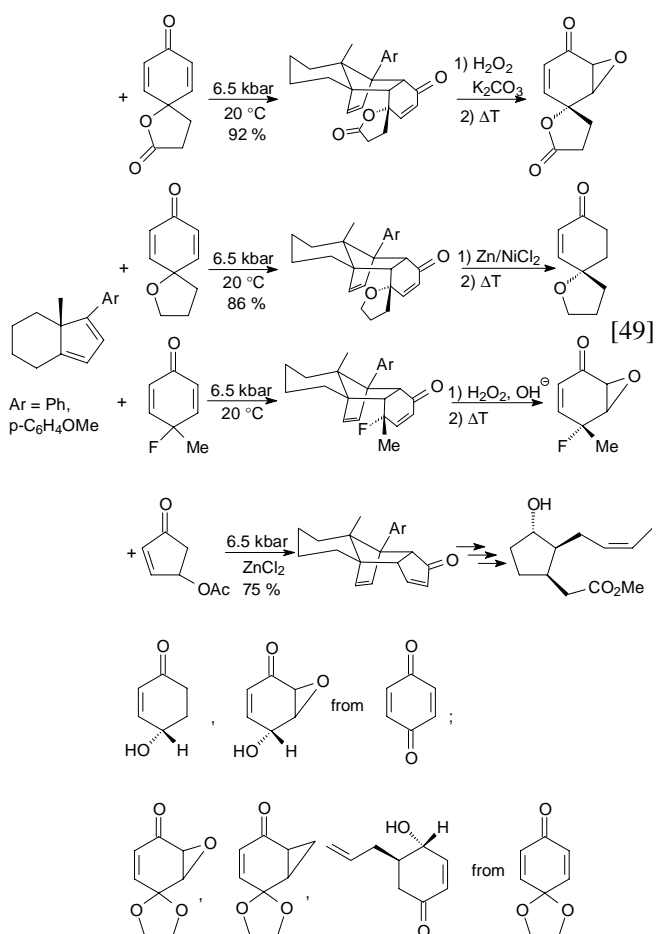
An interesting example is the pressure induced reaction of buckminsterfullerene C_{60} with 1,3,5-cycloheptatriene [50]. Generally C_{60} reacts as electron-deficient dienophile or dipolarophile in numerous Diels–Alder or 1,3-dipolar cycloadditions and 1,3,5-cycloheptatriene as a diene. The reaction with C_{60} is a rare example where both adducts derived from the norcaradiene as well as the cycloheptatriene are observed.

The effect of pressure on *hetero*-Diels–Alder reactions is comparable to that on the discussed Diels–Alder reactions leading to carbocyclic products. The reac-

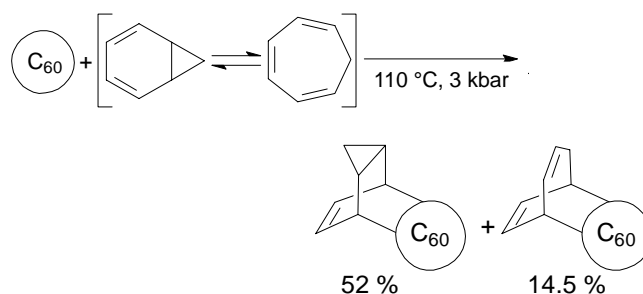
(1) Kinetic resolution of racemic dienophiles



(2) Enantioselective synthesis of optically active compounds from achiral dienophiles



Scheme 10 Chiral discrimination in pressure-induced Diels–Alder reactions of chiral dienes

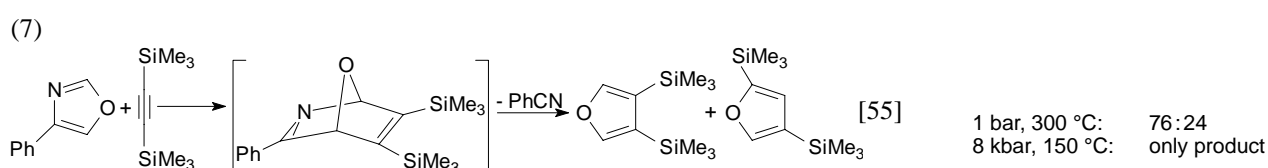
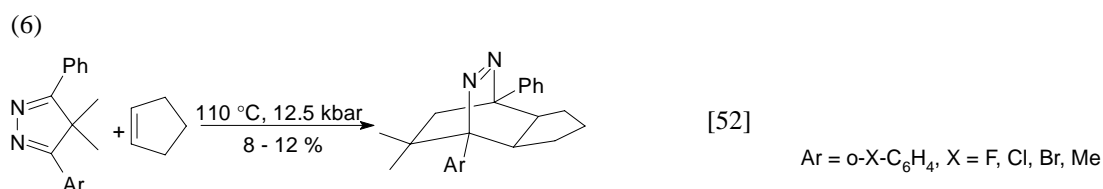
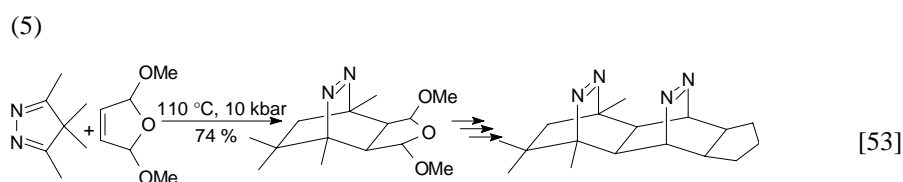
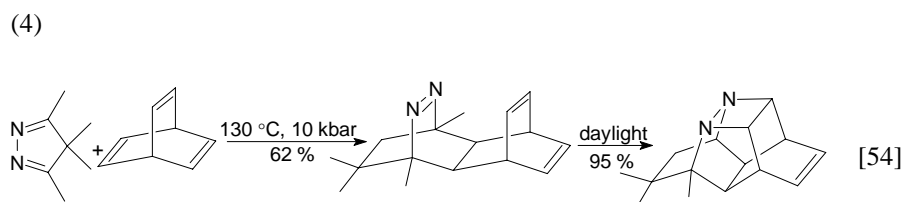
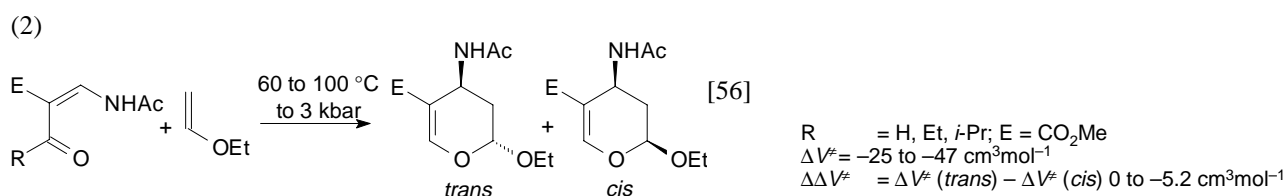
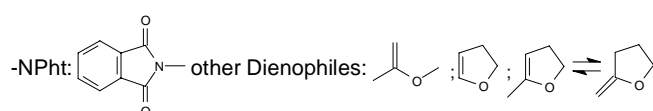
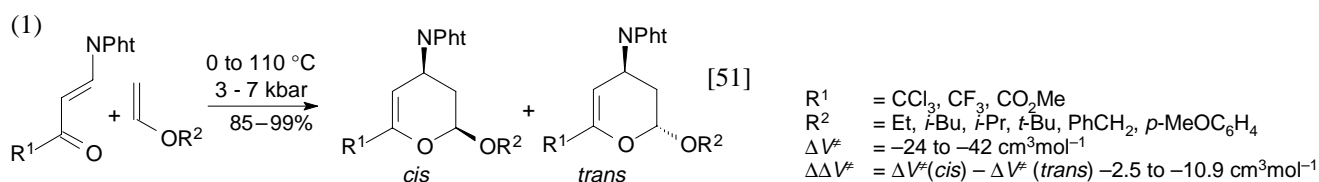


Scheme 11 Pressure-induced Diels–Alder reaction of cycloheptatriene and norcaradiene with C_{60} as dienophile

tions are strongly accelerated by pressure showing highly negative volumes of activation (Scheme 12, entry (1)). The reaction (1) is a good example of the interplay between pressure and temperature [51]. At high pressure the rate of reaction as well as the diastereoselectivity (in favour of the *cis*-adducts due to the negative $\Delta\Delta V^\ddagger$

values) are increased. The pressure-induced acceleration allows the temperature to be lowered, that leads to a further increase in diastereoselectivity. The Diels–Alder reactions of unreactive dienes such as pyrazole [52–54] and oxazole [55] derivatives (Scheme 12, entry (4)

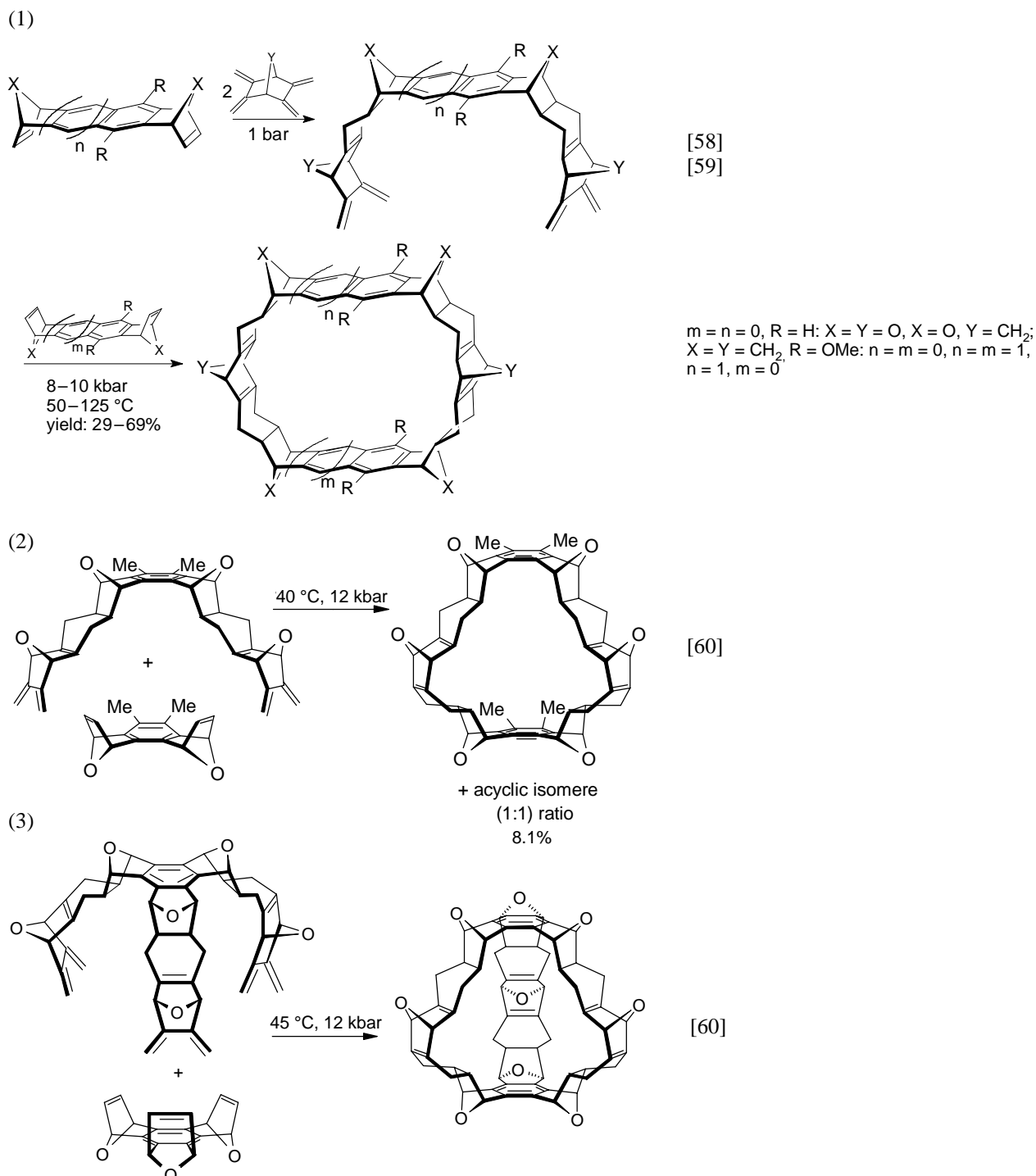
– (7)) are accelerated by high pressure which allows the temperature of reaction to be lowered so that the thermally labile cycloadducts and the 3,4-di-(trimethylsilyl)furan, respectively, can be isolated.



Scheme 12 The effect of pressure on *hetero*-Diels–Alder reactions

The macrocycles shown in Scheme 13 can be synthesized by repetitive, highly stereoselective Diels–Alder reactions between the tetramethylene-substituted norbornane or 7-oxanorbornane derivatives as bis-dienes and the benzoannellated norbornadiene derivatives as bis- or tris-dienophiles, containing all oxo or methano bridges *syn* to one another. Whereas in each case the first reaction leading to the acyclic all-*syn*-configured bis-

or tris-diene occurs at atmospheric pressure, the subsequent inter- and intramolecular Diels–Alder reactions only succeed at high pressure. Obviously, the inter- as well as intramolecular Diels–Alder reactions are accelerated by pressure. The macrocycles are of interest in supramolecular chemistry because of their well defined cavities with different sizes depending on the arene spacer-units.



Scheme 13 Synthesis of macrocycles by means of pressure-induced repetitive Diels–Alder reactions

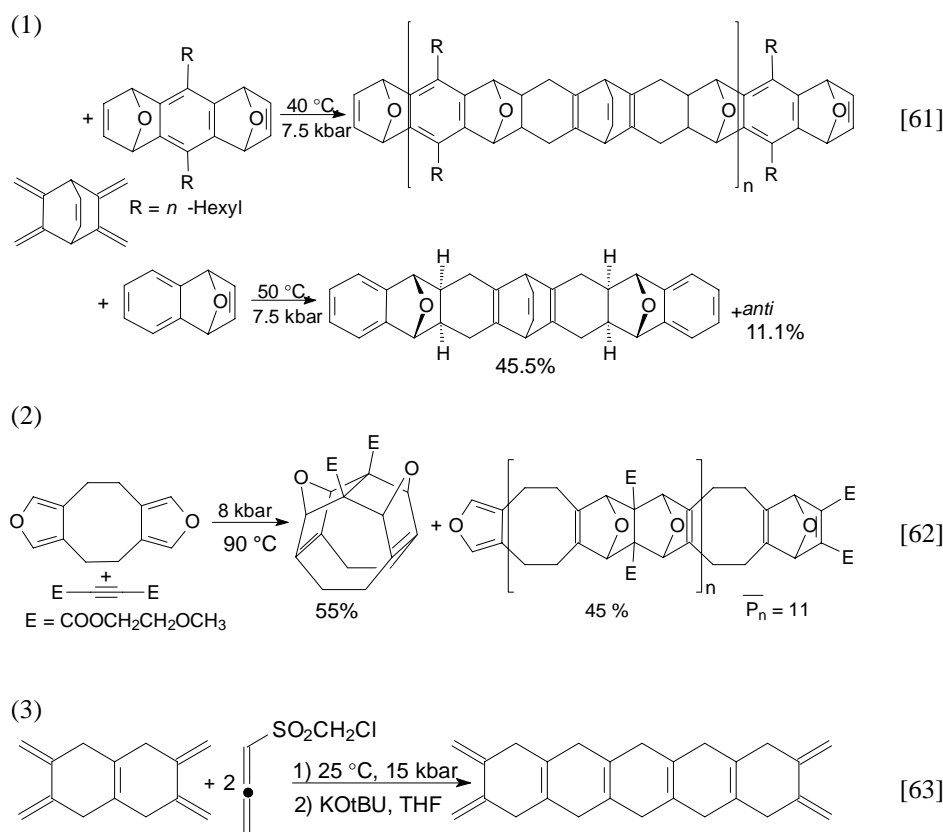
If the oxo (or methano) bridges are not exclusively *syn* to one another either in the bis-dienophiles or bis-dienes (Scheme 14) or if the bis-diene is too large for the formation of a macrocycle, then the pressure-induced repetitive Diels–Alder reactions (proceeding again highly stereoselectively) produce rigid ribbon-type oligomers on a nanometer-scale. The ethano-bridged bis-diene reacts less stereoselectively than the methano- or oxo-bridged bis-dienes [61]. It forms with oxabenzonorbornadiene as dienophile a (2:1)cycloadduct and with bis-dienophiles the ribbon-type oligomers with long chain-lengths. A more flexible ribbon-type structure can be obtained by repetitive Diels–Alder reactions of the difuranocyclooctane as bis-diene with dimethyl acetylenedicarboxylate as bis-dienophile. The cage compound is formed in an undesired side-reaction [62]. The extension of the spacer-unit of a bis-diene can be achieved by the pressure-induced Diels–Alder reaction of the bis-diene with allenylchloromethylsulfone followed by basic HCl and SO₂ elimination [63].

High pressure can be also useful in tandem reactions consisting of a Diels–Alder [4+2] cycloaddition followed by a 1,3-dipolar [3+2] cycloaddition or a Claisen–Ireland rearrangement (Scheme 15). Tandem [4+2]/[3+2] cycloadditions of nitroalkenes and with electron-rich dienophiles and electron-poor dipolarophiles have

been applied in the synthesis of several natural alkaloids [64]. At atmospheric pressure this reaction needs either strongly activated nitroalkenes or a stoichiometric amount of Lewis acid as “catalyst”. At high pressure the tandem reaction occurs with nonactivated nitroalkenes and a variety of different dienophiles and dipolarophiles readily at 20 °C [65]. By the use of electron-rich dienophile and electron-poor or neutral dipolarophiles an one-pot-three-component tandem cycloaddition can be run (Scheme 15, entry (1)) [66]. In the second tandem reaction (Scheme 15, entry (2)) high pressure highly accelerates the Diels–Alder reaction which proceeds in the rate-determining step. Thus, pressure has a strong effect on the overall reaction [67]. The consecutive reactions of quadricyclane and norbornadiene, respectively, consisting of a homo-Diels–Alder reaction with dimethylacetylenedicarboxylate followed by a Diels–Alder reaction of the primary adduct with 1,3-diene leading to polycyclic compounds profit from high pressure, so that in some reactions the final bisadducts can be observed only at high pressure [68].

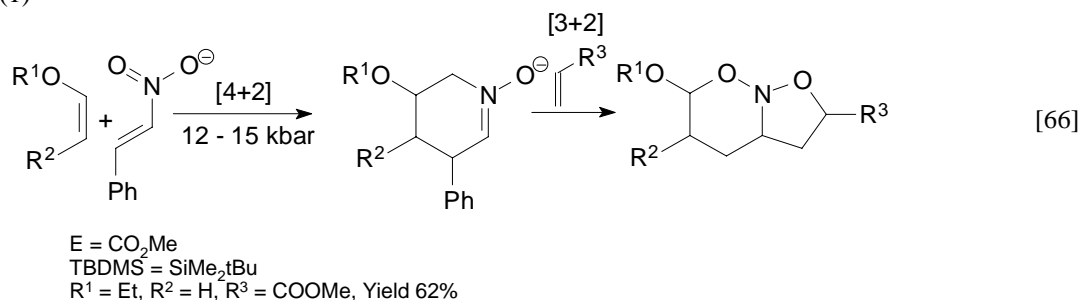
2.3 1,3-Dipolar [3+2] Cycloadditions

1,3-Dipolar cycloadditions usually occur stereospecifically with retention of configuration in the dipolaro-

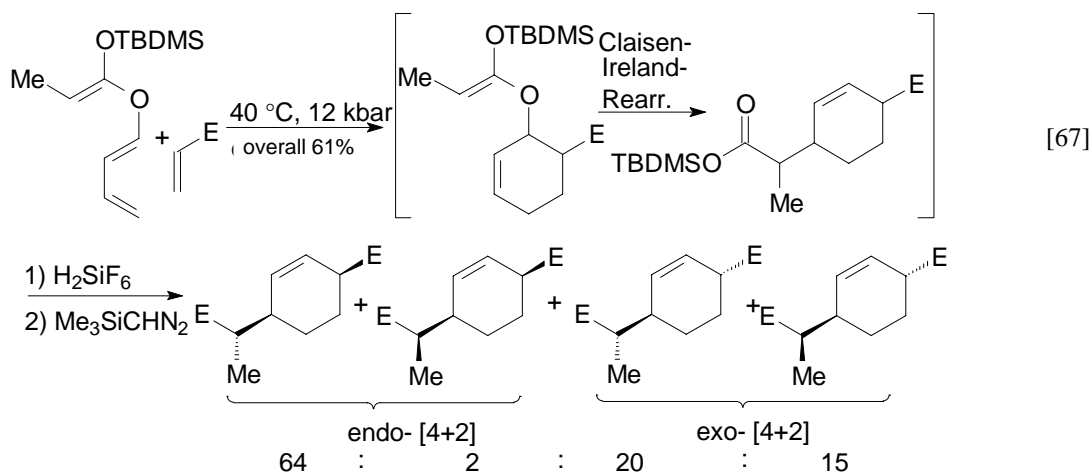


Scheme 14 Synthesis of ribbon-type oligomers by means of pressure-induced repetitive Diels–Alder reactions

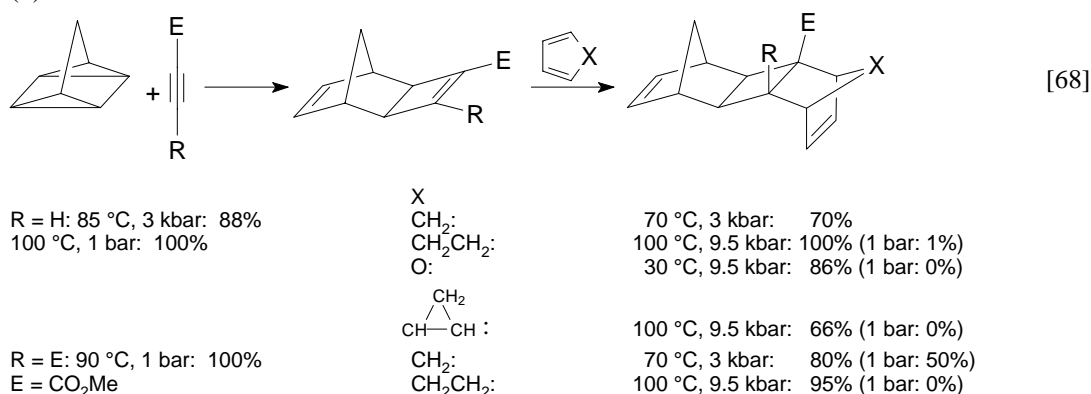
(1)



(2)



(3)

**Scheme 15** The effect of pressure on tandem reactions

philes, and their rates are relatively insensitive to solvent polarity [69]. These results have been taken as an evidence for a concerted process. Only few exceptions are known where the non stereospecific course of reaction suggests a stepwise mechanism [70]. Activation and reaction volumes were measured for few reactions of diazoalkanes, nitrones, and alkyl azides as dipoles with electron-deficient or neutral alkenes as dipolarophiles already in the early 1980 s. They are generally in the range of $\Delta V^\ddagger = -(21 \pm 3) \text{ cm}^3 \text{ mol}^{-1}$ and $\Delta V =$

$-(25 \pm 2) \text{ cm}^3 \text{ mol}^{-1}$ [71]. The relatively large ratios ($\Delta V^\ddagger : \Delta V$) have been regarded as an indicator for a pericyclic mechanism. The absolute values of ΔV and ΔV^\ddagger for 1,3-dipolar cycloadditions, however, are about 5 to 10 $\text{cm}^3 \text{ mol}^{-1}$ smaller than those of Diels–Alder reactions. No clear explanation has been given for this difference. But one can assume, that one reason might be the ring-size dependence of the volume change in cyclizations. According to the information provided later the decrease in volume seems to be larger for the for-

mation of a six-membered ring rather than of a five-membered ring [72].

At 12 kbar and 25 °C benzylazide undergoes a regioselective 1,3-dipolar cycloaddition with a substituted methyl methoxymethacrylate whereas at 1 bar and 80% a (1:1) mixture of the two regioisomeric cycloadducts is formed (Scheme 16, entry (1)) [73]. In the pressure-induced cycloaddition of nitrones with electron-deficient alkenes, alkynes and nitriles the yields and the selectivities of the cycloadducts are better than at 1 bar and higher temperatures. The silyloxazoline resulting from the pressure-induced reaction of benzylphenylnitron with trimethylsilylacetylene can be used for the synthesis of β -lactam antibiotics [74]. The 1,3-dipolar cycloadditions of nitrones with electron-rich enoethers are less influenced by pressure. Moderate pressure of ca. 2 kbar and a Lewis acid catalyst turned out to be the optimum conditions for some of these reactions. The first step in the reaction of diazomethane with 1-phenylphosphole (Scheme 16, entry (3)) is certainly the addition of diazomethane to the phosphorus ($R_3P + CH_2N_2 \rightarrow R_3P=N=N=CH_2$) followed by hydrolysis leading to the highly reactive 1-phenylphosphole-1-oxide which reacts with

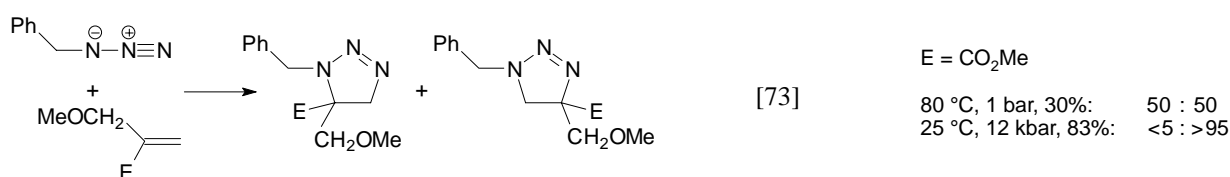
diazomethane to the phosphole and the 1,3-dipolar cycloaddition as well, so that the overall reaction is almost completed at 12 kbar within 12 hours compared to 10 day at 3–5 bar where the monoadduct is formed, preferentially.

2.4 [2+2] Cycloadditions

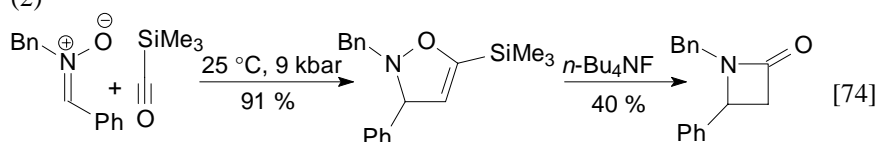
[2+2] Cycloadditions involving ketene derivatives as one or both reaction partners are assumed to be rare examples of concerted $[\pi_s^2 + \pi_a^2]$ cycloadditions [76]. The activation volumes determined for the [2+2] cycloaddition of diphenylketene [77] and the [2+2] cycloadditions of diphenylketene to various enoethers [78] turned out to be with $-30 \text{ cm}^3 \text{ mol}^{-1}$ and -22 to $-52 \text{ cm}^3 \text{ mol}^{-1}$, respectively, highly negative. Thus, the effect of pressure leads to a powerful acceleration of these [2+2] cycloadditions comparable to that of Diels–Alder reactions which is useful for synthetic purposes. For example, various β -lactams can be easily synthesized by pressure-induced [2+2] cycloadditions of alkyl and aryl isocyanates and enoethers [79].

Dolbier and Weaver investigated the effect of pressure on the stereo- and regioselectivity in a certainly

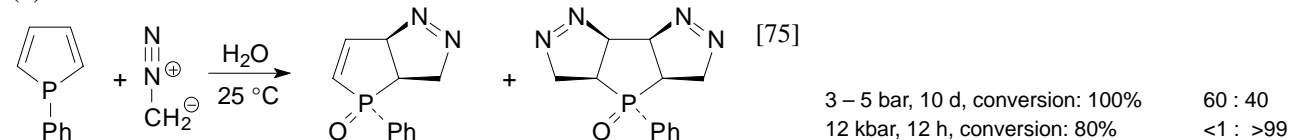
(1)



(2)



(3)



Scheme 16 Pressure-induced 1,3-dipolar cycloadditions

diazomethane in the fashion of a 1,3-dipolar cycloaddition to form the monoadduct and subsequently the bisadduct [75]. (In the absence of water none of the cycloadducts are formed.) Apparently, high pressure has a strongly rate-enhancing effect on the first addition of

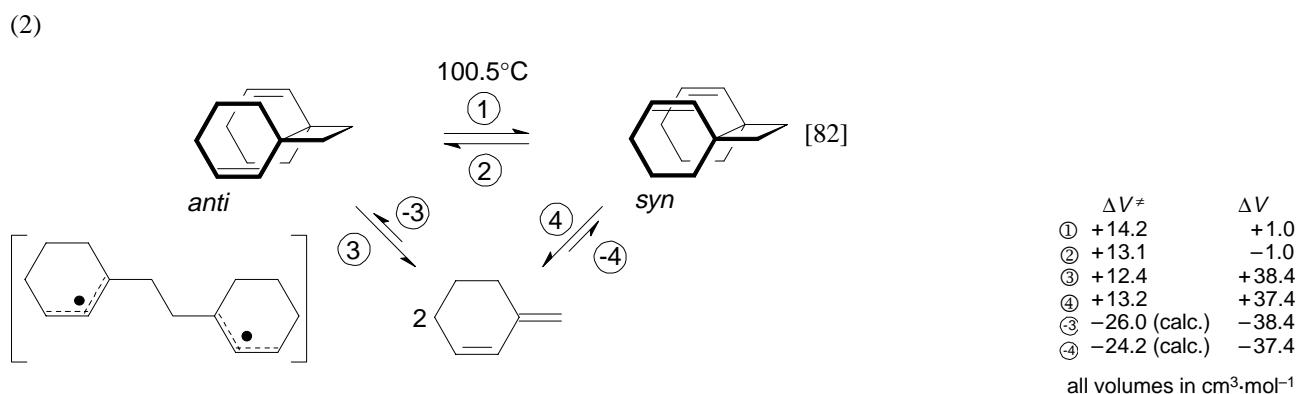
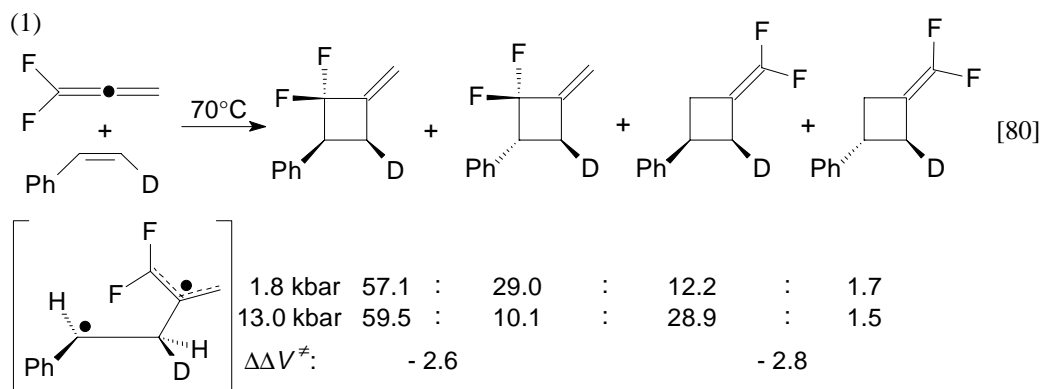
stepwise [2+2] cycloaddition of 1,1-difluoroallene to (*Z*)- β -deuteriostyrene involving a diradical intermediate (Scheme 17) [80]. In order to explain the pressure-induced increase in stereoselectivity corresponding to $\Delta\Delta V^\ddagger = \Delta V^\ddagger(Z) - \Delta V^\ddagger(E) = -2.6$ and $-2.8 \text{ cm}^3 \text{ mol}^{-1}$ (pro-

vided that there is a linear relationship between $\ln(Z/E)$ and pressure up to the very high pressure of 13 kbar) the authors concluded that at high pressure the ring-closure in the diradical intermediate leading to the (*Z*)-configured methylenecyclobutane derivatives are favoured over bond rotation which is a prerequisite for the formation of (*E*)-configured methylenecyclobutanes.

The activation volumes of stepwise [2+2] cycloadditions in non polar systems proceeding *via* diradical intermediates are negative but significantly less negative than those of pericyclic Diels–Alder reactions as already mentioned. An example is the cyclodimerization of 1,3-butadiene [81]. The activation volume ($\Delta V^\ddagger = -20.9 \text{ cm}^3 \text{ mol}^{-1}$) of the [2+2] cyclodimerization leading to *trans*-1,2-divinylcyclobutane is less negative by $-17.5 \text{ cm}^3 \text{ mol}^{-1}$ than that of the competing Diels–Alder [4+2] cycloaddition ($\Delta V^\ddagger = -38.4 \text{ cm}^3 \text{ mol}^{-1}$) leading to 4-vinylcyclohexene so that the [2+2] cyclodimerization can be almost completely suppressed by the use of high pressure. The semicyclic 1,3-diene system of the 3-methylenecyclohexene is confined strictly to a *transoid* conformation. Thus, its reactions are limited to the [2+2] cyclodimerization. The thermally induced cyclodimerization of 3-methylenecyclohexene, however, cannot be observed because of the unfavorable position of the

equilibrium which is on the side of the starting material even at high pressure (at 7.5–8.0 kbar and 25–60 °C: *syn* and *anti*-cyclodimers $\leq 1\%$). Starting from the photochemically accessible *syn*- and *anti*-cyclodimers the activation and reaction volumes of the mutual *syn-anti* interconversion and the [2+2] cycloreversions were determined [82]. From these data the activation volumes of the not directly observable [2+2] cyclodimerizations can be calculated which are comparable to those determined for the [2+2] cyclodimerization of chloroprene (23 °C: $\Delta V^\ddagger = -22 \text{ cm}^3 \text{ mol}^{-1}$) [15], 1,3-cyclohexadiene (70.5 °C: $\Delta\Delta V^\ddagger = -22$ and $-18 \text{ cm}^3 \text{ mol}^{-1}$ for the formation of the *syn*- and *anti*- [2+2] cyclodimer, respectively) [16], and 1,3-butadiene [81]. The finding, that volumes of activation of the mutual *syn-anti* interconversion and the [2+2] cycloreversion of the cyclodimers of 3-methylenecyclohexene dimers are positive and of the same order of magnitude, is good evidence that the cyclobutane ring-opening leading to corresponding diradical intermediate occurs in the rate-determining steps of both reactions.

The [2+2] cycloaddition of tetracyanoethene (TCNE) to vinyl ethers shows a powerful pressure-induced acceleration resulting in highly negative activation volumes (for example $\Delta V^\ddagger = -55.0 \text{ cm}^3 \text{ mol}^{-1}$, $\Delta V = -31.9 \text{ cm}^3 \text{ mol}^{-1}$ (25 °C, CH_2Cl_2) for the cycloaddition



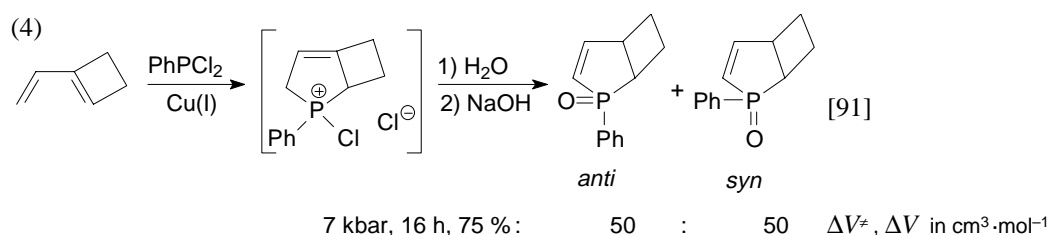
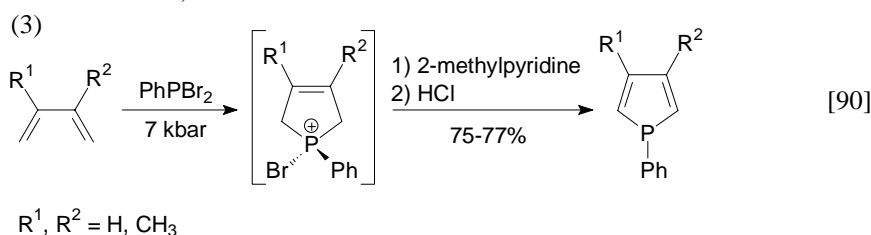
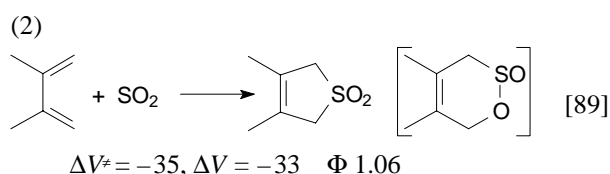
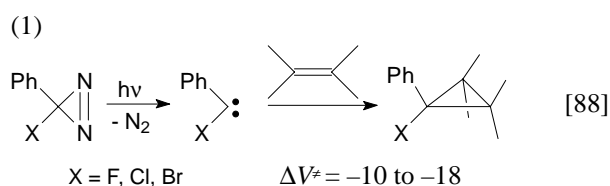
Scheme 17 The effect of pressure on stepwise [2+2] cycloadditions and [2+2] cycloreversions

of TCNE to ethylvinylether) [83]. Detailed mechanistic studies [84] allow the conclusion that these reactions proceed stepwisely passing through interceptable dipolar intermediates. The observation, that the activation volumes are generally more negative than the corresponding reaction volumes ($\Phi = \Delta V^\ddagger/\Delta V > 1$) has been confirmed by the finding that [2+2] cycloreversion of a TCNE-vinylether cycloadduct is also accelerated by pressure and, hence, its activation volume is negative, too [85]. Due to the effect of electrostriction the partial molar volumes of the dipolar intermediate and the polar transition states for its formation are smaller than those of the reactants (TCNE and vinylether) and the cycloadduct. This powerful effect of pressure on polar cycloadditions has been used in the synthesis of various dicyanoalkoxy-substituted cyclobutane derivatives [86].

2.5 Cheletropic Reactions

Cheletropic reactions were defined by Woodward and Hoffmann to be processes in which two σ bonds directed to the same atom are formed or cleaved in one step [87]. The addition of a singlet carbene to an alkene is an example of a non-linear cheletropic reaction. Turro,

Moss and coworkers generated phenylhalogenocarbenes (Ph-C-X : $X = \text{F, Cl, Br}$) by flash photolysis of the corresponding azirines and studied the pressure-dependence of their addition to tetramethylethene and (*E*)-2-pentene at room temperature up to 2 kbar (Scheme 18, entry (1)) [88]. The activation volumes ($\Delta V^\ddagger = -10$ to $-18 \text{ cm}^3 \text{ mol}^{-1}$) were found to be less negative (by about 20 to $30 \text{ cm}^3 \text{ mol}^{-1}$) than those found for Diels–Alder reactions. This result can be explained by the interdependence between the effect of pressure and ring size (*vide infra*). The addition of SO_2 to 1,3-dienes (Scheme 18, entry (2)) is an example of a linear cheletropic reaction. The activation volume for the reaction between SO_2 and 2,3-dimethyl-1,3-butadiene was found by Isaacs and Laila to be more negative than the reaction volume comparable to many Diels–Alder reactions [89]. For that reason one may speculate that in the rate-determining step the Diels–Alder adduct (the six-membered ring sulfonic ester) is formed followed by a rearrangement to the observed five-membered ring sulfone. The cheletropic addition of PhPBr_2 to 1,3-dienes leading to the corresponding phospholes after basic HBr elimination of the primary adduct can be dramatically accelerated by high pressure [90]. In the analogous reaction of PhPCl_2 with 1-vinylcyclobutene the time of reaction could be reduced from two months to 16 h by raising the pressure from 1 bar to 7 kbar (Scheme 18, entry (3) and (4)) [91].



3. Pericyclic Rearrangements

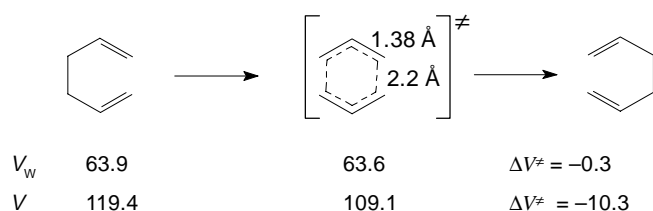
Many pericyclic rearrangements show a pressure-induced acceleration which is characterized by negative volumes of activation [6]. The effect of pressure on rearrangements is usually smaller than that on intermolecular cycloadditions and may be explained with larg-

Scheme 18 The effect of pressure on cheletropic reactions

er packing coefficients of the pericyclic transition states compared to those of the corresponding acyclic ground states as already discussed for the pericyclic and stepwise cycloadditions.

3.1 Sigmatropic [3.3] Shifts: Cope and Claisen Rearrangement

On the basis of stereochemical, kinetic investigations and quantum-mechanical calculations, most Cope rearrangements are regarded as being pericyclic processes [14, 92, 93]. The van der Waals volumes calculated for the parent 1,5-hexadiene and the pericyclic transition state [72, 94] are approximately the same (Scheme 19). This is understandable since in the symmetrical transition state the bond breaking and making have proceeded to the same extent so that the effects of the two processes on the van der Waals volume compensate each other and no great overall effect of pressure on the Cope rearrangement is to be expected. However, it is reasonable to assume that the pericyclic transition state exhibits a larger packing coefficient than the acyclic ground state. Therefore, the activation volume is expected to be negative. The activation volume of the degenerate Cope rearrangement of 1,5-hexadiene can be estimated to approximately $-10 \text{ cm}^3 \text{ mol}^{-1}$ if the packing coefficient determined for cyclohexene [4] is used for the unknown packing coefficient of the pericyclic transition state.



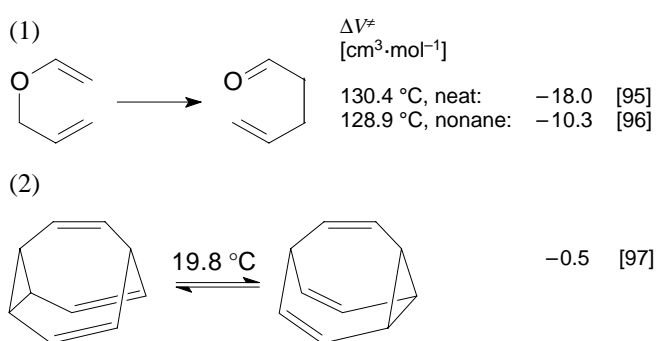
All volumes are given in $\text{cm}^3 \cdot \text{mol}^{-1}$. The structural parameters necessary for the calculation of the van der Waals volume for the transition structure (TS) were taken from *ab initio* [14, 93] calculations. The partial molar volume for the TS was calculated from the equation:

$$V(\text{TS}) = V_w(\text{TS})/\eta \text{ (cyclohexene)}; \quad \eta \equiv V_w/V = 0.5829 \text{ (cyclohexene)}.$$

Scheme 19 Partial molar volume (V), van der Waals volume (V_w) of 1,5-hexadiene and the pericyclic transition state of the Cope rearrangement

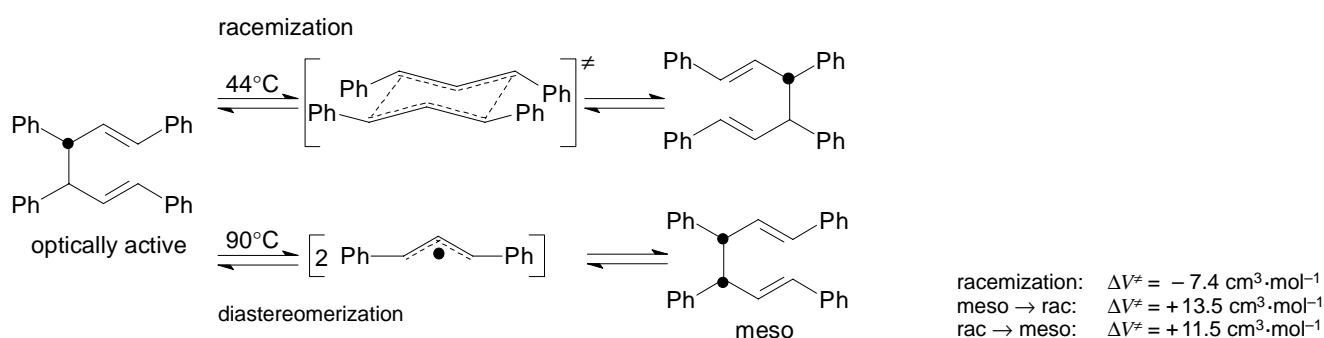
In fact, negative activation volumes of the expected size ($\Delta V^\ddagger = -7$ to $-13 \text{ cm}^3 \text{ mol}^{-1}$) were found for several Cope rearrangements and related Claisen rearrangements [95]. The only exception is the activation volume of the Claisen rearrangement of the neat parent allylvinylether (Scheme 20, entry (1)) which was determined to be $\Delta V^\ddagger = -18 \text{ cm}^3 \text{ mol}^{-1}$ [96]. A new meas-

urement of the pressure-dependent kinetics of this rearrangement in solution led to an activation volume $\Delta V^\ddagger = -10.3 \text{ cm}^3 \text{ mol}^{-1}$ [97] which is of similar size as those determined for the other Cope and Claisen rearrangements. With the concept of cyclic interaction, introduced here, we can understand why the degenerate Cope rearrangement in bullvalene, investigated by Merbach, le Noble and coworkers [98] with pressure- and temperature-dependent NMR spectroscopy, shows no significant pressure effect ($\Delta V^\ddagger = -0.5 \text{ cm}^3 \text{ mol}^{-1}$) (Scheme 20, entry (2)). As a result of the rigid bullvalene skeleton no such cyclic interaction appears in the transition state.



Scheme 20 The effect of pressure on the Claisen rearrangement of allylvinylether and the degenerate Cope rearrangement in bullvalene

The utility of high pressure in the elucidation of reaction mechanisms can be also demonstrated by the example of the racemization and diastereomerization in 1,3,4,6-tetraphenyl-1,5-hexadiene (Scheme 21) indicating that a pericyclic Cope rearrangement competes here with a dissociative process involving free-radical intermediates [99]. Optically active tetraphenylhexadiene undergoes a facile racemization at temperatures just above room temperature. At $90 \text{ }^\circ\text{C}$ *racemic* tetraphenylhexadiene shows a mutual interconversion to the *meso*-diastereomer. Whereas the racemization may be the result of a pericyclic Cope rearrangement involving a chair-like transition state, the mutual diastereomerization cannot be explained by one or a sequence of Cope rearrangements involving chair- or boat-like transition states. The effect of pressure allowed an unambiguous mechanistic conclusion. The observation, that the racemization is accelerated by pressure and, therewith, exhibits a negative volume of activation, is good evidence for a pericyclic Cope mechanism in this case. The finding, that the diastereomerization is retarded by pressure, excludes a pericyclic mechanism or a cyclization by one-bond closure in the rate-determining step and suggests a homolytic bond cleavage in the rate-determining step leading to the 1,3-diphenylallyl radicals as intermediates which can recombine to the two observed diastereomers.

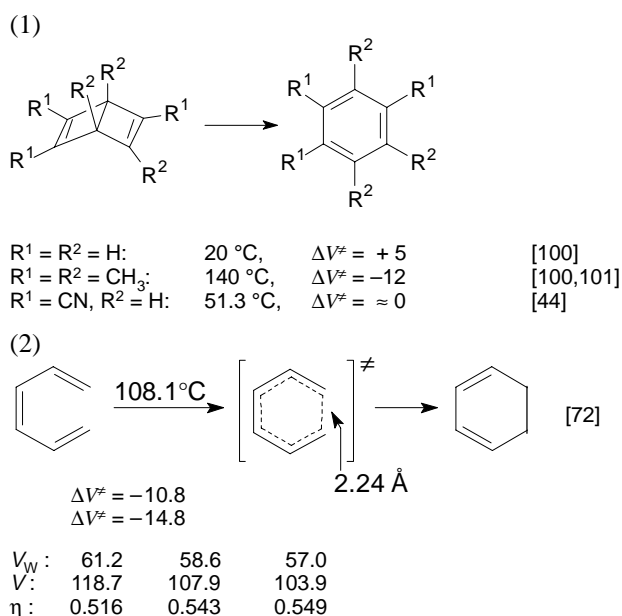


Scheme 21 Activation volumes of the racemization of optically active 1,3,4,6-tetraphenyl-1,5-hexadiene and the mutual interconversion of the *meso* into the racemic diastereomer

3.2 Electrocyclic Rearrangements

The electrocyclic ring-opening of heavily substituted cyclobutene derivatives investigated by Plieninger *et al.* [100] shows negative volumes of activation of different size dependent on the substitution pattern contrary to the expectation of positive activation volumes resulting from the ring-opening. This result indicates that, for example, steric effects contribute substantially to the observed negative activation volumes overcompensating the increase in volume expected from the ring-opening. Clear-cut examples showing both effects are the isomerization of parent [101] and hexamethyl-Dewar benzene [101, 102] leading to benzene and hexamethylbenzene, respectively (Scheme 22, entry (1)). The isomerization of the parent Dewar benzene is retarded by pressure (20 °C: $\Delta V^\ddagger = +5 \text{ cm}^3 \text{ mol}^{-1}$) whereas that of the hexamethyl derivative is accelerated by pressure (140 °C: $\Delta V^\ddagger = -12 \text{ cm}^3 \text{ mol}^{-1}$, $\Delta V = -22 \text{ cm}^3 \text{ mol}^{-1}$). Evidently, the steric crowding of the six methyl groups in the planar hexamethyl benzene is larger than in the nonplanar hexamethyl Dewar benzene overcompensating, the volume-increasing effect of the ring-opening. In the ring-opening of 2,3,5-tricyano Dewar benzene leading to 1,2,4-tricyanobenzene [44] the two effects obviously compensate each other so that this rearrangement is almost pressure-independent (51.3°C: $\Delta V^\ddagger \approx 0 \text{ cm}^3 \text{ mol}^{-1}$).

In the transition state of the electrocyclozation of (*Z*)-1,3,5-hexatriene to 1,3-cyclohexadiene (Scheme 22, entry (2)) a new six-membered ring develops analogously to that of the Cope rearrangement [72]. The electrocyclozation is accelerated by pressure, showing a negative activation volume of $\Delta V^\ddagger = -10.8 \text{ cm}^3 \text{ mol}^{-1}$ which is similar to those of the Cope rearrangements. From the volume data listed in Scheme 22, entry (2) the packing coefficient of the transition state is calculated to equal approximately that of the cyclic product and differs significantly from that of the acyclic reactant. This result again provides good evidence for the assumption that the packing coefficients of pericyclic transition states resemble those of the corresponding cyclic ground states.

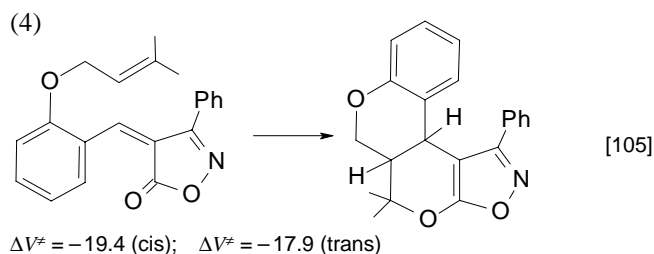
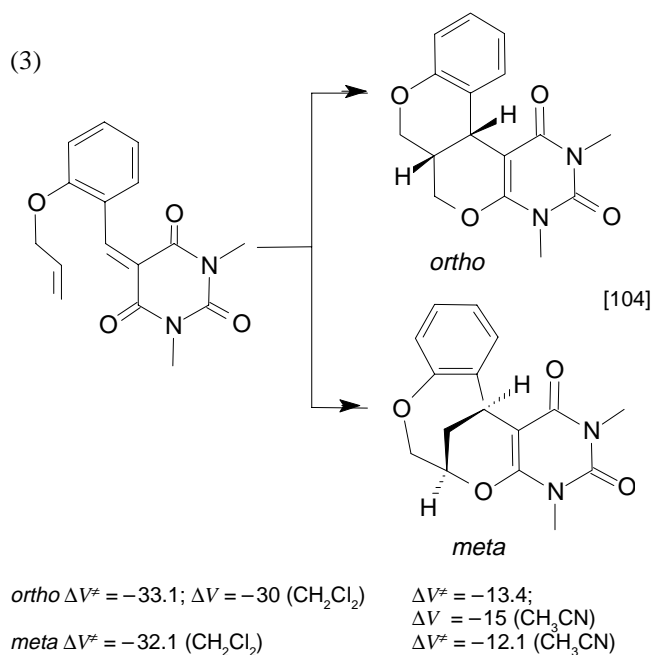
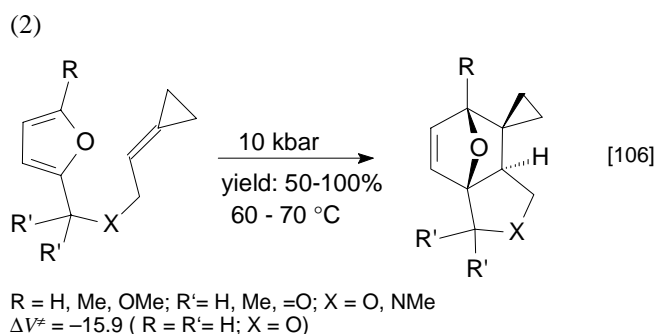
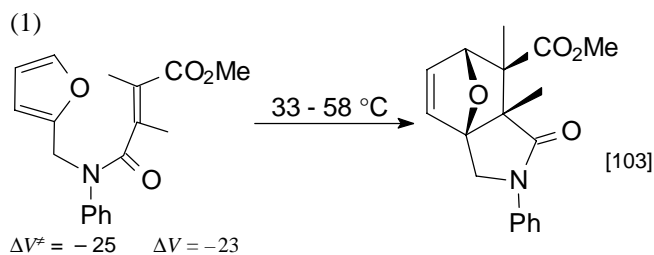


Scheme 22 Electrocyclic rearrangements of substituted Dewar benzene derivatives and (*Z*)-1,3,5-hexatriene. All volumes are given in $\text{cm}^3 \cdot \text{mol}^{-1}$

3.3 Intramolecular Diels–Alder Reactions

In intramolecular Diels–Alder reactions, two new rings are formed. There are examples of relatively large pressure-induced accelerations comparable to the acceleration observed in intermolecular Diels–Alder reactions which can be exploited for preparative purposes [38, 103–114]. All the hitherto studied systems contain polar groups and are, therefore, not very suitable for the analysis of the relation between pressure effect and ring formation. The strong solvent dependence of the activation volume of the intramolecular Diels–Alder reaction shown in Scheme 23 indicates that other effects than ring formation, for example electrostriction, may also be important for the size of the activation volume [104].

To analyze the effect of ring-size and ring-number on the volume changes. The activation and reaction volumes of the intramolecular Diels–Alder reactions in the nonplanar pure hydrocarbon systems (*E*)-1,3,8-nonatri-

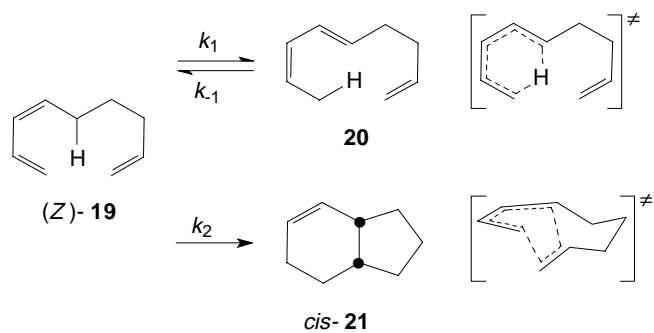


Scheme 23 Pressure dependence of intramolecular Diels–Alder reactions (ΔV^\ddagger , ΔV in cm³·mol⁻¹)

ene [94] and (*E*)-1,3,9-decatriene [72] were determined (Table 2). The packing coefficients η of the transition states are calculated to be equal to or even larger than those of the corresponding bicyclic products compar-

able to the packing coefficients calculated for the electrocyclic ring-closure of (*Z*)-1,3,5-hexatriene to 1,3-cyclohexatriene (Scheme 22, entry (2)). The absolute values of the activation volumes of intramolecular Diels–Alder reactions are approximately twice as large as or even larger than those determined for the Cope rearrangements or the electrocyclization of 1,3,5-hexatriene to 1,3-cyclohexadiene (Scheme 22). From this it was extrapolated that each additional five- or six-membered ring formed in the rate-determining step of a pericyclic reaction contributes about -10 to -15 cm³ mol⁻¹ to its activation volume.

A particularly instructive example is the thermolysis of (*Z*)-1,3,8-nonatriene in which an intramolecular Diels–Alder reaction competes with a sigmatropic [1.5] hydrogen shift (Scheme 24) [94]. The use of high pressure leads to a significant acceleration of the overall reaction and allows a reversal of the selectivity. At 150 °C and 1 bar the [1.5] hydrogen shift passing through a monocyclic transition state is preferred. At 7.7 kbar the intramolecular Diels–Alder reaction is the favored process, evidently due to its bicyclic transition state. The difference in the activation volumes of the two processes extrapolated from the pressure dependence of the product ratio ($\Delta\Delta V^\ddagger \leq -10$ cm³ mol⁻¹) is comparable to those observed for the pericyclic rearrangements involving monocyclic and bicyclic transition states.



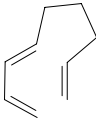
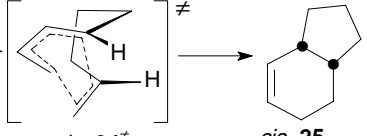
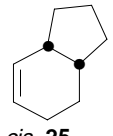
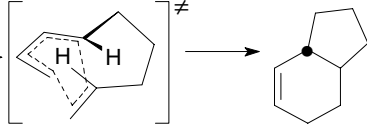
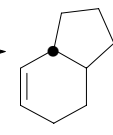
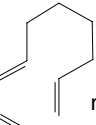
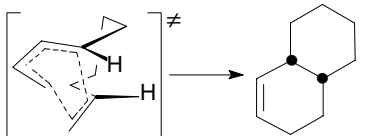
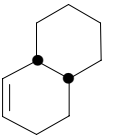
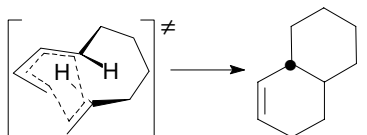
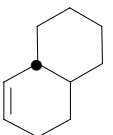
150.2 °C, 24 h, *n*-Pentane:
 1 bar: 80.2% (*Z*)-19, 13.7% 20, 6.1% *cis*-21
 7.7 kbar: 5.5% (*Z*)-19, 18.2% 20, 76.4% *cis*-21
 $\Delta\Delta V^\ddagger = \Delta V^\ddagger$ (*Z*-19 \rightarrow *cis*-21) - ΔV^\ddagger (*Z*-19 \rightarrow 20)
 ≤ -10 cm³·mol⁻¹

Scheme 24 Pressure dependence of the thermolysis of (*Z*)-19

3.4 The Relationship between Activation or Reaction Volume and Ring-Size

A first hint for the ring-size dependence of volume data came from the observation, that the ring-enlargement of *cis*-1,2-divinylcyclobutane to 1,5-cyclooctadiene ($\Delta V = -12.8$ cm³ mol⁻¹) and *trans*-1,2-divinylcyclo-

Table 2 Volume data of the intramolecular Diels–Alder reactions of nonatriene (*E*)-**22** and decatriene (*E*)-**23**

		reaction	ΔV^\ddagger	ΔV	θ		
 (<i>E</i>)- 22 V_W 91.6 V 180.9 η 0.506	153.2°C n-hexane	 $cis\text{-}24^\ddagger$ 87.0 156.1 0.557	 $cis\text{-}25$ 83.3 148.9 0.559	-24.8	-32.0	0.78	
		 $trans\text{-}24^\ddagger$ 87.0 156.1 0.557	 $trans\text{-}25$ 83.4 152.4 0.547	-24.8	-28.5	0.87	
	 (<i>E</i>)- 23 V_W 102.8 V 202.0 η 0.509	172.5°C n-heptane	 $cis\text{-}26^\ddagger$ 97.7 164.4 0.594	 $cis\text{-}27$ 93.8 156.7 0.599	-37.6	-45.4	0.83
			 $trans\text{-}26^\ddagger$ 97.7 167.0 0.585	 $trans\text{-}27$ 93.8 164.6 0.570	-35.0	-37.4	0.94

All Volumes are given in $\text{cm}^3 \text{mol}^{-1}$ and related to the reaction temperatures at 153.2°C and 172.5°C , respectively, $\eta = V_W/V$ is the packing coefficient and $\theta = \Delta V^\ddagger/\Delta V$ the ratio of activation volume to reaction volume.

butane to 4-vinylcyclohexene and 1,5-cyclooctadiene ($\Delta V = -9.6$ and $-17.4 \text{ cm}^3 \text{mol}^{-1}$, respectively) shows highly negative reaction volumes [115]. This means that the ring-enlargement from a four- to a six- and finally eight-membered ring is accompanied by a substantial volume contraction. The volumes of reaction calculated for the hypothetical cyclizations of 1-alkenes from their partial volumes ($\Delta V = V(\text{cycloalkane}) - V(1\text{-alkene})$) confirm this trend (Table 3) [72]. They decrease continuously from the formation of the three-membered ring ($\Delta V = -5.5 \text{ cm}^3 \text{mol}^{-1}$) up to the formation of the ten-membered ring ($\Delta V = -32.3 \text{ cm}^3 \text{mol}^{-1}$) and then, seem to be constant for the larger rings, whereas the van der Waals volumes of reaction (ΔV_W) are approxi-

mately equal, with the exceptions of the cyclopropane, cyclobutane, and cyclopentane formation, and cannot explain the dramatic decrease found for the volumes of reaction. Therefore, this ring-size dependent decrease in volume observed for the cyclizations of the 1-alkenes to the cycloalkanes results from the different packing of the cyclic and open-chained compounds rather than from the changes in their intrinsic molecular volumes.

A simple explanation may come from the assumption that the empty space between the single molecules, which can be attributed to the so-called void volume and expansion volume required for the thermally induced motions and collisions of the molecules in the liquid state, as pointed out by Asano and le Noble al-

Table 3 Volume of reaction (ΔV), van der Waals volumes of reaction (ΔV_w), enthalpies, entropies, and Gibbs enthalpie of reaction calculated for the hypothetical cyclizations of 1-alkenes to cycloalkanes by means of the corresponding thermodynamic parameters [72].

			$\Delta V_w^a)$	$\Delta V^a)$	$\Delta H^b)$	$\Delta S^c)$	$\Delta G^b)$
	→		-1.7	-5.5	7.86	-7.0	9.95
	→		-2.5	-6.6	6.43	-10.3	9.50
	→		-3.8	-14.7	-13.46	-13.1	-9.56
	→		-4.4	-16.5	-19.47	-21.0	-13.21
	→		-4.7	-21.2	-13.41	-19.6	-7.57
	→		-4.9	-25.6	-9.88	-18.8	-4.28
	→		-4.7	-30.9			
	→		-4.6	-32.3			
	→		-4.7	-32.8			
	→		-4.7	-32.3			
	→		-4.6	-27.6			

^{a)} $\text{cm}^3 \cdot \text{mol}^{-1}$. V (n -alkene) calculated by the use of Exner increments [18]. V (cycloalkane) determined from density measurements in n -hexane; ^{b)} kcal mol^{-1} ; ^{c)} $\text{cal mol}^{-1} \text{K}^{-1}$.

ready in 1973 [5], is reduced by the ring-closure of an open chain largely due to the restriction of rotational degrees of freedom during the cyclization. Apparently, the larger the ring is, the more degrees of freedom have to be restricted resulting in the observed ring-size dependent volume contraction. An upper limit of this effect seems to be the formation of cyclodecane. The increasing conformational flexibility in the rings larger

than $\text{C}_{10}\text{H}_{20}$ obviously requires a larger volume, which compensates the volume contracting effect of ring-closure so that the volume of reaction observed for the formation of these larger rings remains constant. It is interesting to note that the ΔV -values do not correlate with any other thermodynamic parameter such as enthalpy, entropy, or Gibbs enthalpy of reaction included in Table 3 for the formation of cyclopropane to cyclooctane.

From these parameters the entropy of reaction should reflect best the restriction of the degrees of freedom as it is assumed for the explanation of the volume contractions. The entropy of reaction decreases from the formation of cyclopropane to that of cyclohexane, but increases again for the formation of the larger rings, cycloheptane and cyclooctane, which can be explained with the increasing conformational flexibility of the rings larger than cyclohexane. A better but not a linear correlation is found between the entropies of formation of the cycloalkanes related each to one CH₂ group ($\Delta S_f^0(\text{CH}_2) = \Delta S_f^0(\text{CH}_2)_n/n$) and the packing coefficients, $\eta(\text{CH}_2)_n$, which are identical with those related each to an CH₂ group (Figure 1) [72]. According to nonlinear correlation the entropy parameter responds to conformational flexibility in the medium-sized rings at an earlier state than the volume parameter. In the homologous sequence of *n*-alkanes, however, the entropy of formation per CH₂ group ($\Delta S_f^0(\text{CH}_2) = 9.5 \text{ cal mol}^{-1} \text{ K}^{-1}$) as well as the packing coefficient per CH₂ group ($\eta(\text{CH}_2) = V_w(\text{CH}_2)/V(\text{CH}_2) = 10.4/16.2 = 0.64$) remains constant with the increasing member of chain atoms.

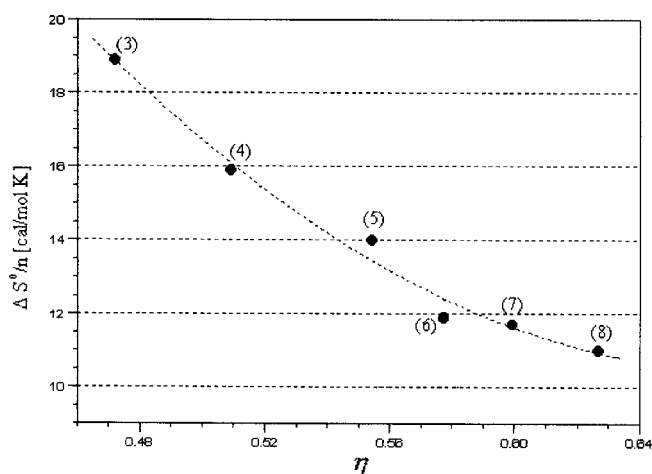


Figure 1 The plot of the entropy of formation of cycloalkanes, from (CH₂)₃ to (CH₂)₈, per CH₂ Group $\Delta S_f^0(\text{CH}_2) = \Delta S_f^0/n$ against their packing coefficients $\eta(\text{CH}_2)_n = V_w(\text{CH}_2)_n/V(\text{CH}_2)_n \equiv \eta(\text{CH}_2)$.

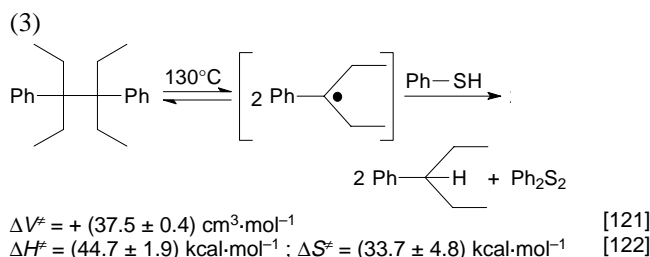
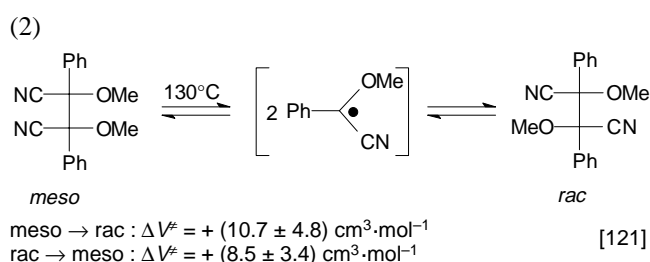
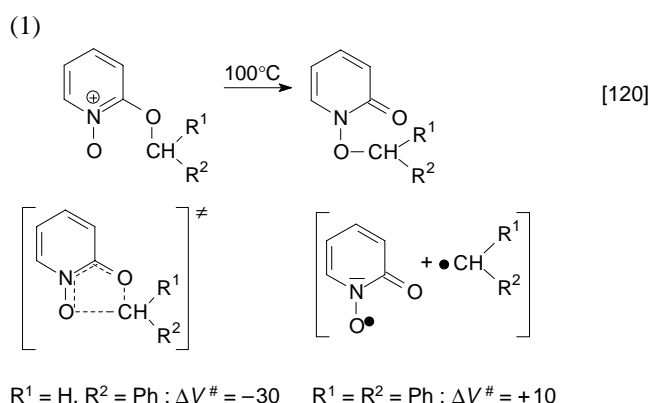
Provided, that the activation volumes depend similarly on the ring-size, the formation of larger rings should be dramatically accelerated by pressure. The intramolecular Diels–Alder reactions of (*E*)-1,3,8-nonatriene and (*E*)-1,3,9-decatriene, in which either a new five- and six-membered ring or two new six-membered rings are formed, seems to be the first example for the validity of this assumption (Table 2). Furthermore, this ring-size effect explains why the activation volume of the formation of three-membered ring in cheletropic reactions of carbenes with alkenes (Scheme 18) and of the

five-membered rings in 1,3-dipolar cycloadditions are substantially less negative than those of the formation of six-membered rings in the Diels–Alder reactions (for example, the 1,3-dipolar cycloaddition of diphenyldiazomethane to ADM: $\Delta V^\ddagger = -23.2 \text{ cm}^3 \text{ mol}^{-1}$, $\Delta V = -26.8 \text{ cm}^3 \text{ mol}^{-1}$ [116], and the Diels–Alder reaction of 2,3-dimethylbutadiene to ADM: $\Delta V^\ddagger = -34.1 \text{ cm}^3 \text{ mol}^{-1}$; $\Delta V = -38.8 \text{ cm}^3 \text{ mol}^{-1}$ [12]; ADM – methyl acetylenedicarboxylate).

4. Free-Radical Reactions

4.1 Homolytic Bond Dissociations

A volume expansion is expected for homolytic bond dissociations as already pointed out in the introduction. This expectation has been confirmed for several homolytic bond cleavages showing positive activation volumes near $\Delta V^\ddagger = +10 \text{ cm}^3 \text{ mol}^{-1}$ [117]. The analysis of the pressure effect on the cleavage of azo compounds is, however, complicated by the possibility of one- and two-bond scission processes [118, 119]. The benzylic



Scheme 25 The effect of pressure on homolytic bond dissociations

and benzhydrylic 1,4-shifts in the substituted pyridiminioxides (Scheme 25, entry (1)) [120] illustrate the utility of high pressure for the distinction between a pericyclic and dissociative mechanism comparable to the rearrangements of 1,3,4,6-tetraphenyl-1,5-hexadiene already mentioned. The negative activation volume determined for the benzylic shift is good evidence for a pericyclic rearrangement whereas the positive activation volume determined for the benzhydrylic shift is in accord with the C–O bond cleavage in the rate-determining step. The large difference between activation volumes observed for rearrangements proceeding *via* homolytic bond cleavage and recombination of the resulting free-radical intermediates ($\Delta V^\ddagger = +6$ to $+13$ cm³ mol⁻¹) on the one hand and for the thiophenol-trapped dissociation of 3,4-diethyl-3,4-diphenylhexane ($\Delta V^\ddagger = +35.7$ cm³ mol⁻¹) on the other hand is remarkable and may be indicative for reactions of caged or solvent-separated radical pairs, respectively [121].

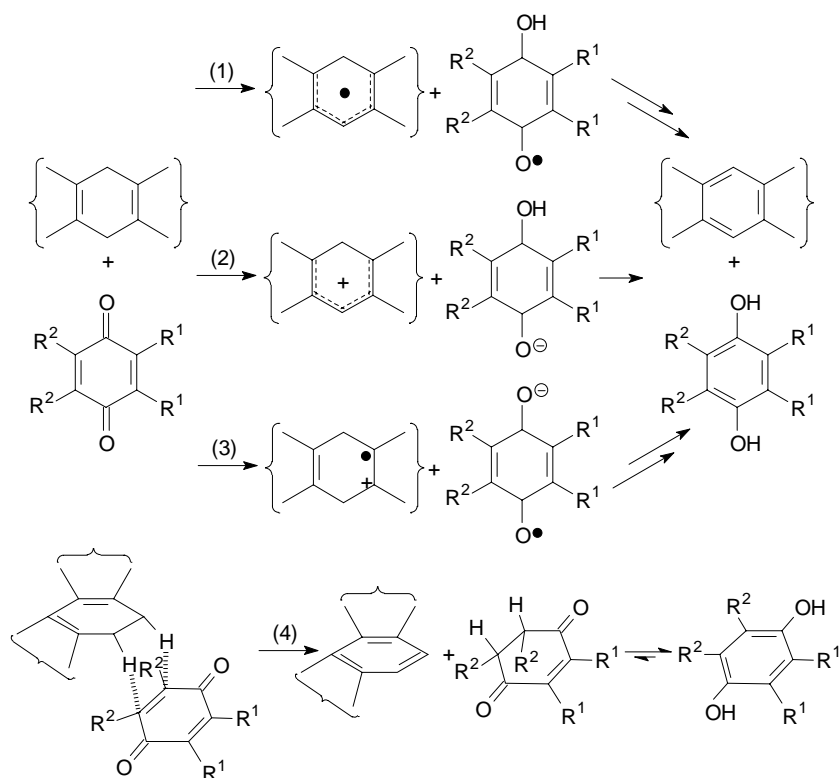
4.2 Quinone Oxidations (Hydrogen Transfer Reactions)

The oxidation of hydroarenes to arenes by quinones such as 2,3-dichloro-5,6-dicyano-1,4-quinone (DDQ) is frequently used for the synthesis of aromatic compounds. Brower *et al.* have already shown that the dehydrogen-

ation 1,4-cyclohexadiene to benzene [123] or tetraline to naphthalene [124] by thymoquinone is accelerated by pressure showing a negative volume of activation ($(\Delta V^\ddagger = -33$ (75 °C) and -28 (175 °C) cm³ mol⁻¹, respectively). A similar effect of pressure has been observed for the oxidation of leuco crystal violet with chloranil ($\Delta V^\ddagger = -25$ cm³ mol⁻¹ (21 °C)) [125]. The pressure-dependent kinetic isotope effect of this reaction (29 °C: $k_H/k_D = 11.5$ (1 bar) and 8.2 (1.5 kbar)) indicates that the hydrogen transfer occurs in the rate-determining step. The large k_H/k_D value at 1 bar and its pressure dependence was attributed to a quantum mechanical tunnelling.

Four mechanisms are discussed for the quinone oxidation of hydroarenes [126]: (1) hydrogen atom transfer leading to a pair of free radicals in the rate-determining step followed by fast subsequent reactions such as disproportionation or single-electron transfer (SET) producing finally the observed arene and hydroquinone, (2) the direct hydride transfer leading to a pair of ions from which the observed products can be formed by proton transfer, (3) single-electron transfer followed by proton transfer producing the same radicals as direct hydrogen transfer, and (4) the pericyclic hydrogen transfer which is limited to systems with vicinal C–H bonds.

Most recent investigations by Rüdhardt *et al.* [126]



Scheme 26 Mechanistic alternatives of quinone dehydrogenations of hydroaromatic compounds. (1) Hydrogen atom transfer, (2) direct hydride transfer, (3) single electron transfer, and (4) pericyclic hydrogen transfer

Table 4 The activation volumes in $\text{cm}^3\text{mol}^{-1}$ of the oxidation of hydroarenes to the corresponding arenes by 2,3-dichloro-5,6-dicyano-1,4-quinone (DDQ) [127]

hydroarene	T (°C)	ΔV^\ddagger (MTBE) ^{a)}	ΔV^\ddagger (MeCN/AcOEt) ^{b)}
1,4-cyclohexadiene	25.1	-24.5	-29.6
9,10-dihydroanthracene	25.1	-25.3	-26.9
9,9,10,10-tetradeutero-9,10-dihydroanthracene	25.1	-35.3 ^{c)}	-
9,9-dimethyl-9,10-dihydroanthracene ^{d)}	39.9	-25.2	-22.8
9,10-dihydrophenanthrene	39.9	-25.1	-29.4
1,4-dihydronaphthalene	24.9	-24.8	-28.8
1,2-dihydronaphthalene	39.9	-25.7	-28.3
tetraline ^{e)}	64.9	-	-26.8

a) methyl-*t*-butylether; b) acetonitrile and ethylacetate (1:1); c) $k_H/k_D = 8.0$ (1 bar) and 4.3 (3 kbar); d) the product is 10,10-dimethyl-9-anthrone. e) the product is 1,2-dihydronaphthalene

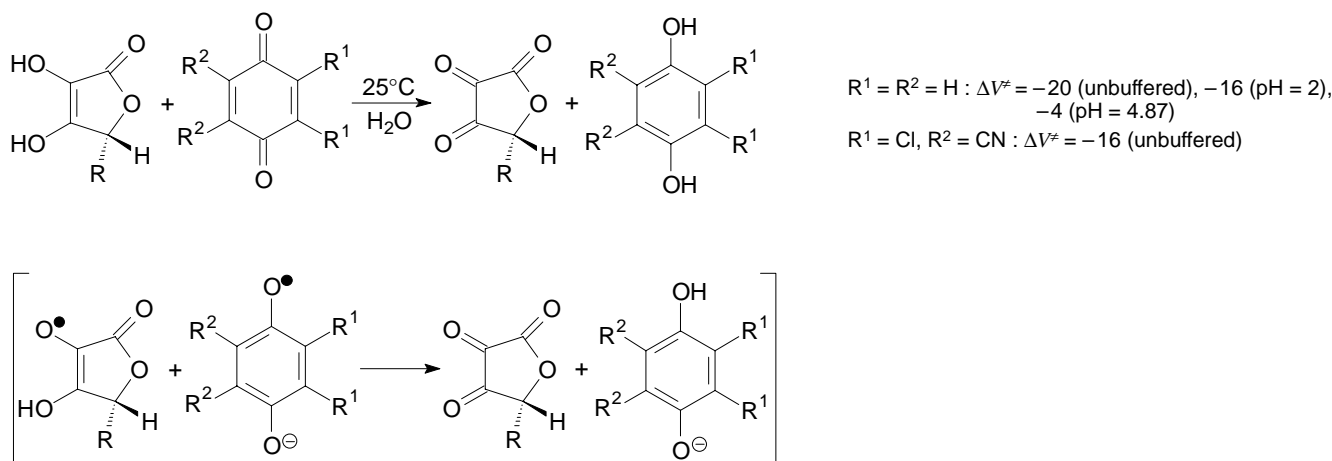
provided good evidence that the DDQ oxidation occurs via atom transfer (Scheme 26, mechanism (1)) comparable to other uncatalyzed transfer hydrogenations. The mechanism (1) suggested by Rüdhardt is further supported by the pressure dependence of the DDQ oxidation of various hydroarenes (Table 4) [127]. The finding, that the activation volumes are not much dependent from the solvent polarity, excludes mechanism (2) of a direct hydride transfer. In this case a strong effect of electrostriction is expected due to the production of charged species in the rate-determining step. Accordingly, the activation volume of one and the same reaction should be more negative in the less polar solvent (dielectric constant: $\epsilon = 4.5$ (MTBE), 6.03 (AcOEt), 35.9 (MeCN) [128]). Just the opposite is found for the experimental data (provided that there is any tendency in these data at all). The pericyclic hydrogen transfer (mechanism (4)) can only occur in formal 1,3-dienes such as 1,2-dihydronaphthalene or 9,10-dihydrophenanthrene and should show a significantly more negative activation volume because of the pericyclic transition state than the hydrogen atom transfer of 1,4-dihydronaphthalene or 9,10-dihydroanthracene proceeding through acyclic transition states. But this is not found

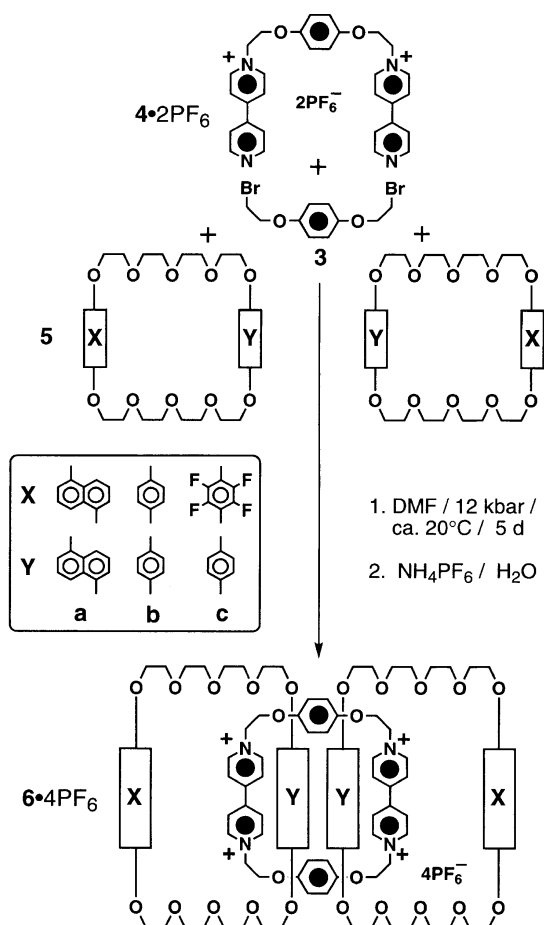
which indicates that all reactions shown in Table 4 proceed with the same mechanism *via* hydrogen atom transfer. Further mechanistic support comes from the primary kinetic isotope effect observed for the DDQ oxidation of 9,10-dihydroanthracene. The strong pressure dependence of the isotope effect may be attributed to a tunnelling component of the hydrogen transfer comparable to that observed by Isaacs *et al.* for the chloranil oxidation of leuco crystal violet [125].

The strongly pH-dependent activation volumes of the quinone oxidations of ascorbic acid (vitamine C) in water or methanol studied by N. S. Isaacs and R. van Eldik [129] are significantly less negative than those found for the oxidation of hydroarenes indicating different mechanisms. The results were explained by a rapid and reversible single electron transfer from the deprotonated anion of ascorbic acid to the quinone followed by a hydrogen atom transfer.

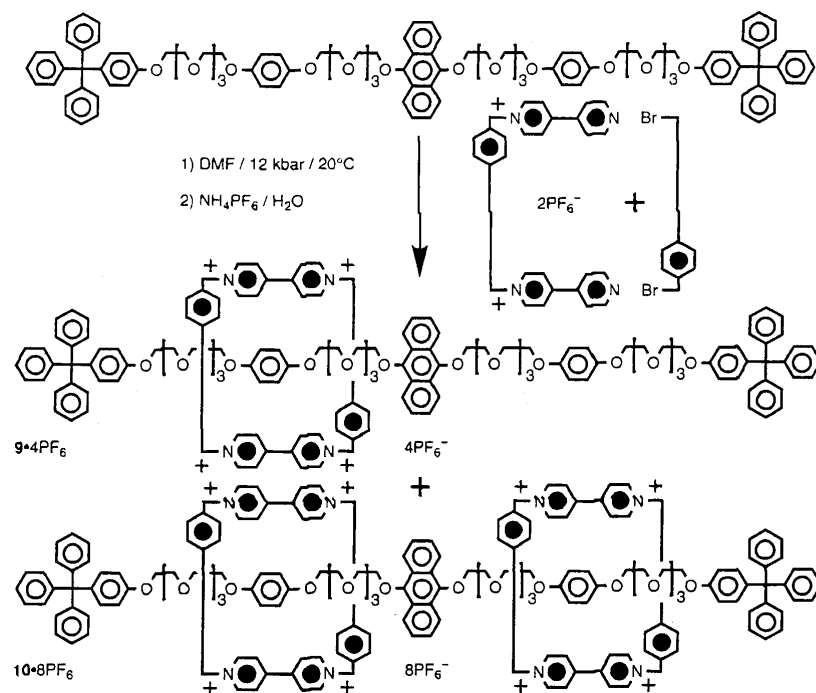
5. Ionic Reactions

Reactions, in which ionic species are generated, show a large volume contraction and, hence a powerful pres-

**Scheme 27** pH and pressure dependence of the oxidation of ascorbic acid (vitamine C) with quinones



Scheme 28 Synthesis of catenanes by pressure-induced alkylation of pyridines



Scheme 29 Synthesis of rotaxanes by pressure-induced alkylation of pyridines

sure-induced acceleration which can be exploited for synthetic purposes. Among the nucleophilic substitutions and additions (such as the aliphatic and aromatic S_N reactions [130], peptide formation (from esters) [131–133], or the addition of nucleophiles to electron-deficient alkenes [134] or oxiranes [135]) the Menshutkin-type S_N2 reactions are particularly worth-mentioning. It is well established that the solvent-dependent activation volumes of the alkylation of pyridine derivatives are highly negative ($\Delta V^\ddagger = -20$ to -50 cm³ mol⁻¹) [8]. Stoddart *et al.* used this high-pressure reaction to construct several catenanes [136] and rotaxanes [137] which are of interest as supramolecular devices. The [3] catenanes (Scheme 28) can be synthesized in one step at high pressure (25 °C, 12 kbar, 5 d) in reasonable yields of 31–33% whereas the yield of those catenanes in the reaction at 1 bar is only ca. 1% and below after 9 weeks [138]. The rotaxanes shown in Scheme 29 were only obtained in the high-pressure reaction [137].

6. Concluding Remarks

It has been demonstrated that cyclizations are accompanied by a contraction of volume. The magnitude of this contraction depends on the number and the size of the forming rings and is a result of the different packing coefficients of cyclic and acyclic structures rather than of the changes in their intrinsic molecular volumes during the cyclization. This effect is most important in cycloadditions and pericyclic rearrangements and explains

the pressure-induced acceleration and the therewith related negative activation volumes of these reactions. In reactions, in which charged species are generated, the effect of electrostriction lead also to a substantial contraction of volume and, hence, to a rate enhancement at high pressure. The utility of high pressure exploiting particularly these two effects for the elucidation of reaction mechanisms and for the organic synthesis is described. Recently, interesting applications of high pressure in transition metal-catalyzed reactions[139] and in supramolecular chemistry [140, 141] have been described which are not considered in this review.

We are grateful to the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support of our work. F.-G. K. thanks the coworkers mentioned in the references for their committed and skillful collaboration, and Ms. I. Reiter and Ms. H. Wöll for their skilled assistance with the preparation of the manuscript, the tables, and schemes.

Referenes

- [1] T. Asano, T. Okada, *J. Phys. Chem.* **1984**, *88*, 238
- [2] Y. Yoshimura, J. Osugi, M. Nakahara, *J. Am. Chem. Soc.* **1983**, *105*, 5414
- [3] A. Bondi, *J. Chem. Phys.* **1964**, *68*, 441
- [4] Y. Yoshimura, J. Osugi, M. Nakahara, *Bull. Chem. Soc. Jpn.* **1983**, *56*, 680
- [5] T. Asano, W. J. le Noble, *Rev. Phys. Soc. Jpn.* **1973**, *43*, 82
- [6] Monographs: N. S. Isaacs, *Liquid High Pressure Chemistry*, Wiley, New York 1981; W. J. le Noble (Ed.), *Organic High Pressure Chemistry*, Elsevier, Amsterdam 1988; R. M. Acheson, E. K. Matsumoto, *Organic Synthesis at High Pressure*, Wiley, New York 1991; R. van Eldik, C. D. Hubbard, *Chemistry under Extreme and Non-Classic Conditions*, Wiley, New York 1997
- [7] Reviews: W. J. le Noble, H. Kelm, *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 841; W. J. le Noble, *Chem. Unserer Zeit* **1983**, *17*, 152; G. Jenner, *J. Chem. Soc., Faraday Trans.1* **1985**, *81*, 2437; K. Matsumoto, A. Sera, T. Uchida, *Synthesis* **1985**, *1*, 999; F.-G. Klärner, *Chem. Unserer Zeit* **1989**, *23*, 53; M. Ciobanu, K. Matsumoto, *Liebigs Ann. Chem.* **1997**, *623*; K. Matsumoto, M. Kaneko, H. Katsura, N. Nayashi, T. Uchida, R. M. Acheson, *Heterocycles* **1998**, *47*, 1135
- [8] T. Asano, W. J. le Noble, *Chem. Rev.* **1978**, *78*, 407
- [9] A. Drljaca, C. D. Hubbard, R. van Eldik, T. Asano, M. V. Basilevsky, W. J. le Noble, *Chem. Rev.* **1998**, *98*, 2167
- [10] R. van Eldik, T. Asano, W. J. le Noble, *Chem. Rev.* **1989**, *89*, 549
- [11] F.-G. Klärner, M. K. Diedrich in: *The Chemistry of Dienes and Polyenes* (Z. Rappoport, Ed.), Vol. 1, 547, Wiley, New York 1997
- [12] G. Jenner, *New J. Chem.* **1991**, *15*, 897
- [13] Y. Li, K. N. Houk, *J. Am. Chem. Soc.* **1993**, *115*, 5414
- [14] K. N. Houk, Y. Li, J. D. Evanseck, *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 682
- [15] C. A. Steward Jr., *J. Am. Chem. Soc.* **1972**, *94*, 635
- [16] F.-G. Klärner, B. M. J. Dogan, O. Ermer, W. v. E. Doering, M. P. Cohen, *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 110
- [17] see ref. [27]
- [18] O. Exner in: *Organic High Pressure Chemistry* (W. J. le Noble, Ed.), 19, Elsevier, Amsterdam, **1988**
- [19] PCMODEL, Serena Software, **1992**
- [20] M. A. Firestone, M. Vitale, *J. Org. Chem.* **1981**, *46*, 2160; L. N. Kowa, D. Schwarzer, J. Troe, J. Schroeder, *J. Chem. Phys.* **1992**, *97*, 4827
- [21] T. Asano, H. Furika, H. Sumi, *J. Am. Chem. Soc.* **1994**, *116*, 5545; H. Sumi, T. Asano, *J. Chem. Phys.* **1995**, *102*, 9565; T. Asano, K. Crosstick, H. Furuta, K. Matsuo, H. Sumi, *Bull. Chem. Soc. Jpn.* **1996**, *69*, 551
- [22] R. A. Firestone, G. M. Smith, *Chem. Ber.* **1989**, *122*, 1089
- [23] G. Jenner, M. Papadopoulos, J. Rimmelin, *J. Org. Chem.* **1983**, *48*, 748
- [24] A. George, N. S. Isaacs, *J. Chem. Soc., Perkin Trans. 2* **1985**, 1845
- [25] F.-G. Klärner, V. Breitkopf, *Eur. J. Org. Chem.* **1999**, 2757
- [26] R. A. Grieger, C. A. Eckert, *J. Am. Chem. Soc.* **1970**, *92*, 2918; R. A. Grieger, C. A. Eckert, *J. Chem. Soc., Faraday Trans.* **1970**, *66*, 2579
- [27] F.-G. Klärner, B. Krawczyk, V. Ruster, U. K. Deiters, *J. Am. Chem. Soc.* **1994**, *116*, 7646
- [28] J. F. Blake, W. L. Jorgensen, *J. Am. Chem. Soc.* **1991**, *113*, 7430
- [29] R. Breslow, *Acc. Chem. Res.* **1991**, *24*, 159
- [30] P. A. Grieco, J. J. Nunes, M. D. Gaul, *J. Am. Chem. Soc.* **1990**, *112*, 4595
- [31] W. Blokzijl, M. J. Blandamer, J. B. F. N. Engberts, *J. Am. Chem. Soc.* **1991**, *113*, 4241
- [32] U. Pindur, G. Lutz, C. Otto, *Chem. Rev.* **1993**, *93*, 741
- [33] G. Jenner, *J. Phys. Org. Chem.* **1999**, *12*, 619
- [34] N. S. Isaacs, L. Maksimovic, A. Laila, *J. Chem. Soc., Perkin Trans. 2* **1994**, 495
- [35] B. Poling, C. A. Eckert, *Ind. Eng. Chem. Fundam.* **1972**, *11*, 451
- [36] G. Jenner, *New J. Chem.* **1997**, *21*, 1087
- [37] L. Minuti, A. Taticchi, E. Gaes-Beitz, E. Wenkert, *Tetrahedron* **1995**, *51*, 10033
- [38] L. F. Tietze, C. Ott, K. Gerke, M. Buback, *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1485
- [39] W. G. Dauben, J. M. Gerdes, D. B. Smith, *J. Org. Chem.* **1985**, *50*, 2576
- [40] W. G. Dauben, J. L. Lam, Z. R. Guo, *J. Org. Chem.* **1996**, *61*, 4816
- [41] V. Breitkopf, P. Bubenitschek, H. Hopf, P. G. Jones, F.-G. Klärner, D. Schomburg, B. Witulski, B. Zimny, *Liebigs Ann. Chem.* **1997**, *127* and unpublished results
- [42] G. I. Fray, R. G. Saxton, *The Chemistry of Cyclooctatetraene and its Derivatives*, Cambridge University Press, Cambridge **1978** P. G. Wentholt, D. A. Hrovat, W. T. Borden, W. C. Lineberger, *Science* **1996**, *272*, 1456
- [43] F.-G. Klärner, R. Ehrhardt, H. Bandmann, R. Boese, D. Bläser, K. N. Houk, B. R. Beno, *Chem. Eur. J.* **1999**, *5*, 2119
- [44] Review: H. Hopf, B. Witulski, *Pure Appl. Chem.* **1993**, *65*, 47; V. Breitkopf, H. Hopf, F.-G. Klärner, B. Witulski, B. Zimny, *Liebigs Ann. Chem.* **1995**, 613
- [45] C. Born, D. Meibom, E. Winterfeldt, *Chem. Commun.* **1996**, 887
- [46] S. Röhrig, L. Hennig, M. Findeisen, P. Welzel, D. Müller, *Tetrahedron* **1998**, *54*, 3439
- [47] G. Silvero, M. J. Lucero, E. Winterfeldt, K. N. Houk, *Tetrahedron* **1998**, *54*, 7293
- [48] B. Wegener, M. Hausen, E. Winterfeldt, *Tetrahedron Asymmetry* **1993**, *4*, 345
- [49] H. Weinmann, E. Winterfeldt, *Synthesis* **1996**, 357; C. Born, E. Winterfeldt, *Liebigs Ann. Chem.* **1996**, 1209; P. G. Jones, H. Weinmann, E. Winterfeldt, *Angew. Chem.* **1995**, *107*, 489
- [50] J.-F. Lin, N. Keto, A. Mori, H. Takeshita, R. Isobe, *Bull. Chem. Soc. Jpn.* **1994**, *67*, 1507
- [51] M. Buback, W. Trost, T. Hübsch, E. Voss, L. F. Tietze, *Chem. Ber.* **1989**, *122*, 1179; L. F. Tietze, T. Hübsch, J. Oelze, C. Ott, W. Trost, G. Wörner, M. Buback, *Chem. Ber.* **1992**, *125*, 2249; M. Buback, G. Kuchta, A. Niklaus, M. Henrich, I. Rothert, L. F. Tietze, *Liebigs Ann. Chem.* **1996**, 1151
- [52] W. Adam, C. Barneveld van, J.-S. Gehrke, F.-G. Klärner, *J. Chem. Soc., Perkin Trans. 2* **1999**, 2723
- [53] K. Exner, D. Hochstrate, M. Keller, F.-G. Klärner, H. Prinzbach, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2256
- [54] S. Hünig, P. Kraft, F.-G. Klärner, U. Artschwanger-Perl, K. Peters, H.-G. Schnering, *Liebigs Ann. Chem.* **1995**, 351
- [55] Z. Z. Song, Z. Y. Zhon, T. C. W. Mak, H. N. C. Wong, *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 432
- [56] L. F. Tietze, T. Hübsch, C. Ott, G. Kuchta, M. Buback, *Liebigs Ann. Chem.* **1995**, 1
- [57] V. M. Zhulin, E. B. Kabotyanskaya, M. V. Kel'tseva, V. S. Bogdanov, Y. D. Koreshkov, *Izv. Akad. Nauk. SSSR, Ser. Khim.* **1990**, 2651
- [58] F. H. Kohnke, A. M. Z. Slawin, J. F. Stoddart, D. J. Williams, *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 892; F. H. Kohnke, J. F. Stoddart, *Pure Appl. Chem.* **1989**, *61*, 1581; P. R. Ashton, G. R. Brown, N. S. Isaacs, D. Guiffrida, F. H. Kohnke, J. P. Mathias, A. M. Z. Slawin, D. R. Smith, J. F. Stoddart, D. J. Williams, *J. Am. Chem. Soc.* **1992**, *114*, 6330; J. P. Mathias, J. F. Stoddart, *Chem. Soc. Rev.* **1992**, *21*, 215; P. R. Ashton, U. Girreser, D. Guiffrida, F. H. Kohnke,

- J. P. Mathias, F. M. Raymo, A. M. Z. Slawin, J. F. Stoddart, D. J. Williams, *J. Am. Chem. Soc.* **1993**, *115*, 5422
- [59] J. Benkhoff, R. Boese, F.-G. Klärner, A. E. Wigger, *Tetrahedron Lett.* **1994**, *35*, 73
- [60] P. R. Ashton, J. F. Stoddart, *J. Am. Chem. Soc.* **1993**, *115*, 5422
- [61] S. Wegener, K. Müllen, *Macromolecules* **1993**, *26*, 3037
- [62] M. Pollmann, K. Müllen, *J. Am. Chem. Soc.* **1994**, *116*, 2318
- [63] R. M. Graham, L. A. Paquette, *J. Org. Chem.* **1995**, *60*, 5770
- [64] S. E. Denmark, *J. Org. Chem.* **1997**, *62*, 435; S. E. Denmark, A. Thorarensen, *Chem. Rev.* **1996**, *96*, 137; S. E. Denmark, M. E. Schunite, *J. Org. Chem.* **1994**, *59*, 4576
- [65] G. J. Kuster, F. Kalmoua, R. Gelder, H. W. Scheeren, *Chem. Commun.* **1999**, 855 and references cited therein
- [66] R. M. Uittenbogaard, J.-P. G. Seerden, H. W. Scheeren, *Tetrahedron* **1997**, *53*, 11929
- [67] J. Velker, J.-P. Roblin, A. Neels, A. Tesuoro, H. Stoeckli-Evans, F.-G. Klärner, J.-S. Gehrke, R. Neier, *Synlett* **1999**, *51*, 925
- [68] G. Jenner, *High Pressure Research* **1996**, *15*, 51
- [69] R. Sustmann, *Heterocycles* **1995**, *40*, 1; A. Padwa (Ed.), *1,3-Dipolar Cycloaddition Chemistry*, Wiley Interscience, New York 1984
- [70] R. Huisgen, G. Mloston, E. Langhals, *J. Am. Chem. Soc.* **1986**, *108*, 6401
- [71] V. M. Zhulin, Z. G. Makarov, M. M. Krayushkin, E. B. Zhuravleva, A. M. Beskopyl'nyi, *Dokl. Akad. Nauk. SSSR* **1985**, *280*, 917; V. M. Zhulin, E. B. Zhuravleva, *Dokl. Akad. Nauk. SSSR* **1986**, *290*, 383
- [72] M. K. Diedrich, F.-G. Klärner, *J. Am. Chem. Soc.* **1998**, *120*, 6212
- [73] G. T. Anderson, J. R. Henry, S. M. Weinreb, *J. Org. Chem.* **1991**, *56*, 6946
- [74] C. Ahn, J. W. Kennington, P. DeShong, *J. Org. Chem.* **1994**, *21*, 6282
- [75] F.-G. Klärner, D. Oebels, W. S. Sheldrick, *Chem. Ber.* **1993**, *126*, 473
- [76] L. Ghozec, M. J. O'Donnel in: *Pericyclic Reactions*, Volume II (A. P. Marchand and R. E. Lehr, Eds.), Academic Press, New York 1977
- [77] N. S. Isaacs, E. Rannala, *J. Chem. Soc., Perkin Trans. 2* **1975**, 1555
- [78] G. Swieton, J. v. Jouanne, H. Kelm, R. Huisgen, *J. Chem. Soc., Perkin Trans. 2* **1983**, 37
- [79] M. Chmielewski, Z. Kaluza, P. Salanski, J. Jurczak, *High Pressure Research* **1992**, *11*, 171; R. W. M. Aben, E. P. Limburg, H. W. Scheeren, *High Pressure Research* **1992**, *11*, 167; Y. Taguchi, T. Tsuchiya, A. Oishi, I. Shibuya, *Bull. Chem. Soc. Jpn.* **1996**, *69*, 1667
- [80] W. R. Dolbier, S. L. Waeber, *J. Org. Chem.* **1990**, *55*, 711
- [81] U. Deiters, F.-G. Klärner, B. Krawczyk, V. Ruster, *J. Am. Chem. Soc.* **1994**, *116*, 7646
- [82] B. Krawczyk, Dimerisierungen von 1,3-Dienen bei hohem Druck: Das Volumenprofil von konzentrierten und mehrstufigen Cycloadditionen, Ph. D. Dissertation, Universität Essen 1996; W. v. E. Doering, J. Ekmanis, K. D. Belfield, F.-G. Klärner, B. Krawczyk, Manuscript in preparation
- [83] J. Jouanne, H. Kelm, R. Huisgen, *J. Am. Chem. Soc.* **1979**, *101*, 151
- [84] R. Huisgen, *Acc. Chem. Res.* **1977**, *10*, 117
- [85] W. J. le Noble, R. Muhktar, *J. Am. Chem. Soc.* **1975**, *97*, 5938
- [86] R. W. M. Aben, J. Goudriaan, J. M. M. Smits, H. W. Scheeren, *Synthesis* **1993**, 37
- [87] R. B. Woodward, R. Hoffmann, *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 781
- [88] N. J. Turro, M. Okamoto, I. R. Gould, R. A. Moss, W. Lawrynowicz, L. M. Hadel, *J. Am. Chem. Soc.* **1987**, *109*, 4973
- [89] N. S. Isaacs, A. Laila, *J. Phys. Org. Chem.* **1994**, *7*, 178
- [90] N. S. Isaacs, G. N. El-Din, *Synthesis* **1989**, 967; *Tetrahedron* **1989**, *45*, 7083
- [91] F.-G. Klärner, S. Yaslak, R. Drewes, C. Gesenberg, M. Peter, *Liebigs Ann. Chem.* **1995**, 203
- [92] D. A. Hrovat, B. R. Beno, H. Lange, H.-Y. Yoo, K. N. Houk, W. T. Borden, *J. Am. Chem. Soc.* **1999**, *121*, 10529; W. v. E. Doering, Y. Wang, *J. Am. Chem. Soc.* **1999**, *121*, 10112; 10967
- [93] K. Morokuma, W. T. Borden, D. A. Hrovat, *J. Am. Chem. Soc.* **1988**, *110*, 4474
- [94] M. K. Diedrich, D. Hochstrate, F.-G. Klärner, B. Zimny, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1079
- [95] C. Walling, M. Naiman, *J. Am. Chem. Soc.* **1962**, *84*, 2628; G. A. Stashina, E. N. Vasil'vitskaya, G. D. Gamelevich, B. S. El'yanov, E. P. Serebryakov, V. M. Zhulin, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1986**, 329; M. K. Diedrich, D. Hochstrate, F.-G. Klärner, B. Zimny, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1079; W. v. E. Doering, L. Birladeanu, K. Sarma, J. H. Teles, F.-G. Klärner, J. S. Gehrke, *J. Am. Chem. Soc.* **1994**, *116*, 4289; P. Jansen, Diploma Thesis, Universität Essen, Bochum 1994
- [96] C. Walling, J. Naiman, *J. Am. Chem. Soc.* **1962**, *84*, 2628
- [97] F.-G. Klärner, D. Müller, unpublished results; D. Müller, Diploma Thesis, Universität Essen 1998. The temperature-dependent kinetic analysis was carried out for this rearrangement in the gas phase between 142° and 173 °C leading to the Arrhenius equation $\log k = (11.1 \pm 0.3) - (29.3 \pm 0.5) \text{ kcal mol}^{-1}/RT$. In the gas phase the resulting activation enthalpy and entropy, $\Delta H^\ddagger = 28.5 \text{ kcal mol}^{-1}$ and $\Delta S^\ddagger = -10.6 \text{ cal/mol K}$, are larger than those in benzene solution (80 °C: $\Delta H^\ddagger = 25.4 \text{ kcal mol}^{-1}$ and $\Delta S^\ddagger = -15.9 \text{ cal/mol K}$: J. Burrows, B. K. Carpenter, *J. Am. Chem. Soc.* **1981**, *103*, 6983)
- [98] E. M. Schulman, A. E. Merbach, M. Turin, R. Wedinger, W. J. le Noble, *J. Am. Chem. Soc.* **1983**, *105*, 3988
- [99] W. v. E. Doering, L. Birladeanu, K. Sarma, G. Blaschke, U. Scheidemann, R. Boese, J. Benet-Buchholz, F.-G. Klärner, J.-S. Gehrke, B. Zimny, H.-G. Korth, *J. Am. Chem. Soc.* **2000**, *122*, 193
- [100] R. Mündlich, H. Plieninger, H. Vogler, *Tetrahedron* **1977**, *33*, 2261; R. Mündlich, H. Plieninger, *Tetrahedron* **1978**, *34*, 887
- [101] W. J. le Noble, K. R. Brower, C. Brower, C. S., *J. Am. Chem. Soc.* **1982**, *104*, 3150
- [102] R. Mündlich, H. Plieninger, *Tetrahedron* **1976**, *32*, 2335
- [103] N. S. Isaacs, P. G. van der Becke, *J. Chem. Soc., Perkin Trans. 2* **1982**, 1205
- [104] M. Buback, K. Gerke, C. Ott, L. F. Tietze, *Chem. Ber.* **1994**, *127*, 2241
- [105] M. Buback, J. Abeln, T. Hübsch, C. Ott, L. F. Tietze, *Liebigs Ann.* **1995**, 9
- [106] T. Heiner, K. Michalsky, K. Gerke, G. Kuchta, M. Buback, A. de Meijere, *Synlett* **1995**, 355
- [107] T. Heiner, S. I. Kozhushkov, K. Gerke, T. Haumann, R. Boese, A. de Meijere, *Tetrahedron* **1996**, *37*, 12185
- [108] T. Butz, J. Sauer, *Tetrahedron Asymmetry* **1997**, *8*, 703
- [109] A. C. Brickwood, M. G. B. Drew, L. M. Harwood, T. Ishikawa, P. Marais, V. Morrison, *J. Chem. Soc., Perkin Trans. 1* **1999**, 913
- [110] S. Jarosz, E. Kozłowska, A. Jerzowski, *Tetrahedron* **1997**, *31*, 10775
- [111] Y. Araki, T. Konoike, *J. Org. Chem.* **1997**, *62*, 5299
- [112] A. Tahari, D. Uguen, *Tetrahedron Lett.* **1994**, *23*, 3945
- [113] G. Galley, M. Pätz, *J. Chem. Soc., Perkin Trans. 1* **1996**, 2297
- [114] L. F. Tietze, A. Schuffenhauer, *Eur. J. Org. Chem.* **1998**, 1629
- [115] W. v. E. Doering, L. Birladeanu, K. Sarma, J. H. Teles, F.-G. Klärner, J.-S. Gehrke, *J. Am. Chem. Soc.* **1994**, *116*, 4289
- [116] G. Swieton, J. Jouanne, H. Kelm, *J. Org. Chem.* **1983**, *48*, 1035
- [117] U. B. Imashev, V. V. Zorin, S. M. Kalashnikov, S. S. Zlotskii, V. M. Zhulin, D. L. Rakhmankulov, *Dokl. Akad. Nauk SSSR* **1978**, *242*, 140; A. A. Lapshova, G. A. Stashina, V. V. Zorin, S. S. Zlotskii, V. M. Zhulin, D. L. Rakhmankulov, *Zh. Org. Khim.* **1980**, *16*, 1251; M. Y. Botnikov, S. S. Zlotskii, V. V. Zorin, E. K. Kravets, V. M. Zhulin, D. L. Rakhmankulov, *Izv. Acad. Nauk SSSR, Ser. Khim.* **1977**, 690; E. V. Pastushenko, M. Y. Botnikov, S. S. Zlotskii, V. M. Zhulin, D. L. Rakhmankulov, *React. Kinet. Catal. Lett.* **1981**, *16*, 195; M. Buback, H. Lendle, *Z. Naturforsch.* **1979**, *34a*, 1482; Y. Kimura, Y. Yoshimura, M. Nakahara, *Chem. Lett.* **1987**, 617
- [118] R. C. Neuman, G. D. Lockyer, *J. Am. Chem. Soc.* **1983**, *105*, 3982; R. C. Neuman, M. J. Amrich, *J. Org. Chem.* **1980**, *45*, 4629; V. M. Zhulin, G. A. Stashina, E. G. Rozantsev, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1979**, 977; Y. Ogo, M. Kojima, *High Temp. - High Press.* **1981**, *13*, 321
- [119] R. C. Neuman, C. T. Berge, G. A. Binengar, W. Adam, Y. Nishizawa, *J. Org. Chem.* **1990**, *55*, 4564
- [120] W. J. le Noble, M. R. Daka, *J. Am. Chem. Soc.* **1978**, *100*, 5961
- [121] G. Dierkes, Dissertation, Universität Essen, in preparation
- [122] G. Kratt, H.-D. Beckhaus, C. Rüdhardt, *Chem. Ber.* **1984**, *117*, 1748
- [123] J. Pajak, K. R. Brower, *J. Org. Chem.* **1985**, *50*, 2210
- [124] K. R. Brower, *J. Org. Chem.* **1982**, *47*, 1889
- [125] N. S. Isaacs, K. Javid, E. Rannala, *J. Chem. Soc., Perkin Trans. 2* **1978**, 709
- [126] C. Höfler, C. Rüdhardt, *Liebigs Ann. Chem.* **1996**, 183
- [127] F. Wurche, Dissertation, Universität Essen, in preparation
- [128] C. Reichardt, *Solvents and Solvent Effects in Organic Chemistry*; VCH, Weinheim 1990
- [129] N. S. Isaacs, R. van Eldik, *J. Chem. Soc., Perkin Trans. 2* **1997**, 1465
- [130] See e.g. I. Barrett, M. A. Kerr, *Tetrahedron Lett.* **1999**, *40*, 2439; T.

- Ibata, M.-H. Shang, T. Demura, *Bull. Chem. Soc. Jpn.* **1995**, *68*, 2941; K. Matsumoto, S. Hashimoto, S. Otani, *J. Chem. Soc., Chem. Commun.* **1991**, 306
- [131] F.-G. Klärner, U. Kalthof, J. Gante, *J. Prakt. Chem.* **1997**, *339*, 359
- [132] T. Yamada, Y. Omote, Y. Yamanka, T. Miyazawa, S. Kuwata, *Synthesis* **1998**, 991
- [133] T. Shioiri, T. Imaeda, Y. Hamada, *Heterocycles* **1997**, *46*, 421
- [134] See e. g. S. Pinheiro, A. Guignant, D. Desmaele, J. d'Angelo, *Tetrahedron Assymetry* **1992**, *3*, 1003; G. Jenner, *Tetrahedron Lett.* **1995**, *36*, 233
- [135] H. Kotsuki, M. Wakao, H. Hayakawa, T. Shimanouchi, M. Shito, *J. Org. Chem.* **1996**, *61*, 8915
- [136] D. B. Amabilino, P. R. Ashton, V. Balzani, S. E. Boyd, A. Credi, J. Y. Lee, S. Menzer, J. F. Stoddart, M. Venturi, D. J. Williams, *J. Am. Chem. Soc.* **1998**, *120*, 4295 and references cited therein
- [137] R. Ballardini, V. Balzani, W. Dehaen, A. E. Dell'Erba, F. M. Raymo, J. F. Stoddart, M. Venturi, *Eur. J. Org. Chem.* **2000**, 591
- [138] P. R. Ashton, S. E. Boyd, C. G. Claessens, R. E. Gillard, S. Menzer, J. F. Stoddart, M. S. Tolley, A. J. P. White, D. J. Williams, *Chem. Eur. J.* **1997**, *3*, 788
- [139] O. Reiser, *Rev. High Pressure Sci. Techn.* **1998**, *8*, 111
- [140] A. Abou-Hamdan, P. Bugnon, C. Saudan, P. G. Lye, A. E. Merbach, *J. Am. Chem. Soc.* **2000**, *122*, 592
- [141] N. S. Issacs, P. J. Nichols, C. L. Raston, C. A. Sandova, D. J. Young, *Chem. Commun.* **1997**, 1839

Address for correspondence:
Prof. Dr. Frank-Gerrit Klärner
Universität Essen
Institut für Organische Chemie
Universitätsstr. 5
D-45117 Essen
Fax: Internat. code (0)201-183-4252
e-Mail: klaerner@oc1.orgchem.uni-essen.de