Elimination and Addition Reactions. Part 40.[1] The Insignificant Effect of Strain in Higher Order Eliminations in 1,1-bis(phenylsulphonyl) Carbanions with ω-Leaving Groups

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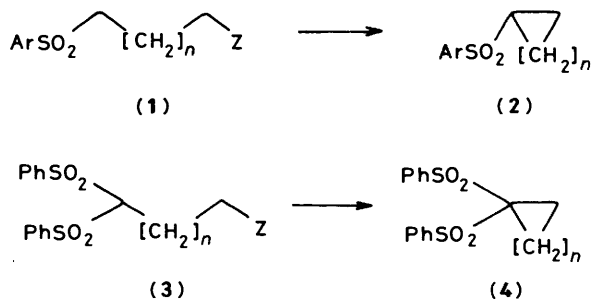
Rates of cyclisation of 1,1-bis(phenylsulphonyl) carbanions bearing distal leaving groups have been determined. The response of the system to solvent effects and to leaving group is similar to that in intermolecular nucleophilic substitution.

The system is very sensitive to the size of the ring formed; for iodides in ethanol the ratios for ring sizes 3:4:5:6:7 are $1:1.1 \times 10^{-5}:1.0 \times 10^{-2}:1.6 \times 10^{-6}:7.3 \times 10^{-10}$. The contribution of strain in the product to the enthalpy of activation is slight and inconsistent; the entropy of activation for cyclopropane formation is so favourable as to make this by far the most rapid process observed.

The factors which are significant in determining the ease of intramolecular nucleophilic substitution were outlined in a classical paper by Ruzicka and his colleagues[2] in 1926. The Ruzicka generalisations were not based on experimental data because, at the time, only very few kinetic measurements had been made on systems capable of yielding general answers to the questions: (i) what is the impact of strain on reactivity? and (ii) what is the significance of activation entropy in such reactions?

The Ruzicka generalisations, interpreted according to expected trends in enthalpy and entropy terms, led to the conclusion that the likely order of ring closure rate as a function of ring size formed would be $3 \approx 4 \ll 5 < 6 > 7$. Early kinetic work on cyclisation of ω-amino halides,[3] reinforced by recent determinations,[4] gave the order $5 \gg 6 > 3 > 7 \gg 4$. Similarly, in intramolecular displacement reactions of oxygen nucleophiles, three- and four-membered rings are formed substantially more slowly than their five-membered analogues.[5] Until 1967 no results appeared which were quantitatively contrary to the Ruzicka generalisation. It had already been observed, however, in the formation of cyclic sulphonium salts from ω-chloro sulphides, $RS[CH_2]_nCl$, that whereas for R = alkyl, five-membered rings (probably) were formed much faster than three-membered,[6a] with R = aryl, production of thiiranium salts was much faster than that of tetrahydrothiophenium salts.[6b]

In the course of an investigation of the behaviour of ω-bromoalkyl aryl sulphones[7] (**1**) with bases, it was found that whereas four-membered rings (**2**; $n = 2$) were formed much more slowly than five-membered rings ($n = 3$), cyclopropanes ($n = 1$), the most strained of all, were obtained at least 100 times more rapidly than cyclopentanes. Similar results were obtained for a corresponding series of ω-halogenoalkyl malonates;[8] in this series, cyclopropanes were formed so rapidly that accurate kinetic measurements could not be made. Unambiguous mechanisms could be assigned to all of these cycloalkane-forming reactions; either rapidly established pre-equilibrium formation of carbanions was implicated[7] or *E*1 anion reactions were involved.[8] Activation parameters for these reactions were not obtained and so no clear picture of the role of strain emerged. Much more recently, and following the preliminary communication of part of the present work,[9] Mandolini and his collaborators[10] reported quantitative results on the cyclisation of ω-halogenoalkyl malonates promoted by bases in dimethyl sulphoxide. They found that enthalpies of activation, evaluated by subtraction of intramolecular from intermolecular terms, varied little with ring size in comparison with the considerable variations in cycloalkane strain energies. Results for cyclopropanes were not available because reactions were too fast for the analytical procedures used.



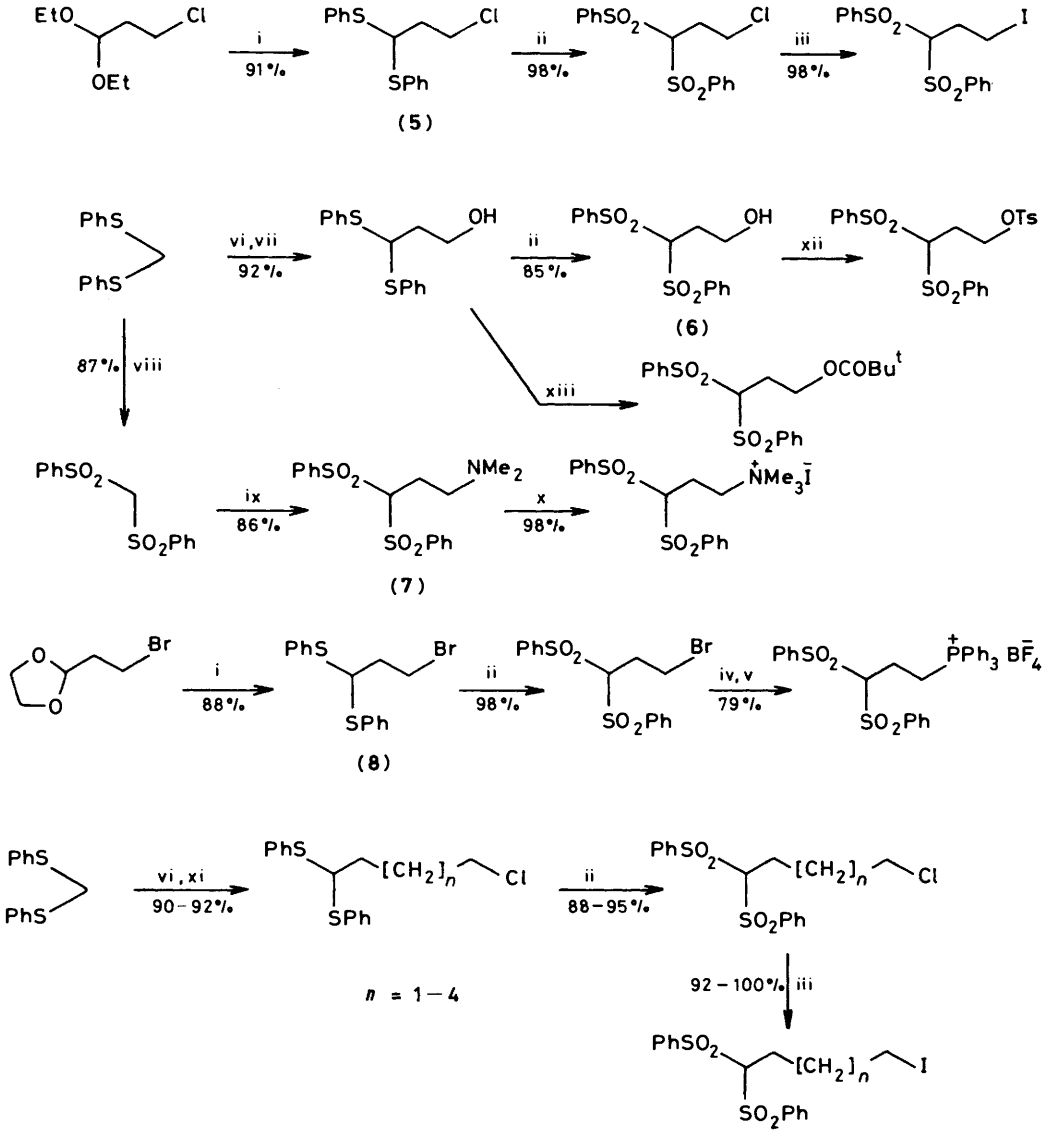
As part of our programme[11] on the evaluation of the effect of strain on reactivity we have examined the behaviour of the bis-sulphones (**3**; $n = 1$—5, Z = Cl, Br, I, OTs, $^+PPh_3$, $^+NMe_3$, SPh, or SO_2Ph). Our purpose was to test the sensitivity of the cyclisation reaction to the strain energy of the cyclic product obtained. These substrates were chosen for their high acidities [pK_a (H_2O) 11—13],[12] which ensure complete conversion into the conjugate bases under the reactions conditions chosen. Any complexities due to pre-equilibria dependent upon the nature of the leaving group[13] are thus avoided and, in addition, reactions could conveniently be followed by loss of the u.v. absorbance of the carbanion.

The ω-halogenoalkyl bis-sulphones were obtained by the routes shown in the Scheme.

Results and Discussion

Products.—From reactions in the standard solvent–base system ethoxide–ethanol, all substrates gave the bis-sulphonylcycloalkane (**4**) in high yield except for the halides (**3**; $n = 5$, Z = Cl or I). In the case of the chloride (**3**; $n = 5$, Z = Cl), intermolecular competition with the external nucleophile, ethoxide ion, gave the ethoxy compound (**3**; $n = 5$, Z = OEt) only. From the iodide, both ethoxy compound and cycloheptane (**4**; $n = 5$) were obtained. Results are in Tables 1, 4, and 5.

Kinetics.—In all cases, ring-closure reactions were first order in substrate and zero order in base provided that the amount of the latter was in excess of 1 mol. equiv. Reactions were followed by monitoring the loss of the u.v. absorption of the bis-sulphonyl carbanion at 290—300 nm. Stopped-flow spectrometry was used for the iodide (**3**; $n = 3$, Z = I) and for reactions giving cyclopropanes, except for the ammonium compound. Results are in Table 1. Activation parameters (Table



Scheme. *Reagents:* i, PhSH, HCl, $CHCl_3$, room temp.; ii, *m*-$ClC_6H_4CO_3H$, $CHCl_3$, room temp.; iii, NaI, Me_2CO, reflux; iv, PPh_3, dioxane, reflux; v, $NaBF_4$, MeOH–H_2O; vi, n-Bu^{n}Li, tetrahydrofuran, −75 °C; vii, oxirane, −20 °C; viii, H_2O_2, AcOH, 70 °C; ix, $ClCH_2CH_2\overset{+}{N}HMe_2\bar{C}l$, $E\bar{t}ONa$, EtOH, reflux; x, MeI, $CHCl_3$, room temp.; xi, $Br[CH_2]_{n+2}Cl$, −20 °C; xii, TsCl, pyridine; xiii, Me_3CCOCl, CH_2Cl_2

2) were determined from runs in the temperature range 20–60 °C.

Mechanism.—The kinetic behaviour of the substrates which give only 1,1-bisphenylsulphonylcycloalkanes is unambiguous as regards mechanism. The high acidity of the starting material results in complete conversion into the bis-sulphonyl-stabilised carbanion and consistently reactions are zero order in base. This confirmation of the *E*1 anion mechanism is free from the need to calibrate pre-equilibria which has characterised our earlier work [1] on higher order eliminations. Reactions are thus free from the effect of the leaving group on processes other than those in which the bond to the leaving group is broken. In the case of the iodide (**3**; $n = 5$), the rate of cyclisation to the cycloheptane (first order in substrate, zero order in base) was followed as before but part of the reaction pathway is the formation of the ethoxy compound, which results from a (presumably) second-order process.

Role of Strain.—The relationship between strain in the product and the rate constants and activation parameters is evident from Tables 1 and 2. Clearly, strain in the most strained product, the cyclopropane, has little inhibitory effect. It is striking that the relative reactivities for ring sizes 3:4:5:6 in the series of chlorides are in the order $1:6.7 \times 10^{-6}:1.6 \times 10^{-2}:2.9 \times 10^{-6}$, and that these values are similar to those obtained earlier for ω-bromoalkyl malonates ($1:1.5 \times 10^{-6}:1 \times 10^{-2}:7.5 \times 10^{-6}$). When the free energy of activation is dissected into its component parts (Table 2), the striking fact emerges that the range of variation in $\Delta H^{\ddagger}$ for the whole series investigated is only 5.5 kcal mol^{-1},* against a variation in strain energy of 26.9 kcal mol^{-1}. Clearly, any effect of strain is both restricted and erratic. Enthalpies of activation for formation of the small rings *are* higher than for the cyclopentane, but little different from that for the least strained member of the series.

*1 kcal = 4.184 kJ.

Table 1. Cyclisation of ω-chloroalkyl 1,1-bis(phenylsulphonyl) carbanions[a]

n	Ring size	Z = Cl k_{rel}	Z = I k_{rel}	k^I/k^{Cl}	Cycloalkane yield (%) Z = Cl	Z = I
1	3	61	101	397	99	100
2	4	4.1×10^{-4}	1.1×10^{-3}	644	97	98
3	5	1[b]	1[c]	240	97	96
4	6	1.7×10^{-4}	1.6×10^{-4}	226	93	95
5	7		7.2×10^{-8}[g]		91[d]	70[e,f]

[a] In ethanolic sodium ethoxide at 25 °C. [b] k 1.5×10^{-2} s^{-1}. [c] k 3.6 s^{-1}. [d] No cyclisation; the percentage is of product (**3**; n = 5, Z = OEt) at 78.5 °C. [e] By n.m.r.; the remainder is (**3**; n = 5, Z = OEt). [f] 47% Isolated. [g] Extrapolated from measurements at 57.8, 50.0, and 38.7 °C.

Table 2. Activation parameters for cyclisation of bis(phenylsulphonyl) carbanions derived from chlorides (**3**; n = 1—4)

Ring size	$\Delta H^{\ddagger}$[a]	ΔS[b]	Strain energy[c]
3	20.5	+10	28.3
4	21.8	−9	27.4
5	16.3	−12	7.3
6	19.8	−18	1.4

[a] In kcal mol^{-1}. [b] In cal mol^{-1} K^{-1}. [c] In kcal mol^{-1}; data from ref. 14. Values refer to the parent hydrocarbon.

Table 3. Influence of solvent in cyclisation of bis-sulphonyl-stabilised carbanions

Ring size	k (40% v/v EtOH–H_2O[a] *vs.* EtOH) Z = Cl	Z = I
3	20.4	*b*
4	15.9	3.0
5	5.9	2.1
6	4.3	2.2
7		4.4[c]

[a] At 25 °C. [b] Too fast for stopped-flow determination. [c] At 50 °C.

Table 4. Medium effects on activation parameters for the formation of 1,1-bis(phenylsulphonyl)cyclobutane

Medium	k (25 °C)/s^{-1}	$\Delta G^{\ddagger}$/kcal mol^{-1}	$\Delta H^{\ddagger}$/kcal mol^{-1}	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}
100% EtOH	6.05×10^{-6}	24.5	21.8	−9.3
40:60 EtOH–H_2O	9.60×10^{-5}	22.9	19.5	11.3

Table 5. Leaving groups in cyclisation of 1,1-bis(phenylsulphonyl) carbanions to give cyclopropanes

Leaving group, Z	k_{obs}[a]	k_{rel}	$pK_a(H_2O)$ Z–H	Cycloalkane yield (%)
Cl	0.91	1	−7	99
Br	103	114	−9	100
I	359	397	−9.5	100
OTs	46	50	−7	96
$^+PPh_3$	0.40	0.44	0	84
$^+NMe_3$	3×10^{-5}	$<3 \times 10^{-5}$	9.8	95[c]
^+SPhEt	12	13.2	−5	91
SPh	*b*		+6.6	
SO_2Ph	*b*		+2.1	
$OCOBu^t$	*d*		+5.3	

[a] In s^{-1} at 25 °C in EtOH. [b] No reaction. [c] At 78.5 °C. [d] Transesterification only; see text.

These results show that the Ruzicka generalisation is not a safe one so far as enthalpies of activation are concerned. This is not surprising the incidence of strain in alteration of the enthalpy of a transition structure will, of course, be profoundly influenced by the nature of that transition structure, just as is, for example, nucleofugality. The transition structures of reactions involving carbanions clearly vary tremendously. For example, there are very large differences in leaving group sensitivity between 1,2-[13] and 1,3-eliminations.[1]

For ω-bromoalkyl malonate ions in Me_2SO,[10] the Rome group found that the sensitivity of transition state energies to ring size was low in comparison with strain energies of the corresponding cycloalkanes. Their work is in entire agreement with the Ruzicka generalisation if this is updated to take account of the more recently determined strain energies of the medium-sized rings.[14]

The insensitive response of the enthalpy of activation to ring strain is not necessarily indicative of a small degree of ring formation in the transition state. We have calculated[15] that in the reverse process of ring fission, the excess of enthalpies of the three- and four-membered rings falls away very rapidly as a function of the extension of one ring bond.

DeTar[16] has commented on the energetics of S_N2-type ring-closure reactions. He suggests that cyclic products are not appropriate models for transition structures, and that for rings of five members and upwards there are interactions (especially torsional) in the transition structure which are not present in the products. While a cyclobutane may be an appropriate model for a four-membered ring transition structure, a cyclopentane or cyclohexane as a model for the appropriate transition structure may lead to an underestimate of the strain inherent in such a structure.

The fact that the enthalpy of activation for cyclobutane formation is actually *higher* than for cyclopropane is remarkable. The finding is another example of what has recently become a well established phenomenon; four-membered rings are reluctant, by comparison with their similarly strained cyclopropane counterparts, either to open or to close. Reluctant fission of four-membered rings is seen in nucleophilic eliminative ring fission,[15] in homolytic eliminative ring fission,[17] in carbonyl-forming ring fission,[18] and in nucleophilic substitution.[19] We have tentatively ascribed this significant difference in behaviour (a factor of nearly 10^6 in k_{rel} in the present examples) to the distribution of strain in such systems. For cyclopropane, the significant factors which determine strain are valence angle distortion and torsional interaction.[20] For cyclobutane, by contrast, more than half of the excess of enthalpy is to be ascribed to transannular repulsion.[21] This builds up more rapidly than the components of cyclopropane strain as cyclisation proceeds and so even in a transition state with quite a modest extent of ring formation, a four-membered ring may be disadvantaged relative to a three-membered ring.

The *X*-ray crystal structure of compound (**4**; n = 2) shows the cyclobutane ring to be planar.[22a] To this extent, therefore, the

three- and four-membered ring systems are more similar than if the four-membered ring were puckered. A very recent paper from the Rome group[22b] deals with the sticking variations in ring-closure rates as a function of structure which are displayed by three-membered rings.

Entropies of Activation.—The Ruzicka generalisations are borne out by the entropies of activation for the carbanion cyclisations (Table 2). There have been few previous examples of determination of entropies of activation for this type of reaction. Earlier work[23] in this series showed that for cyclisations leading to 'onium salts, $\Delta S^{\ddagger}$ values behaved in a random fashion, a circumstance to be associated with varying degrees of solvation of the highly polar transition structures. In the present work the trend of increasingly negative $\Delta S^{\ddagger}$ values as ring size in the product increases is unmistakable. Page[24] has pointed out that each internal rotation lost in the act of cyclisation reduces the entropy by 5 cal mol^{-1} K^{-1}. Table 2 shows a variable extent of expression of this change. The progression from four- to five- to six-membered rings is broadly consistent with this calculation. The most significant decrease is, of course, that between the three- and four-membered rings, which contributes more than 75% of the rate ratio at 25 °C. It is the very highly favourable entropy of activation that makes three-membered ring-forming reactions so successful against a background of the very limited role of strain.

Medium Effects, Leaving Group Effects, and the Transition State.—The effect of transfer of the ω-halogenoalkyl carbanions from pure ethanol to 40% ethanol–water is seen in Table 3. The range of acceleration is roughly 2—20 fold, being significantly larger for the chlorides than for the iodides and being insensitive to ring size within a small variation. The substantial values of k^{I}/k^{Cl} are consistent with substantial separation of the leaving group in the transition structure and the observed solvent effect is similar to that found for intermolecular displacements, for which the general consensus of opinion[25] is for the considerable bond formation to the nucleophile and considerable separation of the leaving group. The values obtained may be compared with those for the Ramberg–Bäcklund reaction[26] (k^{Br}/k^{Cl} for $PhCH_2SO_2CH_2Z$ = 207 in 40% dioxane-H_2O) and for the reaction of CH_3Z with N_3 (k^{I}/k^{Cl} = 2 000 in Me_2NCHO, 100 in H_2O).[27]

The fact that rates are *increased* on transfer to the more solvating, higher dielectric medium suggests that hydrogen bonding to the carbanion is not very important and that better solvation of the partially separated leaving group (more with chloride than with iodide) is the dominant effect. It can be seen from Table 4 that transfer of the cyclobutane-forming substrate (**3**; n = 2, Z = Cl) from 100% ethanol to 40:60 ethanol–water produces a fifteen-fold increase in rate which is the result of a *decrease* in $\Delta H^{\ddagger}$ accompanied by a *decrease* in $\Delta S^{\ddagger}$. This behaviour, so far as the solvent is concerned, corresponds to that of reaction of an uncharged (poorly solvated) nucleophile with a neutral electrophile, giving rise to greater solvation of the transition structure than of the ground state. S_N2 Hydrolysis of 2-bromopropane, for example, is accelerated 66.7 times on transfer from ethanol to 40% v/v water–ethanol.[28]

The behaviour of other leaving groups studied provides confirmation of a transition structure in which cleavage of the bond to the leaving group is well advanced. The reactivity of the systems with 'onium leaving groups is severely retarded on transfer to more aqueous media. This behaviour is, in fact, more consistent with a system in which nucleophile and electrophile possess opposite charges.[29]

The tosylate is very similar in reactivity to the bromide. No particular conclusions are to be derived from this fact; the phenylthio and phenylsulphonyl leaving groups do not depart. These leaving groups were studied in our earlier work on mono-sulphonyl-stabilised carbanions and ranks (≡ nucleofugalities) were assigned to them.[1] Evidently, the much reduced nucleophilicity of the bis-stabilised carbanion prevents expulsion of what must be regarded, by the standards of displacement (rather than elimination) reactions, as rather poor nucleofuges. It is possible that ring closure of the sulphide (**3**; n = 1, Z = SPh) and the corresponding sulphone does in fact occur, but, under the forcing conditions required to obtain any reaction, the cyclopropane formed would be unstable. Trost and his collaborators[30] have shown that this compound undergoes nucleophilic ring fission with benzyloxide in dimethylformamide. It was impossible to evaluate alkoxycarbonyl leaving groups in this system; the pivalate (**3**; n = 1, Z = OCO-Bu^t) gave exclusively the alcohol (**6**) by transesterification and no cyclopropane was obtained.

In our earlier work with mono-stabilised carbanions, a remarkably close connection emerged between leaving group rank and the pK_a of the conjugate acid of the leaving group in the solvent concerned (Bu^{t}OH). In the present work, a broad correlation is obtained for uncharged leaving groups. For the charged leaving groups, however, gross departure from such a naïve expectation is seen; the 'onium and particularly ammonium groups are much more reactive than the pK_a projection would predict. We have work in hand to calibrate the transition structures of reactions with this type of leaving group.

Conclusions.—Cyclisation of bis-stabilised carbanions bearing distal leaving groups follows the pattern for intermolecular displacement reactions in its response to the leaving group and change of medium. These manifestations are insensitive to the size of the product ring and the insensitivity of the reactions to the strain in the product points to a transition structure in which rather little ring closure has occurred.

Experimental

Extractions were performed with dichloromethane unless otherwise stated. Light petroleum refers to the fraction of b.p. 40—60 °C. Reactions were carried out under dry nitrogen or argon. N.m.r. (^{1}H, ^{13}C) and i.r. spectra were consistent with assigned structures. Ethanol was dried with magnesium and iodine.

Bis(phenylsulphonyl)methane had m.p. 122.1 °C (lit.,[31] 119—120 °C), bis(phenylthio)methane had m.p. 37 °C (lit.,[32] 39.5—40.5 °C), 1,1-bis(phenylsulphonyl)cyclopropane had m.p. 148 °C (lit.,[33] 149 °C), 1,1-bis(phenylsulphonyl)cyclobutane had m.p. 118 °C (lit.,[34] 118—119 °C), 1,1-bis(phenylsulphonyl)-cyclopentane had m.p. 145 °C (lit.,[35] 149 °C), and 1,1-bis(phenylsulphonyl)cyclohexane had m.p. 165 °C (lit.,[36] 163—164 °C).

1,1-*Bis*(*phenylsulphonyl*)*cycloheptane.*—A mixture of cycloheptanone (25 mmol) and benzenethiol (55 mmol) in dry chloroform (80 cm^3) was saturated with dry hydrogen chloride and then kept at 25 °C for 12 h. The mixture was washed successively with water and aqueous sodium hydroxide; removal of the solvent left crude 1,1-bis(phenylthio)cycloheptane (94%) containing about 5% of cycloheptanone. Oxidation of the thioacetal (10 mmol) with *m*-chloroperoxybenzoic acid (4.5 equiv.) in chloroform (50 cm^3) at 25 °C for 24 h gave the *bis-sulphone* (90%), m.p. 201 °C (from ethanol) (79%) (Found: C, 60.3; H, 5.8; S, 17.1 $C_{19}H_{22}O_4S_2$ requires C, 60.3; H, 5.9; S, 16.9%).

3-*Bromo*-1,1-*bis*(*phenylsulphonyl*)*propane* (**3**; n = 1, Z = Br).—A mixture of benzenethiol (332 mmol) and 2-(2-bromoethyl)-1,3-dioxolane (83 mmol) in chloroform (250 cm^3) was

Table 6. Cyclisation reactions: substrates and products

Substrate	Z	Yield (%)	M.p. (°C)	Found (%) C	H	S	Formula	Reqd. (%) C	H	S	Product	M.p. (°C)	Yield (%)	Found (%) C	H	S	Formula	Reqd. (%) C	H	S
(3; $n = 1$)	I	91[f]	117	40.3	3.2		$C_{15}H_{15}IO_4S_2$	40.0	3.4		(4; $n = 1$)	149[a,b]	100							
(3; $n = 2$)	I	99[f]	137	40.9	3.65		$C_{16}H_{17}IO_4S_2$	41.4	3.7		(4; $n = 2$)	118[a,c]	98							
(3; $n = 3$)	I	92[f]	114[c]	42.7	4.3		$C_{17}H_{19}IO_4S_2$	42.7	4.0		(4; $n = 3$)	145[a,c]	85							
(3; $n = 4$)	I	100[f]	85	44.1	4.4	12.7	$C_{18}H_{21}IO_4S_2$	43.9	4.3	13.0	(4; $n = 4$)	165[a,c]	97							
(3; $n = 5$)	I	99[f]	68[c]	45.3	4.5	12.8	$C_{19}H_{23}IO_4S_2$	45.1	4.6	12.7	(4; $n = 5$)	201[a,c,d]	79	60.3	5.8	17.1	$C_{19}H_{22}O_4S_2$	60.3	5.9	17.0
(3; $n = 1$)	Cl	91	91	50.4	4.2		$C_{15}H_{15}ClO_4S_2$	50.2	4.2		(4; $n = 1$)	149[a,b]	99							
(3; $n = 2$)	Cl	95	115	51.2	4.6		$C_{16}H_{17}ClO_4S_2$	51.5	4.6		(4; $n = 2$)	118[a,c]	97	57.2	4.8		$C_{16}H_{16}O_4S$	57.1	4.8	
(3; $n = 3$)	Cl	95	104[c]	53.0	4.8		$C_{17}H_{19}ClO_4S_2$	52.8	4.95		(4; $n = 3$)	145[c,l]	97	58.5	5.8		$C_{17}H_{18}O_4S_2$	58.3	5.2	
(3; $n = 4$)	Cl	94	55[c]	53.5	5.2	16.3	$C_{18}H_{21}ClO_4S_2$	50.4	5.3	16.0	(4; $n = 4$)	165[a,c]	85	59.0	5.7	17.6	$C_{18}H_{20}O_4S_2$	59.3	5.5	17.6
(3; $n = 5$)	Cl	88	85[c]	55.0	5.6	15.5	$C_{19}H_{23}ClO_4S_2$	54.7	5.8	15.4	*e*		91	57.8	6.3		$C_{21}H_{28}O_5S_2$	59.4	6.7	
(3; $n = 1$)	OTs	39	113[c]	53.6	4.6		$C_{22}H_{22}O_7S_3$	53.4	4.5		(4; $n = 1$)	149[a,b]	84							
(3; $n = 1$)	PPh_3BF_4	79	262[c]	58.7	4.2		$C_{27}H_{30}BF_4O_4PS_2$	58.9	4.5											
(3; $n = 1$)	Br	98	107[c]	44.4	3.65		$C_{15}H_{15}BrO_4S_2$	44.7	3.75		(4; $n = 1$)	149[a,b]	98							
(3; $n = 1$)	NMe_3I	98	235[j]	42.6	4.4	2.5[k]	$C_{18}H_{24}INO_4S_2$	42.4	4.75	2.8[k]	(4; $n = 1$)	149[a,b]	95							
(3; $n = 1$)	$SPhEtBF_4$	82		50.2	4.8		$C_{23}H_{25}BF_4O_4S_3$	50.4	4.6		(4; $n = 1$)	149[a,b]								
(3; $n = 1$)	SPh	85	114.5	58.4	5.0		$C_{21}H_{20}O_4S_3$	58.3	4.7		*i*									
(3; $n = 1$)	SO_2Ph	99	142	54.3	4.6		$C_{21}H_{20}O_6S_3$	54.3	4.3		*i*									
(3; $n = 1$)	$OCOBu^t$	90	135[h]	56.4	5.6		$C_{20}H_{24}O_4O_2$	56.6	5.7		*g*									

[a] M.p. and mixed m.p. with an authentic specimen. [b] Lit. m.p. 149 °C (see ref. 33). [c] From ethanol. [d] N.m.r. analysis gave 1,1-bis(phenylsulphonyl)cycloheptane 70%, 7-ethoxy-1,1-bis(phenylsulphonyl)-heptane 30%. Crystallisation from EtOH gave the cycloheptane (47%), m.p. and mixed m.p. 200 °C. [e] Crude 7-ethoxy-1,1-bis(phenylsulphonyl)heptane (see text). [f] From the bromide with NaI–propanone. [g] 3,3-Bis(phenylsulphonyl)propan-1-ol (26%) and its sodium salt (70%). [h] From propan-2-ol. [i] No reaction with 1M-NaOEt–EtOH at 80 °C (1 day). At 150 °C for 115 h, t.l.c. shows starting material and two other products, but not cyclopropane. ^{1}H N.m.r. shows ethoxy groups. [j] From methanol. [k] Analysis for N. [l] From ethanol–hexane.

saturated with dry hydrogen chloride at 20 °C. After 24 h, the mixture was washed with aqueous 5% sodium hydroxide; evaporation left the crude thioacetal (**8**) (88%). Oxidation with *m*-chloroperoxybenzoic acid gave the *bis-sulphone* (98%), m.p. 107 °C (details in Table 6).

3-*Chloro*-1,1-*bis*(*phenylsulphonyl*)*propane*.—Dry hydrogen chloride was bubbled through a solution of 1-chloro-3,3-diethoxypropane (50 mmol) and benzenethiol (300 mmol) in chloroform (150 cm^3) for 1.5 h. After 24 h at 20 °C, removal of the solvent left a residue which on distillation gave the crude thioacetal (**5**), b.p. 135 °C at 2 × 10^{-4} mmHg. Oxidation with *m*-chloroperoxybenzoic acid gave the *sulphone* (**3**; n = 1, Z = Cl) (91%), m.p. 91 °C (details in Table 6).

1,1-*Bis*(*phenylsulphonyl*)-3-*tosyloxypropane* (**3**; n = 1, Z = OTs).—3,3-Bis(phenylthio)propan-1-ol [37] was oxidised with *m*-chloroperoxybenzoic acid (4.4 mol) to give 3,3-*bis*(*phenylsulphonyl*)*propan*-1-*ol* (**6**) (85%), m.p. 121—122 °C (from ethanol) (Found: C, 53.1; H, 4.7. $C_{15}H_{16}O_5S_2$ requires C, 52.9; H, 4.7%). Treatment with tosyl chloride in pyridine at −10 °C gave the *tosylate* (98%), m.p. 113 °C (from ethanol). Details are in Table 6.

1,1-*Bis*(*phenylsulphonyl*)-3-*pivaloyloxypropane* (**3**; n = 1, Z = $OCOBu^t$).—3,3-Bis(phenylsulphonyl)propan-1-ol (**6**) was treated with 3 equiv. of pivaloyl chloride in chloroform at 20 °C. After 20 h, removal of the solvent gave the *ester*, m.p. 135.2 °C (from propan-2-ol). Details are in Table 6.

The ester (0.94 mmol) in ethanolic M-sodium ethoxide was set aside at 20 °C for 24 h. Filtration and evaporation left the alcohol (**6**) (26%) (identified by i.r. and ^{1}H n.m.r.). The residue from filtration, m.p. *ca.* 260 °C (decomp.), was the sodium salt of (**6**), which was converted into the free alcohol (97%) by treatment of a chloroform suspension with aqueous 10% HCl. On similar treatment of the sodium salt with potassium t-butoxide in t-butyl alcohol, the alcohol (**6**) (97%) and pivalic acid (87%) were recovered.

1,1-*Bis*(*phenylsulphonyl*)-3-*phenylthiopropane* (**3**; n = 1, Z = SPh).—Ethanolic 0.5M-sodium ethoxide (15.6 mmol) was added to a refluxing solution of bis(phenylsulphonyl)methane (15 mmol) and 2-bromoethyl phenyl sulphide (16.5 mmol) in ethanol (60 cm^3). After 2 h at reflux, dilution with water and extraction gave the *sulphide* (91%), m.p. 114.5 °C. Oxidation of the sulphide with *m*-chloroperoxybenzoic acid in chloroform gave the sulphone (99%), m.p. 142 °C (details in Table 6).

3,3-*Bis*(*phenylsulphonyl*)*propyltrimethylammonium Iodide* (**3**; n = 1, Z = $^+NMe_3I^-$).—2-Dimethylaminoethyl chloride (10.2 mmol) in ethanol (50 cm^3) was added dropwise to a refluxing solution of bis(phenylsulphonyl)methane (10 mmol) in ethanolic 0.22M-sodium ethoxide (22 mmol). After 3 h at reflux, dilution of the mixture with brine and extraction gave the amino sulphone (**7**) (86%), m.p. 123 °C (from ethanol) (lit.,[35] 124 °C) (Found: C, 55.4; H, 5.9; N, 3.7. Calc. for $C_{17}H_{21}NO_4S_2$: C, 55.6; H, 5.8; N, 3.8%). Methylation of the amine with a 10-fold excess of methyl iodide in chloroform at 20 °C gave the *methiodide* (98%), m.p. 234—236 °C (from methanol) (details in Table 6).

3,3-Bis(*phenylsulphonyl*)*propyltriphenylphosphonium Bromide* (**3**; n = 1, Z = $^+Ph_3PBF_4^-$).—The bromide (**3**; n = 1, Z = Br) (5 mmol) and triphenylphosphine (5 mmol) in dioxane (10 cm^3) containing aqueous 48% hydrobromic acid (1 cm^3) were heated at reflux for 5 days. Dilution with brine and extraction gave the crude phosphonium bromide as an oil, which was dissolved in the minimum of methanol and added to sodium tetrafluoroborate (25 mmol) in water (25 cm^3). The precipitated *salt* (79%) had m.p. 262 °C (from ethanol) (details in Table 6).

3,3-*Bis*(*phenylsulphonyl*)*propyl*(*ethyl*)*phenylsulphonium Tetrafluoroborate* (**3**; n = 1, Z = $^+SEtPhBF_4^-$).—The sulphide (**3**; n = 1, Z = SPh) (1.15 mmol) was heated under reflux for 24 h with a 1M-solution of triethyloxonium tetrafluoroborate in dichloromethane. Evaporation to dryness and trituration with dry ethanol gave the crude *salt* (82%), which was purified by preparative t.l.c. and subsequent crystallisation; m.p. 132—134 °C (from acetonitrile–ether) (details in Table 6).

6-*Chloro*-1,1-*bis*(*phenylsulphonyl*)*hexane*.—n-Butyl-lithium (12.9 cm^3 of a 1.55M-solution in hexane) was added, under argon at −40 °C, to bis(phenylthio)methane (20 mmol) in dry tetrahydrofuran (100 ml). After 15 min at −40 °C, 1-bromo-5-chloropentane (20 mmol) in tetrahydrofuran (7.5 ml) was added. The mixture was kept at −20 °C for 16 h; addition of water and extraction then gave the crude sulphide (92%). Oxidation with *m*-chloroperoxybenzoic acid (4.5 equiv.) in chloroform gave the *bis-sulphone* (85%), m.p. 165 °C (from ethanol). Similar procedures were used for the chlorides (**3**; n = 2—5).

The chloro sulphone (0.78 mmol) and sodium iodide (4.65 mmol) in acetone (7.5 cm^3) were boiled under reflux for 48 h. Addition to water and extraction with chloroform (sodium

Table 7. Kinetics of cyclisation of 5-chloro-1,1-bis(phenylsulphonyl)-pentane [a,b]

Run	$10^2k/s^{-1}$	T/°C
1	1.10 [c,d]	22.3
2	1.13 [d,e]	22.4
3	1.24 [d]	23.3
4	1.70 [d]	26.2
5	1.58 [e,f]	25.7
6	1.66 [e,f]	25.8
7	2.73	31.5
8	2.94	31.7
9	4.23	36.4
10	4.39	36.5
11	6.37	41.3
12	7.14	41.5
13	9.48	45.4
14	9.73	45.7
15	14.36	51.1
16	15.42	51.4
17	22.14	56.8
18	1.41 [g]	25.0
19	1.25 [h]	25.2
20	4.50 [i]	26.2
21	3.78 [j]	25.0
22	5.08 [k]	25.0
23	8.73 [l]	25.0
24	8.75 [m]	25.0
25	8.47 [n]	25.0

[a] In ethanolic sodium ethoxide unless otherwise stated. [b] [substrate] = 4.07 × 10^{-5}M; [EtONa] = 0.125M. [c] [substrate] = 1.02 × 10^{-4}M. [d] [EtONa] = 0.126M. [e] [substrate] = 2.04M. [f] [EtONa] = 0.252M. [g] NaOMe–MeOH; [substrate] = 2.49 × 10^{-4}M; [MeONa] = 0.125—0.25M; mean of five determinations. [h] Bu^tOK–Bu^tOH; [substrate] = 2.03 × 10^{-4}M; [Bu^tOK] = 0.125—0.25M; mean of four determinations. [i] KOH in 50:50 v/v Bu^tOH–H_2O at 26.2 °C; [substrate] = 1.02 × 10^{-4}M; [KOH] = 0.625—0.125M; mean of three determinations. [j] NaOH in EtOH–H_2O (80:20 v/v); [substrate] = 2.56 × 10^{-4}M; [NaOH] = 0.125—0.24M; mean of four determinations. [k] NaOH in EtOH–H_2O (60:40 v/v); [substrate] = 2.0 × 10^{-4}M; [NaOH] = 0.125—0.25M. [l] NaOH in EtOH–H_2O (40:60 v/v); [substrate] = 1.26 × 10^{-4}M; [NaOH] = 0.12M; mean of three determinations. [m] NaOH in EtOH–H_2O (20:80 v/v); [substrate] = 1.03 × 10^{-4}M; [NaOH] = 0.1—0.2; mean of four determinations. [n] NaOH in EtOH–H_2O (10:90 v/v); [substrate] = 1.05—1.2 × 10^{-4}M; [NaOH] = 0.1—0.4M; mean of four determinations.

disulphite wash) gave the *iodide* (92%), m.p. 114 °C (from ethanol).

Similar procedures were used for the iodides (**3**; n = 2—5) (details in Table 6).

Ring Closure of 5-Chloro-1,1-bis(phenylsulphonyl)pentane.—The bis-sulphone (3 mmol) in ethanolic 0.5M-sodium ethoxide (120 cm^3) was kept at 20 °C for 6 h. Addition to saturated brine and extraction gave the cyclopentane (97%), m.p. 145.1 °C (from ethanol–hexane). Other cyclisations (except to cycloheptanes) proceeded similarly; details are in Table 6.

Reaction of 7-Chloro-1,1-bis(phenylsulphonyl)heptane with Ethanolic Sodium Ethoxide.—The chloride (2.5 mmol) in ethanolic 0.5M-sodium ethoxide was set aside for 5 days at 20 °C. Work-up as before gave unchanged chloride (100%), m.p. and mixed m.p. 85 °C. When the reaction was carried out under reflux for 48 h extraction as before gave a residue which, on flash chromatography, gave crude 7′-ethoxy-1,1-bis(phenylsulphonyl)heptane (91%) as an oil, m/z 424 (M^+, 1%); $\delta_H(CDCl_3)$ 1.23 (t, 3 H), 1.3—2.2 (m, 10 H), 3.45 (t, 2 H), 3.48 (q, 2 H), 4.5 (t, 1 H), and 7.6—8.2 (m, 10 H); $\delta_C(CDCl_3)$ 15.1, 25.5 (2 peaks), 27.9, 28.8, 29.5, 66.0, 70.4, 83.8, 129.2, 129.6, 134.7, and 138.2 (Found: C, 57.8; H, 6.3. Calc. for $C_{21}H_{28}O_5S_2$: C, 59.4; H, 6.65%).

Kinetics.—Reactions were followed by monitoring the decrease in u.v. absorption of mixtures of substrate and ethanolic sodium ethoxide near 290 nm. Substrate concentrations were 0.5—2 × 10^{-4}M, base concentrations 0.1—0.5M. The full results for 5-chloro-1,1-bis(phenylsulphonyl)pentane are in Table 7. Results for other substrates were obtained similarly.

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