

The Kinetic Anomalies observed in the Formation of Small Ring Systems explained by Sigma-assistance and Sigma-resistance. Part 4. ¹⁻³ Carbanion Cyclizations

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Cyclization of carbanions to give cyclopropane, cyclobutane, and cyclopentane derivatives shows a behaviour that deviates from that predicted by the Ruzicka hypothesis. This adds to the anomalies, generally observed in the formation of 3-, 4-, 5-, and 6-membered saturated ring systems, *i.e.*, the enthalpy of activation for the formation of the odd-membered rings is consistently found to be lower than that of the less strained next higher even-membered ring. MNDO calculations were performed on the reaction profiles of the carbanion cyclizations for $n = 3, 4,$ and 5 . The results of these calculations support the earlier conclusion that the anomalies in the ΔH^\ddagger values can be adequately explained by the influence of sigma-assistance and sigma-resistance (*i.e.*, by rules for σ -systems analogous to those described extensively for π -electron systems), mediated by through-bond interaction between the reacting centres.

Through the years, it has become clear that in the formation of cycloalkanes and various other saturated ring systems with ring size $n = 3, 4, 5,$ and 6 kinetic anomalies occur.⁴ A classical way of looking at the closure of ring systems (be it *via* a biradical, a radical-olefin, an ionic cyclization, or any other mechanism) is the Ruzicka hypothesis.⁴ In the latter, two competing factors are considered: an unfavourable strain energy that progressively hinders the formation of smaller rings, and an entropy factor which becomes more opposing to ring formation as the chains grow longer. While this simple picture satisfactorily explains the overall kinetic trends for ring closure as a function of n for $n \geq 6$, it has been known for a long time^{5,6} that smaller rings often behave anomalously. Thus, closure of four-membered rings is found to be exceptionally slow, not only when compared with that of five-membered rings but also when compared with the closure of three-membered rings. Furthermore, formation of five-membered rings is, in general, slightly favoured over formation of the less strained six-membered rings.

Until recently, a dearth of activation parameters for the formation of small saturated rings made it impossible to conclude whether these anomalies stem from irregularities in ΔH^\ddagger or in ΔS^\ddagger as functions of n . Recently, one of us has published⁷ the results of measurements of the activation parameters for intramolecular nucleophilic substitution by carbanions (*viz.* the cyclization of bis-sulphonyl-stabilized carbanions to bis-sulphonylcycloalkanes with $n = 3, 4,$ and 5) (Figure 1).

Activation enthalpies of 85.7, 91.2, and 68.3 kJ mol⁻¹ were obtained for $n = 3, 4,$ and 5 , respectively. Thus the activation enthalpy for cyclobutane formation is larger than that for cyclopropane formation. Since the same effect was observed for radical cyclization processes,⁵ the obvious conclusion appears to be that the ubiquitously observed much slower formation of four-membered rings is not only due to a difference in ΔS^\ddagger (which corroborates the Ruzicka model), but also to a difference in ΔH^\ddagger , which is *opposed* to the effect predicted by the Ruzicka hypothesis.

The anomaly of the four-membered ring formation has often been noted but, in our opinion, no adequate explanations have been offered yet. In this connection, a study by DeTar and Luthra⁴ has shown that a molecular mechanics model is not able to produce consistent predictions for the activation

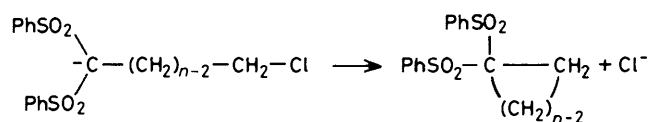


Figure 1. Cyclization of bis-sulphonyl-stabilized carbanions to bis-sulphonylcycloalkanes with $n = 3, 4,$ and 5

enthalpies for the formation of three- and four-membered rings. This problem is quite general and it has often been attributed to 'special electronic factors' (see for example references 4, 6, and 8). In the earlier publication of our Amsterdam group¹⁻³ such electronic factors were discussed more explicitly. The role of through-bond interaction (TBI) in (amongst others) cyclization reactions was invoked; it was established that a given cyclization reaction can be 'sigma-assisted' or 'sigma-resisted'; that is to say, interaction of the frontier orbitals of the reacting (functional) groups, mediated (*via* TBI) by the intervening sigma bonds, can lower or heighten the activation enthalpy of a reaction.

Since a full description of radical cyclizations⁹ is thwarted by the usual problems encountered in theoretical treatments of open-shell systems, we decided to investigate more closely the carbanion cyclizations depicted in Figure 1.

Results and Discussion

Qualitative Description of Sigma-assistance and Sigma-resistance in Carbanion Cyclizations.—It should be realized¹⁻³ that, as recently stipulated also by Dewar,¹⁰ through- σ -bond interactions are fully analogous to interactions occurring in π -systems, in short, to the factors determining the rules well known (amongst others) as those of the conservation of orbital symmetry. In this context, an apt method for the description of the behaviour of the nodes (essential in the application or orbital 'symmetry' arguments) in chains built up from C-C σ -bonds is the so-called C-approximation of Sandorfy and Daudel,^{11,12} and of Herndon.¹³ This approximation (in principle a simple Hückel MO scheme for carbon sp^3 AOs) can be used^{1-3,14} to describe the simplest models of the systems

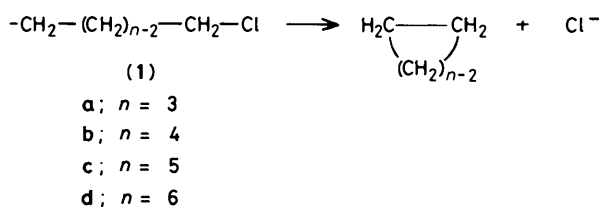


Figure 2. Unsubstituted carbanion system

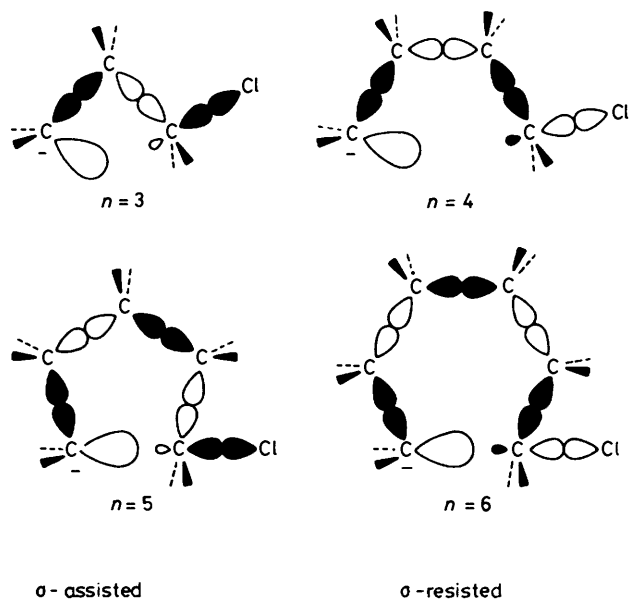


Figure 3. Graphical representation (within the C-approximation¹¹⁻¹³) of the HOMOs of model systems (1a-d). It should be noted that, as in π -MOs, the HOMO is the MO with the maximum number of nodes that still retains full bonding character across all bonds as represented by the Lewis structural formula. Only relative signs of the basis orbitals are shown, the coefficients have not been drawn to scale. However, in the figure it is indicated that each HOMO mainly consists of the lone pair on the negative centre

studied by Benedetti and Stirling,⁷ *viz.* the unsubstituted carbanions (1a-d).

Construction of the highest occupied MOs (HOMOs) of these systems by application of the C-approximation for $n = 3, 4, 5,$ and 6 shows (Figure 3) that only in the systems with $n = 3$ and $n = 5$ do the AOs on C(1) and C(n) have the correct (*i.e.*, the same) sign for a favourable interaction; in the systems with $n = 4$ and $n = 6$ the signs of the AOs on C(1) and C(n) are opposed. It should be noted that in each case the interacting AO on C(n) is the counterpart of the sp^3 lobe forming (part of) the σ -bond to the Cl atom. In the course of the reaction this back-lobe grows into a 'real' sp^3 lobe, while the chloride ion is expelled.

The HOMOs of the transition-state complexes are largely represented by the σ -orbital of the C-C bond formed. Thus, in order for a reaction to take place, in the cases with $n = 4$ and $n = 6$, either the AO on C(1) or that on C(n) has to change its sign. By such a process a state of higher energy is produced, as a consequence of which the activation enthalpy for ring closure is increased.

It was stated earlier¹⁻³ that it cannot be expected that interaction *via* σ -bonds can completely forbid a reaction, as is the case for the π -MO symmetry rules. Rather, it was envisaged that the σ -interaction should exert most of its, moderate, influence in the transition state, in such a way as to facilitate a

Table 1. Transition-state parameters for the *intra*-molecular reactions in model systems (1a-c) ($n = 3, 4,$ and 5)

Compound	n	$r_{1-n}/\text{\AA}$	$r_{1-Cl}/\text{\AA}$	$\Delta H^\ddagger/\text{kJ mol}^{-1}$
(1a)	3	2.107	2.030	12.08
(1b)	4	2.388	1.960	19.58
(1c)	5	2.528	1.959	3.68

reaction or hamper it, hence the terms 'sigma-assistance' and 'sigma-resistance.'

MNDO Study of the Reaction Profiles.—The first series of calculations (MNDO^{15,*}) were carried out on the systems (1a-c), *i.e.*, the unsubstituted carbanions with $n = 3, 4,$ and 5 . Full geometry optimizations were carried out with exception of the 'bond' C(1)-C(n), which was given a range of values lying between the distance C(1)-C(n) in the all-*trans* open-chain molecule and the bond length in the corresponding cyclic compound. Independently, MNDO transition-state calculations were carried out[†] for $n = 3, 4,$ and 5 by a procedure that uses gradient-norm minimization with a non-linear least-squares method. Transition states were characterized by one negative eigenvalue of the Hessian matrix. Both methods gave virtually identical results. For the sake of comparison, similar calculations were performed for a corresponding intermolecular reaction, *viz.* the (S_N2) reaction between the methyl carbanion and methyl chloride. Some pertinent results of the transition-state (TS) calculations are summarized in Table 1, while full TS-geometry data are given in the Appendix (Table 5). Activation enthalpies for the ring-closure reactions were calculated by subtracting from the enthalpies of the transition states the enthalpies obtained for the corresponding all-*trans* open-chain carbanions.

It should be noted that the activation enthalpy found for (1c) ($n = 5$) is in close agreement with the results obtained for the intermolecular reaction: in the latter case no activation barrier was found.

In a second series of calculations on model systems, the influence of charge-stabilizing substituents on C(1) was studied by replacing the two hydrogen atoms on C(1) by CN groups. In view of the difficulties met (see also reference 9) in finding the lowest minima in the calculations for $n = 5$, the intramolecular reaction for the five-membered system was simulated by the intermolecular reactions between the dicyanomethyl carbanion and methyl chloride (see Figure 4). This appears quite reasonable, both in view of the close agreement obtained earlier (*vide supra*) between the activation enthalpies for these two reactions for X = H and in view of the fact that the five-membered ring is (almost) completely free of strain.

The calculations were carried out in the same way as for the unsubstituted molecules. Some pertinent TS parameters are given in Table 2 (see Appendix, Table 5, for full TS-geometry data).

In Table 3 are summarized the differences in activation enthalpies between three-, four-, and five-membered systems (or, for the latter, the intermolecular reaction), as found by Benedetti and Stirling⁷ and in our calculations. It is seen that the agreement is good. Here, it should be noted that MNDO was chosen as the calculational method to be used in corroborating the results of our qualitative nodal-plane approach

* The local MNDO version used was updated by Dr. P. H. M. Budzelaar, to whom the authors express their gratitude.

† For this purpose, the program MOPAC was used. Part of the calculations were carried out by Dr. P. H. M. Budzelaar.

(rather than a method at a higher level of theory), in view of the fact that the major aim of the present investigation was the interpretation of the *relative* values of the activation enthalpies in a *series* of reactions leading to three-, four-, and five-membered rings.

The transition states prove to be reactant-like (as concluded by Benedetti and Stirling⁷); in the transition states the Cl atoms have moved a fair distance away. Inspection of the MOs obtained in each of the series of calculations showed that in the cyclizations to the four-membered rings the AO (in the HOMO) on C(1) is, in the early stages of the reaction, opposed in sign to the AO on C(4) (see Figure 3), so the interaction is indeed antibonding as predicted by the simple C-approximation arguments. For $n = 3$ and $n = 5$ the AOs on C(1) and C(n) have the same sign (in the HOMO) from the onset of the reaction. Therefore it can be concluded that the formation of the three-membered ring is opposed by ring-strain effects, but favoured by electronic effects (σ -assistance); in the formation of the four-membered ring the activation enthalpy is built up from ring strain and σ -resistance.

In going from the open chains to the rings the orbital energies of the HOMOs of the systems with $n = 3$ and $n = 5$ decrease from the start; however, the orbital energy of the HOMO of the system with $n = 4$ first increases until the AO on C(1) has

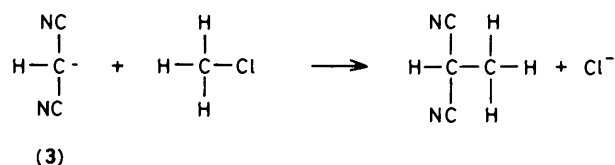
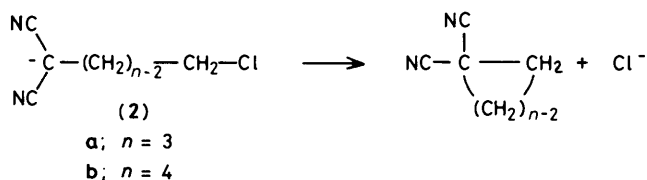


Figure 4. Model systems used to investigate charge-stabilizing substituents on C(1)

Table 2. Transition-state parameters for the *intra*-molecular reactions in model systems (2a and b) ($n = 3, 4$) and for the *inter*-molecular reaction in model system (3)

Compound	$r_{1-n}/\text{\AA}$	$r_{1-\text{Cl}}/\text{\AA}$	$\Delta H^\ddagger/\text{kJ mol}^{-1}$
(2a) <i>intra</i> , $n = 3$	1.821	2.308	125.54
(2b) <i>intra</i> , $n = 4$	2.012	2.212	128.38
(3) <i>inter</i>	2.083	2.080	88.32

changed its sign. This is a clear indication of unfavourable through-bond interaction (σ -resistance), which is further corroborated by the fact that, for comparable C(1)–C(n) distances, the HOMOs of the systems with $n = 3$ and $n = 5$ always have a lower energy than that of the molecule with $n = 4$. In Figure 5 the behaviour of the orbital energies of the HOMOs [$\epsilon(\text{HOMO})$] as a function of the distance C(1)–C(n) is shown (in the early stages of the reactions) for systems (1a, b, and c) ($X = \text{H}$, $n = 3, 4$, and 5, respectively).

The fact that in the transition state for three-ring formation the C(1)–C(n) distance is smaller than in the TS for four-ring formation can be explained geometrically: in order to yield the same amount of overlap the atoms C(1) and C(n) must come closer for $n = 3$ than for $n = 4$, as in the latter case the AOs on C(1) and C(n) are more directed towards each other [at the same C(1)–C(n) distance]. It should be noted that this longer C(1)–C(n) transition-state distance for $n = 4$ makes it even less

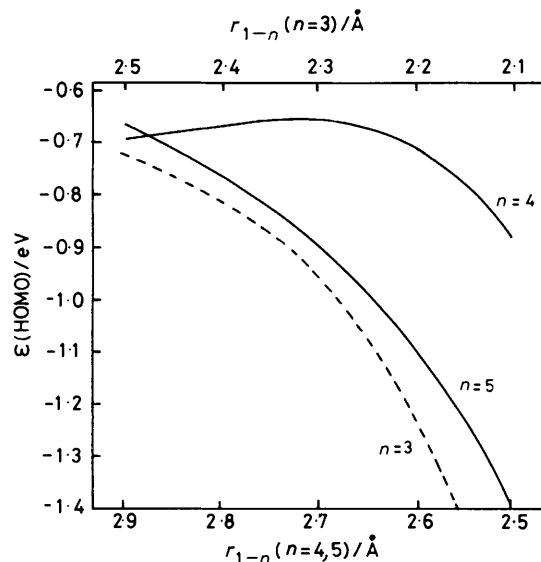


Figure 5. Dependence of $\epsilon(\text{HOMO})$ on the distance C(1)–C(n) for the systems (1a) ($n = 3$), (1b) ($n = 4$), and (1c) ($n = 5$) in the early stages of the reactions. The r -scale for (1a) has been offset by 0.4 Å to compensate for the smaller TS distance

Table 3. Differences in activation enthalpies between three-, four-, and five-membered systems (or, for the latter, the *inter*-molecular reaction)

Source	$\delta\Delta H^\ddagger(4-3)/\text{kJ mol}^{-1}$	$\delta\Delta H^\ddagger(4-5)/\text{kJ mol}^{-1}$
Benedetti and Stirling ⁷	5.5	22.9
This work (1; $X = \text{H}$)	7.50	15.90
This work (2 + 3; $X = \text{CN}$)	2.84	40.06

Table 4. Results of the application of the strain model of Stirling and co-workers¹⁶ on the data obtained in the present investigation. All enthalpies are in kJ mol^{-1}

Compound	TS bond extension (Å)	$\Delta H_{\text{strain}}^c$	ΔH^\ddagger^d	$\delta\Delta H^\ddagger^e$ (σ -effect)
(1a); $n = 3$, $X = \text{H}$	0.59 ^a	24.03	12.08	-11.95
(1b); $n = 4$, $X = \text{H}$	0.82 ^b	19.80	19.58	-0.22
(2a); $n = 3$, $X = \text{CN}$	0.30 ^a	62.75	125.54	62.79
(2b); $n = 4$, $X = \text{CN}$	0.44 ^b	54.54	128.38	73.84
		$\delta_{4-3} = -4.2$	$\delta_{4-3} = +7.5$	$\delta_{4-3} = +11.7$
		$\delta_{4-3} = -8.2$	$\delta_{4-3} = +2.8$	$\delta_{4-3} = +11.1$

^a Based on 1.52 Å bond length for cyclopropane. ^b Based on 1.57 Å bond length for cyclobutane. ^c From the strain model described in reference 16.

^d MNDO calculated (see Tables 1 and 2). ^e $\delta\Delta H^\ddagger = \Delta H^\ddagger - \Delta H_{\text{strain}}$.

Table 5. Calculated transition-state geometries of systems (1a—c), (2a and b), and (3)^{a,b}

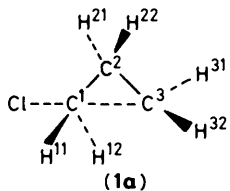
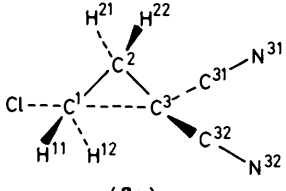
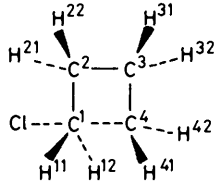
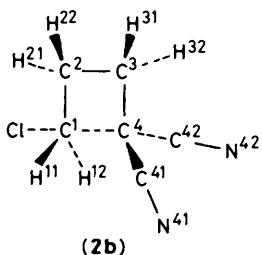
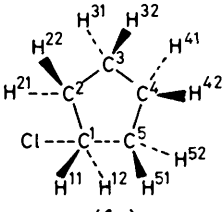
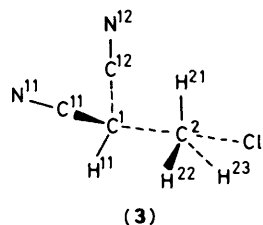
	Bond lengths (Å)	Bond angles (°)	Dihedral angles (°)			
 <p>(1a)</p>	Cl-C(1)	2.030	Cl-C(1)-C(2)	112.8	Cl-C(1)-C(2)-C(3)	180.0
	C(1)-C(2)	1.502	C(1)-C(2)-C(3)	90.4	H(11)-C(1)-C(3)-C(2)	122.0
	C(1)-C(3)	2.107	Cl-C(1)-H(11)	95.3	H(21)-C(2)-C(3)-C(1)	117.1
	C(2)-C(3)	1.466	H(11)-C(1)-H(12)	114.7	C(2)-C(1)-C(3)-H(31)	108.0
	C(1)-H(11)	1.098	C(1)-C(2)-H(21)	114.1		
	C(2)-H(21)	1.112	H(21)-C(2)-H(22)	106.7		
	C(3)-H(31)	1.082	C(2)-C(3)-H(31)	121.0		
			H(31)-C(3)-H(32)	115.7		
 <p>(2a)</p>	Cl-C(1)	2.308	Cl-C(1)-C(2)	103.4	Cl-C(1)-C(2)-C(3)	180.0
	C(1)-C(2)	1.489	C(1)-C(2)-C(3)	74.3	H(11)-C(1)-C(3)-C(2)	117.7
	C(1)-C(3)	1.821	Cl-C(1)-H(11)	85.5	H(21)-C(2)-C(3)-C(1)	114.3
	C(2)-C(3)	1.526	H(11)-C(1)-H(12)	116.7	C(2)-C(1)-C(3)-C(31)	108.1
	C(1)-H(11)	1.093	C(1)-C(2)-H(21)	118.4		
	C(2)-H(21)	1.102	H(21)-C(2)-H(22)	108.8		
	C(3)-C(31)	1.422	C(2)-C(3)-C(31)	120.2		
	C(31)-N(31)	1.165	C(31)-C(3)-C(32)	114.6		
 <p>(1b)</p>	Cl-C(1)	1.960	Cl-C(1)-C(2)	106.7	Cl-C(1)-C(2)-C(3)	179.8
	C(1)-C(2)	1.528	C(1)-C(2)-C(3)	105.4	C(1)-C(2)-C(3)-C(4)	0.4
	C(1)-C(4)	2.388	C(2)-C(3)-C(4)	107.2	H(11)-C(1)-C(2)-C(3)	-72.4
	C(2)-C(3)	1.549	Cl-C(1)-H(11)	97.4	H(12)-C(1)-C(2)-C(3)	71.9
	C(3)-C(4)	1.470	Cl-C(1)-H(12)	97.4	H(21)-C(2)-C(3)-C(1)	-120.7
	C(1)-H(11)	1.098	H(11)-C(1)-H(12)	115.5	H(22)-C(2)-C(3)-C(1)	120.7
	C(1)-H(12)	1.098	C(1)-C(2)-H(21)	111.1	C(1)-C(2)-C(3)-H(31)	-122.5
	C(2)-H(21)	1.112	C(1)-C(2)-H(22)	111.2	C(1)-C(2)-C(3)-H(32)	123.2
	C(2)-H(22)	1.112	H(21)-C(2)-H(22)	106.1	C(2)-C(3)-C(4)-H(41)	104.0
	C(3)-H(31)	1.120	C(2)-C(3)-H(31)	109.1	C(2)-C(3)-C(4)-H(42)	-104.7
	C(3)-H(32)	1.120	C(2)-C(3)-H(32)	109.1		
	C(4)-H(41)	1.085	H(31)-C(3)-H(32)	105.0		
	C(4)-H(42)	1.085	C(3)-C(4)-H(41)	119.8		
			C(3)-C(4)-H(42)	119.8		
		H(41)-C(4)-H(42)	114.5			
 <p>(2b)</p>	Cl-C(1)	2.212	Cl-C(1)-C(2)	98.1	Cl-C(1)-C(2)-C(3)	179.6
	C(1)-C(2)	1.528	C(1)-C(2)-C(3)	98.8	C(1)-C(2)-C(3)-C(4)	0.6
	C(1)-C(4)	2.012	C(2)-C(3)-C(4)	98.9	H(11)-C(1)-C(2)-C(3)	-90.5
	C(2)-C(3)	1.538	Cl-C(1)-H(11)	85.9	H(12)-C(1)-C(2)-C(3)	89.7
	C(3)-C(4)	1.527	Cl-C(1)-H(12)	85.9	H(21)-C(2)-C(3)-C(1)	-119.5
	C(1)-H(11)	1.094	H(11)-C(1)-H(12)	118.5	H(22)-C(2)-C(3)-C(1)	119.5
	C(1)-H(12)	1.094	C(1)-C(2)-H(21)	112.9	C(1)-C(2)-C(3)-H(31)	-119.6
	C(2)-H(21)	1.109	C(1)-C(2)-H(22)	113.1	C(1)-C(2)-C(3)-H(32)	120.9
	C(2)-H(22)	1.109	H(21)-C(2)-H(22)	106.9	C(2)-C(3)-C(4)-C(41)	108.9
	C(3)-H(31)	1.110	C(2)-C(3)-H(31)	112.8	C(2)-C(3)-C(4)-C(42)	-109.7
	C(3)-H(32)	1.110	C(2)-C(3)-H(32)	112.9		
	C(4)-C(41)	1.426	H(31)-C(3)-H(32)	105.9		
	C(4)-C(42)	1.426	C(3)-C(4)-C(41)	117.8		
	C(41)-N(41)	1.165	C(3)-C(4)-C(42)	118.0		
C(42)-N(42)	1.165	C(41)-C(4)-C(42)	113.3			
 <p>(1c)</p>	Cl-C(1)	1.959	Cl-C(1)-C(2)	105.9	Cl-C(1)-C(2)-C(3)	154.7
	C(1)-C(2)	1.526	C(1)-C(2)-C(3)	114.2	C(1)-C(2)-C(3)-C(4)	48.2
	C(1)-C(5)	2.528	C(2)-C(3)-C(4)	113.4	C(2)-C(3)-C(4)-C(5)	-41.8
	C(2)-C(3)	1.539	C(3)-C(4)-C(5)	113.0	H(11)-C(1)-C(2)-C(3)	46.7
	C(3)-C(4)	1.553	Cl-C(1)-H(11)	97.8	H(12)-C(1)-C(2)-C(3)	-99.0
	C(4)-C(5)	1.462	Cl-C(1)-H(12)	96.8	H(21)-C(2)-C(3)-C(4)	171.7
	C(1)-H(11)	1.096	H(11)-C(1)-H(12)	116.5	H(22)-C(2)-C(3)-C(4)	-73.6
	C(1)-H(12)	1.096	C(1)-C(2)-H(21)	110.7	C(1)-C(2)-C(3)-H(31)	171.4
	C(2)-H(21)	1.115	C(1)-C(2)-H(22)	108.7	C(1)-C(2)-C(3)-H(32)	-73.9
	C(2)-H(22)	1.115	H(21)-C(2)-H(22)	106.0	C(2)-C(3)-C(4)-H(41)	-166.6
	C(3)-H(31)	1.116	C(2)-C(3)-H(31)	108.7	C(2)-C(3)-C(4)-H(42)	81.7
	C(3)-H(32)	1.115	C(2)-C(3)-H(32)	109.3	C(3)-C(4)-C(5)-H(51)	-85.4
	C(4)-H(41)	1.126	H(31)-C(3)-H(32)	105.5	C(3)-C(4)-C(5)-H(52)	125.3
	C(4)-H(42)	1.120	C(3)-C(4)-H(41)	106.2		
C(5)-H(51)	1.086	C(3)-C(4)-H(42)	107.8			
C(5)-H(52)	1.085	H(41)-C(4)-H(42)	104.6			
		C(4)-C(5)-H(51)	119.5			
		C(4)-C(5)-H(52)	119.3			
		H(51)-C(5)-H(52)	114.2			

Table 5 (continued)

Bond lengths (Å)	Bond lengths (Å)		Bond angles (°)		Dihedral angles (°)	
	C(1)-C(2)	2.083	H(11)-C(1)-C(2)	96.0	H(11)-C(1)-C(2)-Cl	0.0
	C(2)-Cl	2.080	C(1)-C(2)-Cl	178.0	H(11)-C(1)-C(2)-H(21)	180.0
	C(1)-H(11)	1.101	C(11)-C(1)-C(2)	107.4	H(11)-C(1)-C(2)-H(22)	60.0
	C(1)-C(11)	1.420	C(11)-C(1)-C(12)	116.4	C(11)-C(1)-C(2)-H(21)	63.0
	C(11)-N(11)	1.167	C(1)-C(2)-H(21)	89.8		
	C(2)-H(21)	1.093	C(1)-C(2)-H(22)	87.6		
	C(2)-H(22)	1.094	H(22)-C(2)-H(23)	119.7		



^a Systems (1a), (2a), and (3) were given symmetries C_s . ^b The CN groups in (2a), (2b), and (3) were kept linear.

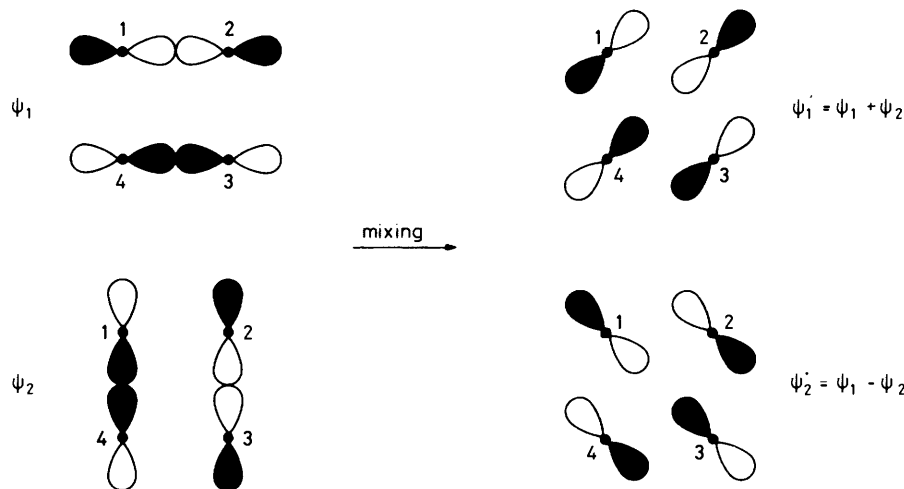


Figure 6. Mixing of MOs

likely that classical ring-strain effects are responsible for the inverted ΔH^\ddagger values as compared with those predicted by the Ruzicka hypothesis. Further, the fact that for the dicyano-substituted anions all C(1)-C(*n*) TS distances are considerably shorter [with retention of the $r(5) > r(4) > r(3)$ order] is in full agreement with the Hammond postulate. In an earlier publication¹⁶ (aimed at rationalizing the remarkable ΔH^\ddagger values for $n = 3$ and $n = 4$) one of us derived an analytical expression for the classical (ring) strain in cyclopropane and cyclobutane as a function of the extension of one of the C-C bonds. Substitution of the C(1)-C(*n*) values calculated by us into this expression allows an estimate of the contribution (ΔH_{strain}) of such classical strain to the activation enthalpies for $n = 3$ and $n = 4$. The ΔH_{strain} values compiled in Table 4 clearly indicate that, owing to the differences in the distances C(1)-C(*n*) in the various transition states, if such strain were the only factor differentiating the $n = 3$ and $n = 4$ cyclizations, the Ruzicka hypothesis would apply fully. From the $\delta\Delta H^\ddagger$ values listed in Table 4 ($\delta\Delta H^\ddagger = \Delta H^\ddagger - \Delta H_{\text{strain}}$) it now appears that the operation of sigma-assistance ($n = 3$) and sigma-resistance ($n = 4$) stabilizes the TS for cyclopropane formation by 11–12 kJ mol⁻¹ relative to that for cyclobutane formation, thereby inverting the order of the overall ΔH^\ddagger values.

Concluding Remarks

In view of the data presented above it is now our conclusion that in the anomalies observed in the rates of cyclization reactions of small saturated rings, the electronic effects of sigma-assistance and sigma-resistance (as described above) play a very important, even dominant, role. It should be realized that,

measured against total enthalpies, the actual contributions are small (as follows from this work and earlier investigations by one of us⁷), but also that slight differences in activation enthalpies can enormously influence reaction rates.

It can never be expected that σ -effects play as decisive a role as π -effects do (e.g., completely forbidding a reaction); however, it appears from this work that their influence on reactivity may be profound.

Appendix

1,3-Interaction in Cyclobutane.—An interesting point is the following. Inspection of the MOs in the cyclization reactions to cyclobutane (both for X = H and X = CN) shows that 1,3-interaction plays a completely insignificant role except in the very last stages of ring closure, well past the transition state. In order to explain this, it is useful to resort to the source of 1,3-interaction in cyclobutane.

In D_{4h} symmetry, the two highest occupied MOs of cyclobutane are degenerate, and are for the most part composed of the carbon 2p AOs lying in the plane of the molecule. The one MO forms the σ -bonds C(1)-C(2) and C(3)-C(4), the other the σ -bonds C(1)-C(4) and C(2)-C(3). Mixing these MOs (ψ_1 and ψ_2) yields hybrids (ψ_1' and ψ_2') which bring about 1,3- and 2,4-interaction (see Figure 6).

However, as (for example) the bond C(1)-C(4) is stretched, the energy of ψ_2 is increased, thus lowering the effective amount of mixing with ψ_1 by (at least) the inverse of the energy difference between ψ_1 and ψ_2 . MNDO calculations on cyclobutane in which one C-C bond was gradually stretched show this energy difference to increase rapidly with increasing

extension of the bond. Therefore 1,3-interaction is concluded to take a significant part in cyclizations only if the transition state of which very much resembles the reaction products.

Transition-state Geometries.—Full geometry data of the calculated TS structures are given in Table 5.

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