Reaction of Chlorosulphonyl Isocyanate with 1,3-Dienes. Control of 1,2- and 1,4-Addition Pathways and the Synthesis of Aza- and Oxa-bicyclic Systems

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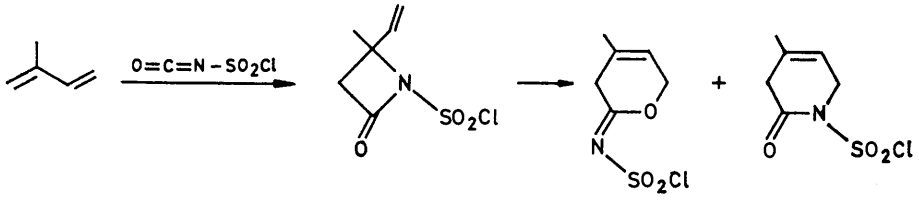
Cyclopenta-, cyclohexa-, cycloheptа- and cyclo-octa-1,3-dienes react with chlorosulphonyl isocyanate to yield, in each case, a single *N*-chlorosulphonyl β-lactam as the primary product. In the first three examples, these 1,2-adducts undergo stepwise thermal rearrangements with varying degrees of ease to thermodynamically more stable products of 1,4-addition (cyclisation occurring through O or N in the ambident anion) or substitution products: the β-lactam from cyclo-octadiene could not be induced to rearrange constructively. The reactivity patterns in acyclic dienes are compared and a dipolar reaction mechanism is discussed. Selected n.m.r. spectra are analysed in detail and examples of conversion of the 1,4-adducts into 2-azabicyclo[2.2.1]-heptanes, -heptenes, and -heptadienes and into 2-oxa- or 2-aza-bicyclo[2.2.2]-octanes and -octenes and -bicyclo[3.3.2]nonenes are recorded.

INTEREST in the addition reactions of chlorosulphonyl isocyanate (CSI) with simple olefins has been extended to include a variety of conjugated olefinic substrates,[1,2] amongst which simple 1,3-dienes have offered particularly interesting reactivity patterns. Isoprene, for example, suffers attack by the uniparticulate electrophile [3] CSI followed by ring closure to yield the product



of 1,2-addition.[1] Such unsaturated *N*-chlorosulphonyl β-lactams are generally unstable and readily rearrange to the products of formal 1,4-addition, cyclisation occurring through O or N in the dipolar intermediate.[1,†]

In contrast, the addition of CSI to homoannular 1,3-dienes has received little attention. 1,2-Addition (*N*-chlorosulphonyl β-lactam formation) has been recorded in addition of CSI to cyclo-octa-1,3-diene [4] and cyclopentadiene,[5] although no details have been published in the latter case.

We were intrigued by the behaviour of CSI with cyclic 1,3-dienes for three main reasons. First, since 1,4-addition was observed with acyclic dienes it seemed reasonable to expect cyclic 1,3-dienes to behave similarly, especially since the diene unit is naturally held in a *cisoid* conformation (as opposed to the usual *transoid* configuration of acyclic dienes). Secondly, 1,4-addition to cyclic dienes might form the basis of an attractive and simple route to azabicyclic systems (*via* 1,4-cyclisation through nitrogen) and oxabicyclic systems (*via* cyclisation through oxygen). Thirdly, there existed the possibility that useful influence might be exerted over

† Significant differences in the reported relative yields of products are apparent in some cases and may be due to differences in experimental conditions and work-up procedures. Disagreement also emerges over the relative importance of unsaturated amides (*e.g.* $ClSO_2{\cdot}NH{\cdot}CO{\cdot}CH{:}CMe{\cdot}CH{:}CH_2$) and whether they are primary products (formed concurrently with the β-lactam) or secondary. Interconversion of the secondary rearrangement products was not recorded.

[1] (*a*) E. J. Moriconi and W. C. Meyer, *J. Org. Chem.*, 1971, **36**, 2841; (*b*) P. Goebel and K. Clauss, *Annalen*, 1969, **722**, 122; (*c*) Th. Haug, F. Lohse, K. Metzger, and H. Batzer, *Helv. Chim. Acta*, 1968, **51**, 2069; (*d*) E. J. Moriconi and W. C. Meyer, *Tetrahedron Letters*, 1968, 3823; (*e*) H. Hoffmann and H. J. Diehr, *ibid.*, 1963, 1875.

[2] (*a*) L. A. Paquette, J. R. Malpass, and T. J. Barton, *J. Amer. Chem. Soc.*, 1969, **91**, 4714; (*b*) E. J. Moriconi, C. F. Hummel, and J. F. Kelly, *Tetrahedron Letters*, 1969, 5325; (*c*) R. J. P. Barends, W. N. Speckamp, and H. O. Huisman, *ibid.*, 1970, 5301; (*d*) J. R. Malpass, *J.C.S. Chem. Comm.*, 1972, 1246.

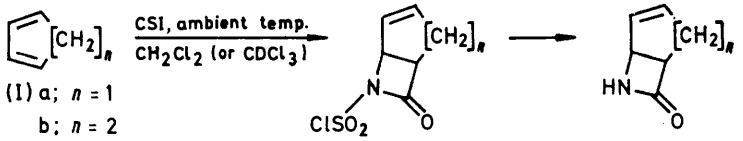
[3] L. A. Paquette, G. R. Allen, jun., and M. J. Broadhurst, *J. Amer. Chem. Soc.*, 1971, **93**, 4503.

[4] T. Durst and M. J. O'Sullivan, *J. Org. Chem.*, 1970, **35**, 2043.

[5] H. Bestian, *Pure Appl. Chem.*, 1971, **27**, 611.

the relative proportion of 1,4-cyclisation through oxygen or nitrogen. If competitive cyclisation through oxygen (to give imino-lactones) and nitrogen (to give lactams) occurred, a precedent existed for manipulation of the product ratio by changing solvent polarity.[6] If energy criteria dictated the *consecutive* formation of imino-lactones and lactams, the work of Speckamp *et al.*[2c] on 1,4-addition of CSI to a vinyl dihydronaphthalene offered encouragement that control might still be achieved by judicious choice of reaction time and temperature.

In the event, we found that both 1,2- and 1,4-addition of CSI to a number of cyclic dienes could be achieved,



(I) a; $n = 1$
b; $n = 2$
c; $n = 3$
b; $n = 4$

(IIa-d) (IIIa-d)

usually with a high degree of control and in synthetically useful yields. Our initial studies on cyclohexadienes [7] are extended here to include a wider range of ring sizes.

RESULTS

The dienes (Ia—d) were studied. Each diene reacted with *ca.* 1 mol. equiv. of CSI in dichloromethane solution at ambient temperature, as shown by the disappearance of the isocyanate i.r. absorption. The appearance of a single high-frequency carbonyl absorption in the region 1 810—1 820 cm^{-1} indicated formation of the *N*-chlorosulphonyl β-lactams (IIa—d) as the sole monomeric carbonyl-containing products. The reactions were also monitored by n.m.r. spectroscopy in deuteriochloroform solution; the spectra of the products (IIa—c) were entirely consistent with the proposed structures [in the case of (IId) spectral data matched literature values [4]]. Acid-catalysed polymerisation of the dienes (Ia and b) was minimised by 'inverse addition' of the diene in solution to a stirred solution of CSI.

The reaction of cyclopentadiene (Ia) with CSI in either solvent was complete within 10 min to give (IIa), $\nu_{max.}$ (CH_2Cl_2) 1 818 cm^{-1}. By using chloroform as a quantitative internal standard in deuteriochloroform solution, the yield of (IIa) was calculated to be 60 ± 5%; the balance of the material appeared to be polymeric. Immediate treatment with aqueous sodium sulphite [4] afforded the stable β-lactam (IIIa) in 40% yield.

Quantitative conversion of cyclohexa-1,3-diene (Ib) into (IIb), $\nu_{max.}$ (CH_2Cl_2) 1 810 cm^{-1}, was complete within 10 min. Again, no attempt was made to isolate (IIb), which was converted directly into (IIIb) by the Graf procedure [8] with benzenethiol, modified for application at low temperatures; [6] the product (IIIb) was isolated in 67% overall yield.

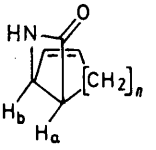
The reaction of cyclohepta-1,3-diene (Ic) with CSI gave a near-quantitative yield of (IIc), $\nu_{max.}$ (CH_2Cl_2) 1 820 cm^{-1}, which was converted into (IIIc) in 38% yield with aqueous sodium sulphite.

The conversion of cyclo-octa-1,3-diene (Id) into (IId) by overnight heating with CSI in benzene at 50 °C has been reported.[4] Use of a more polar solvent (dichloromethane or acetonitrile) allowed the reaction to proceed to completion at ambient temperature in 24 h or 30 min, respectively.

The assignment of the structures (III) was based upon spectroscopic evidence. For example, each compound showed a single NH i.r. absorption (solution) in the region 3 400—3 410 cm^{-1} and a carbonyl band in the region 1 750—1 760 cm^{-1}, characteristic of *N*-unsubstituted β-lactams. The orientation of the β-lactam ring with respect to the remaining double bond was established by n.m.r. spectroscopy (Table 1). The single-

TABLE 1

N.m.r. data for the β-lactams (IIIa—d)



n	$\delta(H_a)$	ΔEu_a †	$\delta(H_b)$	ΔEu_b †	J_{ab}/Hz
1	3.37	−9.7	4.46	−4.3	4.1
2	3.46	−9.0	3.99	−4.0	5.0
3	3.20	−9.3	4.40	−4.2	5.0
4 *	3.2—3.6		4.4—4.7		

* Ref. 4.

† Europium-induced shift parameters [9] (±0.5 p.p.m.) obtained from measurements over a range of molar ratios of $Eu(dpm)_3$ to substrate from 0 to 0.5 : 1 in $CDCl_3$.

proton resonances due to H_a and H_b are clearly in the regions expected for a methine proton adjacent to a lactam carbonyl group (H_a, δ 3.0—3.5) and for a methine proton which is both next to nitrogen and allylic (H_b, δ 4.0—4.5). These assignments were confirmed by the relative magnitudes of the lanthanide-induced shifts of H_a and H_b. The results confirm that H_a is closer to the carbonyl group at which site the shift reagent is known to complex.[9] Europium shift studies and homonuclear spin-decoupling experiments also allowed a more detailed analysis of the remaining features of the n.m.r. spectra; typical results are illustrated for (IIIa) in Table 2.

The *N*-chlorosulphonyl β-lactams (IIIa—c) rearranged

[6] J. R. Malpass and N. J. Tweddle, *J.C.S. Chem. Comm.*, 1972, 1244.

[7] J. R. Malpass and N. J. Tweddle, *J.C.S. Chem. Comm.*, 1972, 1247.

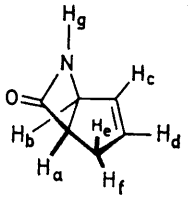
[8] R. Graf, *Annalen*, 1963, **661**, 111; *Angew. Chem. Internat. Edn.*, 1968, **7**, 172.

[9] A. F. Cockerill, G. L. O. Davies, R. C. Harden, and D. M. Rackham, *Chem. Rev.*, 1973, **73**, 555.

thermally, the ease of ring-opening decreasing as the ring size increased. The most instructive reactivity pattern was found in the cyclohexadiene series, and this example will be considered first.

TABLE 2

N.m.r. parameters for the β-lactam (IIIa) ($CDCl_3$ solution; 100 MHz)



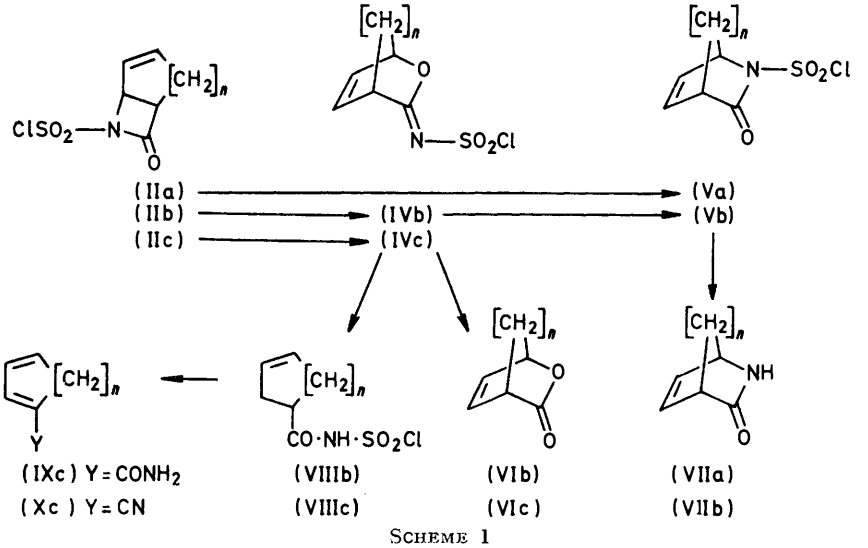
	H_a	H_b	H_c	H_d	H_e	H_f	H_g
δ	3.37	4.46	5.94		2.68	2.38	7.42
ΔEu †	−9.7	−4.3	−2.3/−2.6 §		−7.4	−4.4	−9.0
J_b‡/Hz	4.1						
J_c/J_d	<1	<1	¶	¶			
J_c	3.0	2.4	<1	<1			
J_f	9.5	1.2	1.6	1.6	18		
J_g	<1	<1					

† See Table 1. ‡ Coupling constants (±0.1 Hz) extracted by inspection assuming pseudo-first-order behaviour; <1 signifies that coupling was evident from spin-decoupling studies but was not clearly resolved. § The induced shift parameters of the olefinic protons could not be assigned with confidence owing to the similarity of distances between the carbonyl group and each proton. ¶ The signals of the olefinic protons H_c and H_d were only separated at high concentrations of shift reagent, under which conditions signals were too broad to permit extraction of J_{cd}.

On monitoring the i.r. spectrum of a solution of the *N*-chlorosulphonyl β-lactam (IIb) produced *in situ* from cyclohexadiene in dichloromethane at ambient temperature, there was observed a slow replacement of the carbonyl band at 1 810 cm^{-1} by an intense imine stretching band at 1 588 cm^{-1}. The change was complete within 30 h and removal of solvent under vacuum left a quantitative yield of crude crystalline (IVb). The structure (IVb) was confirmed by the n.m.r. spectrum which showed, in particular, signals at δ 5.74 and 3.90 due to the allylic protons adjacent to oxygen and the imino-groups respectively.[2b] Spin-decoupling studies showed no coupling between the two methine protons nor between the olefinic and methylene protons, consistent with the assigned oxabicyclo[2.2.2]octene structure. In addition, aqueous acid hydrolysed the imino-lactone (IVb) to the bicyclic lactone (VIb) in high yield.

Although compound (IVb) could be isolated with ease and was stable in the crystalline form, further rearrangement to the *N*-chlorosulphonyl δ-lactam (Vb) occurred on heating under reflux in chloroform solution as shown by disappearance of the 1 588 cm^{-1} peak over 17 h and its replacement by a carbonyl band at 1 753 cm^{-1}. After removal of a small amount of polymeric material and evaporation, the *N*-chlorosulphonyl lactam (V) was obtained in 90% yield as an oil. Hydrolysis with aqueous NaOH at pH 6—7 afforded the stable *N*-unsubstituted lactam (VIIb) in 35% yield after chromatography. The i.r. spectrum of (VIIb) showed a single NH stretching absorption at 3 480 cm^{-1} and a carbonyl band at 1 690 cm^{-1}, as expected of a δ-lactam; the n.m.r. spectrum confirmed the azabicyclo[2.2.2]octene structure.

Thus, judicious choice of solvent, reaction time, and temperature allows a choice amongst (IIb), (IVb), and (Vb) (the products of 1,2-addition through nitrogen, 1,4-addition through oxygen, and 1,4-addition through nitrogen, respectively) as the sole product, in high yield in each case. Conversion into the corresponding *N*-unsubstituted lactams or lactone is simple but yields are variable.



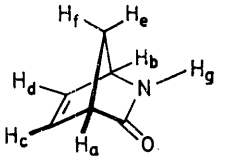
SCHEME 1

A detailed study of the behaviour of the *N*-chlorosulphonyl β-lactam (IIa) as a potential precursor of the related oxa- and aza-bicyclo[2.2.1]heptenes was appropriate. Monitoring a solution of (IIa) in dichloromethane by i.r. spectroscopy showed a gradual decay of

the 1 818 cm^{-1} band accompanied by the appearance of new peaks at 1 790 and 1 775 cm^{-1} (a broad band at 1 695 cm^{-1}, which appeared during the rearrangement, was ascribed to polymeric material). After *ca.* 5 h the rearrangement of (IIa) was almost complete and immediate reduction with sodium sulphite afforded (VIIa) in 27% yield after chromatography. The identity of (VIIa) was confirmed by spectroscopic analysis and comparison with the properties reported for a sample prepared independently *via* hydrolysis of the Diels–Alder adduct of cyclopentadiene and tosyl cyanide.[10] The imino-lactone (IVa) was not observed. A detailed analysis of the n.m.r. spectrum of the *N*-unsubstituted and *N*-deuterio-lactams (VIIa), based on spin-decoupling and europium shift studies, is summarised in Table 3.

TABLE 3

N.m.r. parameters for the 2-azabicyclo[2.2.1]hept-5-en-3-one (VIIa) ($CDCl_3$ solution; 100 MHz)



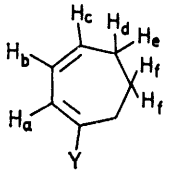
	H_a	H_b	H_c	H_d	H_e	H_f	H_g
δ	3.21	4.34	6.65	6.81	2.38	2.20	6.7—7.1
ΔEu†	−13.3	−3.5	−5.7	−3.2	−6.5	−4.2	−13.5
J_b‡/Hz	2.0						
J_c	3.3	1.5					
J_d	0.9	2.0	5.4				
J_e	1.6	1.8	¶	¶			
J_f	1.4	1.5			7.6		
J_g	§	1.5	¶	¶		1.5	

† See Table 1. ‡ Coupling constants (±0.2 Hz) extracted by inspection assuming pseudo-first order behaviour. § Coupling was evident but could not be measured accurately; estimate 1 ± 0.5 Hz. ¶ Coupling was evident but was too small to be measured.

The appearance of the signal due to the methine proton H_b as a broadened but clearly resolved septet is intriguing: H_b couples with all six other protons in the molecule to approximately the same extent (J 1.5—2.0 Hz) despite the fact that no two protons in the molecule are equivalent.

The *N*-chlorosulphonyl β-lactam (IIc) rearranged slowly in dichloromethane at 30 °C. The decay of the 1 820 cm^{-1} band was matched by growth of an imine stretching band at 1 580 cm^{-1}. After 25 h, removal of the solvent left a crystalline product in quantitative yield whose spectroscopic properties were entirely consistent with its formulation as the *N*-chlorosulphonyl imino-lactone (IVc) [which could be converted into the lactone (VIc) with aqueous acid]. The adduct (IVc) was stable in dichloromethane solution and further rearrangement was induced only in nitromethane at 80 °C over 5 days. No new lactam carbonyl corresponding to (Vc) was observed; there appeared instead a lower frequency carbonyl band at 1 720 cm^{-1} ascribed to the conjugated *N*-chlorosulphonyl amide (VIIIc) together with a nitrile stretching band at 2 210 cm^{-1} assigned to the α,β;γ,δ-unsaturated nitrile (Xc). After treatment of the reaction mixture with sodium sulphite, the nitrile (Xc) was separated chromatographically from a small amount of amide (IXc).

The n.m.r. spectra of (IXc) and (Xc) were very similar, the appearance of the signals due to the olefinic protons H_a, H_b, and H_c as a doublet, a doublet of doublets, and a doublet of triplets, respectively, being diagnostic (J_{ab} 7, J_{bc} 12, $J_{cd} \approx J_{ce}$ 4 Hz). Decoupling experiments



(IXc) Y = CO·NH_2
(Xc) Y = CN

identified the highest field signal in the spectrum of (IXc) (a 2-proton quintet, J 5.5 Hz) as that due to the protons of the central methylene group (H_f). U.v. absorption at 272.5 nm (ε 11 900) was consistent with structure (Xc), and the amide (IXc) showed a characteristically low frequency carbonyl band at 1 665 cm^{-1}, together with u.v. absorption at 274 nm (ε 8 600).

Unsuccessful attempts were made to rearrange *N*-chlorosulphonyl β-lactam (IId). The i.r. spectrum of (IId) in dichloromethane did not change significantly when the solution was heated at reflux over 6 weeks. On warming a solution of (IId) in nitromethane to 50—60 °C over 10 days, the *N*-chlorosulphonyl β-lactam absorption gradually decayed and a broad band at 1 720 cm^{-1} developed. However, after work-up with sodium sulphite, only polymeric material was obtained.

DISCUSSION

Cyclohexa-1,3-diene (Ib) offers the most clearly delineated series of stepwise reactions and will be taken as a basis for mechanistic discussion.

The first step, β-lactam formation, may be viewed either as a thermally allowed $[{}_\pi 2_s + {}_\pi 2_a]$ cycloaddition [1a] [path (A)], as a dipolar addition occurring *via* an associated 1,4-dipole [5,11] [path (B)] or, at the other extreme, as a truly dipolar process [path (C)].[5,8,12]

On the basis of path (A), the preferential formation of 1,2- rather than 1,4-cycloaddition products from acyclic 1,3-dienes might be rationalised in terms of the unfavourable *transoid* conformation adopted by the dienes. However, for cyclic 1,3-dienes which are held in the *cisoid* conformation required for 1,4-cycloaddition, it is not immediately obvious why the highly strained transition state for a $[{}_\pi 2_s + {}_\pi 2_a]$ cycloaddition should be preferred to the $[{}_\pi 2_s + {}_\pi 4_s]$ alternative which, in terms of strain and product stability, might be expected to be of lower energy. It has been suggested [1a] that the participation

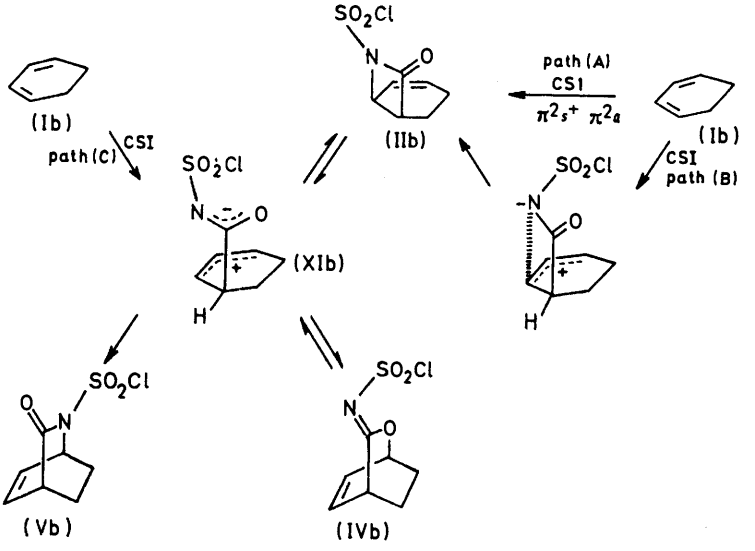
[10] J. C. Jagt and A. M. Van Leusen, *J. Org. Chem.*, 1974, **39**, 564.

[11] E. J. Moriconi, 'Mechanisms of Reactions of Sulphur Compounds,' vol. 3, Intra-Science Research Foundation, Santa Monica, California, 1968, p. 131.

[12] K. Clauss, *Annalen*, 1969, **722**, 110.

of CSI as a $_{\pi}2_s$ component is not facilitated by the orthogonal $\pi_{C=O}$ system on the one side and the $d\pi$–$p_{\pi(SO_2Cl)}$ system on the other. On this basis, it seems that CSI should be as well able as are ketens to behave as the $_{\pi}2_a$ component in concerted reactions with $_{\pi}2_s$ systems.[1a] However, whilst studies on dichloroketen [13] are in full agreement with its behaviour as a $_{\pi}2_a$ component, these same studies point to a marked contrast between the reactivities of dichloroketen and CSI. For example with strained double bonds, the greater reactivity of CSI is more in keeping with a dipolar addition.

The observation in the present work of apparently exclusive initial formation of *cis*-fused *N*-chlorosulphonyl β-lactams with the Markownikov orientation



SCHEME 2

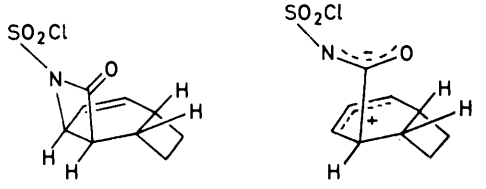
expected of a dipolar addition is in accord with the general behaviour of CSI with the many olefinic substrates investigated to date. Since the early work of Graf [8] a considerable degree of dipolar character has been invoked in order to explain substituent effects on rates of reaction and orientation of addition and to explain the effect of solvent polarity on rates of reaction.[12,14] The qualitative reactivity order (Ia) ~ (IIa) > (IIIa) > (IVa) is comparable to that found for the acid-catalysed hydration of cyclic 1,3-dienes [15] and is certainly consistent with the expected decrease in allylic stabilisation of a developing carbocation centre at the transition state for a dipolar addition of CSI. As the ring size increases, the conformational requirements of the ring will cause the diene system to become progressively more twisted from the preferred coplanar arrangement leading to a decrease in overlap between the olefinic bonds.* Indeed the observed reactivity order is the reverse of that expected in terms of the secondary overlap of the highest occupied orbital of the diene system with the unoccupied π* orbital of the carbonyl group, which has been proposed as a factor favouring a concerted $[_{\pi}2_s + _{\pi}2_a]$ mechanism for the addition of CSI to olefinic systems.[1a] The expected increase in the energy of the highest occupied olefinic π orbitals as the diene system becomes more twisted should lead to a better secondary overlap, owing to the decreasing energy gap between the interacting orbitals. Thus the reactivity of a cyclic diene in a $[_{\pi}2_s + _{\pi}2_a]$ cycloaddition might be expected to increase with increase in ring size.

Having accepted a degree of dipolar character at the transition state for 1,2-addition we can consider paths (B) and (C). The dipolar process [path (C)] offers a mechanistic simplicity the appeal of which has survived since its initial suggestion by Graf,[8] whilst the compromise offered by path (B) has been welcomed by many authors anxious to preserve a degree of 'concertedness' in CSI reactions. A clear dividing line is ultimately unlikely to be drawn in most reactions and the *degree* of dipolar character must be expected to vary from case to case with substitution and solvation. A small but significant observation in closely related studies on bicyclo-octadiene [7] has demonstrated without doubt that the closely related β-lactam (XII) is accessible *via* the truly dipolar species (XIII), and consideration has recently been given to the possibility that the addition of CSI to a conformationally fixed methylenecyclohexane gives the more stable of two β-lactam products directly *via* a dipolar intermediate.[17] We therefore

* A related effect, due to the decrease in overlap between the double bonds as the ring size increases, has also been found in the Diels–Alder addition of maleic anhydride to cyclic dienes where the reactivity order (Ia) > (IIa) > (IIIa) > (IVa) is observed.[16]

[13] L. Ghosez, R. Montaigne, A. Roussel, H. Van Lierde, and P. Mollet, *Tetrahedron*, 1971, **27**, 615.
[14] R. W. Britt, Ph.D. Thesis, 1972, Fordham University, New York.
[15] J. L. Jensen and V. Uaprasert, *J. Org. Chem.*, 1976, **41**, 649.
[16] (*a*) K. Alder and H. H. Mölls, *Chem. Ber.*, 1956, **89**, 1960; (*b*) A. C. Cope and L. L. Estes, jun., *J. Amer. Chem. Soc.*, 1950, **72**, 1128.
[17] E. Dunkelblum, *Tetrahedron*, 1976, **32**, 975.

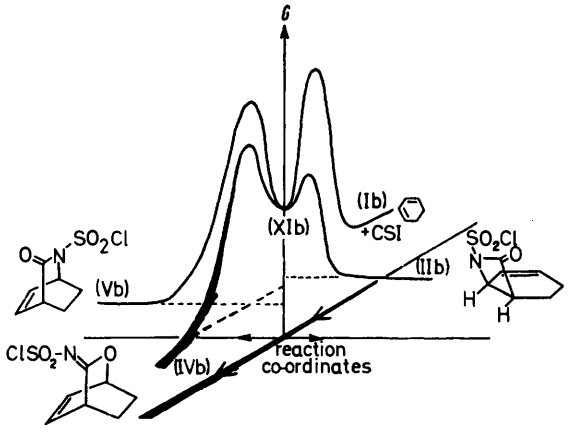
propose to discuss the behaviour of the cyclic dienes in terms of path (C) and a centrally important, common, dipolar intermediate (XIa—d), but in a pragmatic rather than a dogmatic sense.



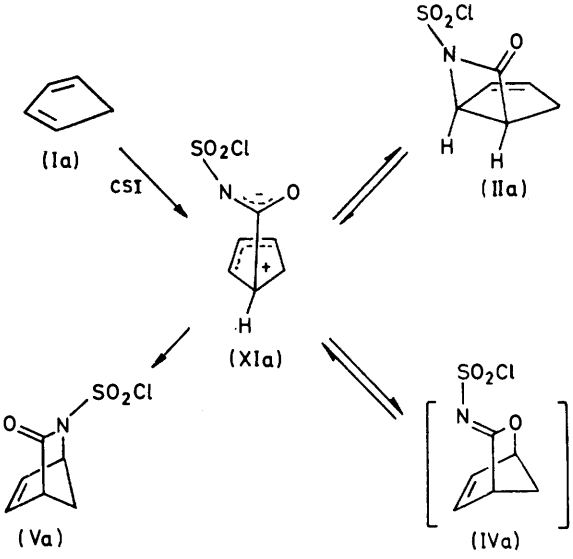
(XII) (XIII)

On this basis, kinetically controlled 1,2-addition to (Ib) *via* (XIb) gives the *N*-chlorosulphonyl β-lactam (IIb) (Scheme 2). Under suitable conditions, heterolytic cleavage of (IIb) re-forms (XIb), which may, more slowly, achieve 1,4-ring closure through oxygen yielding the thermodynamically more stable imino-lactone (IVb). Higher temperatures (or much more polar conditions) allow reopening of (IVb) to the dipole (XIb) and ultimate scaling of the still higher energy barrier to the formation of the thermodynamically most stable product, the *N*-chlorosulphonyl δ-lactam (Vb) *via* 1,4-ring closure through nitrogen in the ambident anion. This process is summarised in a schematic way in the Figure. The consistently greater stability of *N*-chlorosulphonyl lactams compared with *N*-chlorosulphonyl imino-lactones of similar ring size is presumed to be due largely to bond energy differences.

The various rearrangement pathways were not so sharply delineated in the case of the cyclopentadiene series (Scheme 3). The primary product of kinetic control, the *N*-chlorosulphonyl β-lactam (IIa), undergoes heterolysis to the dipolar intermediate (XIa) more easily than (IIb), as might be expected on the basis of (i) the excellent overlap between the π-orbitals and the developing positive charge and (ii) the greater strain of the bicyclo-[3.2.0] system (IIa) than of the bicyclo[4.2.0] system



(IIb). However, the expected imino-lactone (IVa) was not detected, the *N*-chlorosulphonyl lactam (Va) being formed directly. Clearly the highest energy barrier in the conversion of (IIa) into (Va) is now much lower than in the cyclohexadiene series, as indicated by the formation of (Va) at ambient temperature *versus* the slow formation of (Vb) at reflux in chloroform. Perhaps (IVa) is so unstable with respect to the now more accessible product of thermodynamic control (Va) that it is present in too low a stationary concentration to be detected, even by i.r. spectroscopy. Such instability in a strained bicyclic γ-imino-lactone would not be unreasonable; β-imino-lactones have never been detected in CSI–olefin reactions in competition with β-lactam formation. Alternatively, the expected smaller energy difference (in comparison with the cyclohexa-1,3-diene system) between the dipolar intermediate (XIa) and the products of 1,4-addition [(IVa) and (Va)] due to the more efficient stabilisation of the cationic centre and the greater strain in the bicyclo[2.2.1] system may lead to sufficient ' product character ' in the transition state to enable the rearrangement to the



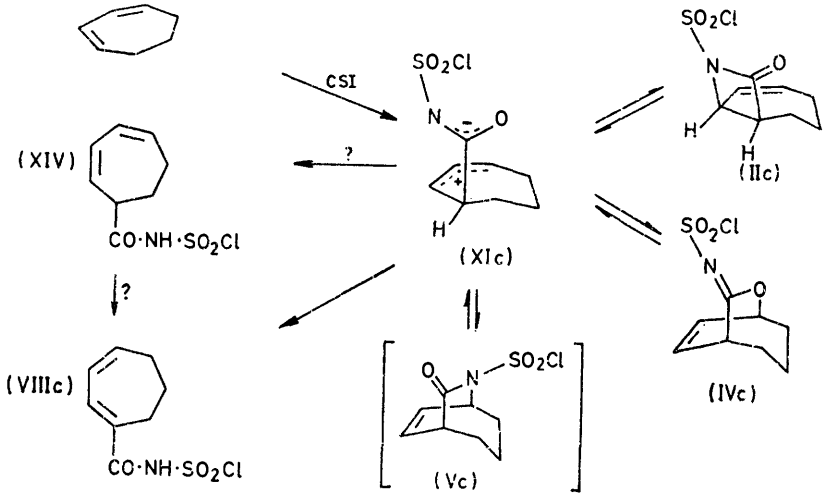
SCHEME 3

lactam (Va) to be both the kinetically and the thermodynamically favoured process.

The energy differences in the cycloheptadiene series (Scheme 4) are significantly greater. The slower reopening of the first-formed *N*-chlorosulphonyl β-lactam (IIc) and the stability of the resulting imino-lactone (IVc) continue the trends anticipated as the methylene chain length increases. There is now less strain in (IIc) and (IVc) relative to the lower homologues and the poorer overlap between the π-system and developing carbocation in moving back from either intermediate to the dipole (XIc) must raise the energy barrier for the process. Indeed the vigour of the conditions necessary to return (IVc) to (XIc) apparently allows the intrusion of a proton transfer process leading to the formal substitution product (VIIIc), and the expected lactam (Vc) is not detected. It is not clear whether (VIIIc) is formed directly *via* transfer of an α-proton (authentic cases of direct α-proton transfer in CSI reactions are not particularly common) [6] or through the intermediacy of the less highly conjugated system (XIV) *via* δ-proton transfer,

in which case rapid isomerisation of (XIV) to the more stable product (VIIIc) would be expected under the reaction conditions.

A decreasing tendency to form 1,4-addition products at the expense of substitution as ring size increases has been observed in other cases, for example in the boron



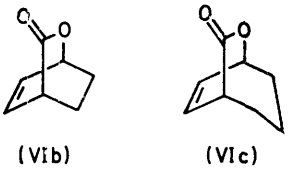
SCHEME 4

trifluoride-catalysed addition of diethyl methylenedicarbamate to cyclic 1,3-dienes.[18]

Extension of the arguments presented above concerning the relative ease of opening of *N*-chlorosulphonyl β-lactams leads to the expectation that the energy barrier to opening of the β-lactam (IId) derived from cyclooctadiene will be higher than any of the cases discussed so far. In fact (IId) was too stable to allow the isolation of any 1,4-addition products. Only polymeric material was produced under the conditions required for ring cleavage.

The major synthetic utility of the CSI–diene reactions described above stems from the degree of control which may be exerted over the addition of either the C=O or C=N moiety across the termini of the diene unit. The conversion of the adducts into more useful oxa- and aza-bicyclic molecules is clearly possible on the basis of simple and well established chemistry. Some examples are now described briefly.

There is evident recent interest in the preparation of β,γ-unsaturated δ-lactones, which have been presented [19] as *formal* products of 1,4-addition of carbon dioxide (itself a poor dienophile) to 1,3-dienes. The novel bicyclic lactones (VIb) and (VIc) [the formal products of addition of CO_2 to the cyclic dienes (Ib) and (Ic)] are easily obtained in good yield *via* acidic hydrolysis of the corresponding *N*-chlorosulphonyl imino-lactones (IVb) and (IVc). CSI is thus an effective 'carbon dioxide equivalent' for the Diels–Alder reaction. The CSI–hydrolysis route should provide a convenient alternative to the diethyl oxomalonate–hydrolysis–bis-Curtius degradation procedure of Ruden [19] in many cases. At first sight, ready thermal loss of CO_2 from the lactones (VI) might be expected *via* a retro-[$_{\pi}4 + _{\pi}2$] cycloaddition. However, even the more highly strained lactone (VIb) is stable up to *ca.* 115 °C, and (VIc) is stable up to 180 °C. The loss of CO_2 at higher temperatures correlates with many studies of CO_2 ejection in retro-Diels–Alder reactions.[20]



A range of simple unsubstituted azabicyclic systems is readily available through the CSI addition reactions. Some examples based on cyclopentadiene and cyclohexadiene are shown in Scheme 5, the conversions being self-explanatory. 2-Azabicyclo[2.2.2]-octene (XV) and -octane systems may be conveniently prepared in this way in yields which compare well with those in the well established route of Cava *et al.* from cyclohexadiene.[21] Alternative routes to the key lactam (VIIIa) in the 2-azabicyclo[2.2.1]heptene series have been described already,[10] though the amine (XVI) has not been reported previously.

The 2-azanorbornadiene system was unknown until the recent preparation of the 3-tosyl derivative.[10] Treatment of (VIIa) with trialkyloxonium salts provides a simple, efficient preparation of further derivatives such as (XVIII), showing a characteristic imine stretching band at 1 620 cm^{-1} in the i.r. spectrum and an n.m.r.

[18] G. R. Krow, R. Rodenbaugh, M. Grippi, G. DeVicaris, C. Hyndman, and J. Marakowski, *J. Org. Chem.*, 1973, **38**, 3094.

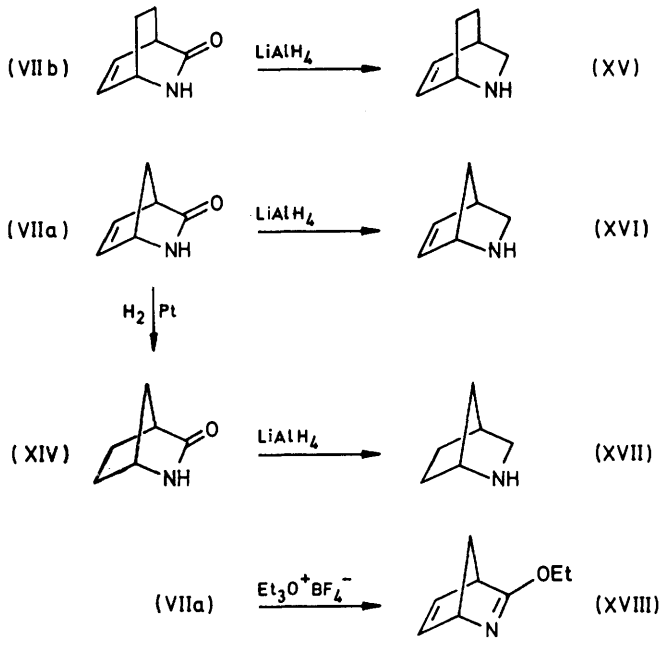
[19] R. A. Ruden and R. Bonjouklian, *J. Amer. Chem. Soc.*, 1975, **97**, 6892.

[20] *E.g.* H. Kwart and K. King, *Chem. Rev.*, 1968, **68**, 415; M. J. Goldstein and G. L. Thayer, *J. Amer. Chem. Soc.*, 1965, **87**, 1925, 1933.

[21] M. P. Cava, C. K. Wilkins, jun., D. R. Dalton, and K. Bessho, *J. Org. Chem.*, 1965, **30**, 3772.

spectrum which (apart from the ethyl signals) closely resembles that of the parent lactam.

In conclusion, the reactions of cyclic 1,3-dienes with CSI are similar to those of acyclic 1,3-dienes in general terms, in that initial Markownikov addition leading to *N*-chlorosulphonyl β-lactams is followed by ring opening to a dipolar intermediate and subsequent rearrangement



SCHEME 5

to products of 1,4-addition through oxygen or nitrogen and/or substitution products. The difference is seen in the manner of the rearrangement. The apparently irreversible cyclisation and proton transfer processes compete to give mixtures in the acyclic series in contrast to the clean, stepwise rearrangement sequences in the cyclic series. In particular, the sharply defined stepwise reaction pathway starting from cyclohexa-1,3-diene and CSI provides a unique example of initial 1,2-cycloaddition followed by successive kinetically and thermodynamically controlled rearrangements to the 1,4-cycloaddition products where, under appropriate conditions, each of the isomers may be isolated in high yield.

EXPERIMENTAL

I.r. spectra were recorded with a Perkin-Elmer 237 grating spectrometer for solutions in dichloromethane (0.1 mm cells). N.m.r. spectra were recorded with a Varian T60 or DA60 or a JEOL JNM PS100 spectrometer, and spin-decoupling studies were performed with the DA60 or PS100 instrument. Apparent *J* values are quoted throughout. Spectra were obtained for solutions in deuteriochloroform, with tetramethylsilane as internal reference unless stated otherwise. U.v. spectra were measured with a Unicam SP800 spectrometer. Mass spectra were recorded with an A.E.I. MS9 spectrometer at 70 eV; the base peak is indicated as '(b)'. A Pye 104 instrument was used for g.l.c. analysis (1.5 m × 6 mm o.d. glass columns packed with 10% E30 on 100—120 mesh Diatomite C AW DMCS or 3% OV 17 on 100—120 mesh Diatomite C 'Q') and for small-scale preparative work (2.1 m × 9 mm o.d. glass column packed with 20% E30 on 60—70 mesh Diatomite C A AW DMCS). All reaction solvents were dried prior to use. Hydrocarbons were dried over sodium wire; chloroform was freed from ethanol before use by shaking with aqueous calcium chloride solution, dried over calcium chloride, and distilled from fresh anhydrous calcium chloride; dichloromethane was refluxed over, and distilled from, calcium hydride; diethyl ether was refluxed over, and distilled from, lithium aluminium hydride; and acetone, acetonitrile, and nitromethane were dried over molecular sieves (Linde 4A). Product solutions and extracts were dried over magnesium sulphate. Chlorosulphonyl isocyanate (CSI) was distilled from anhydrous potassium carbonate before use and reactions with this reagent were carried out by adding the substrate dropwise *via* a syringe to a stirred solution of CSI (or *vice versa*), under dry nitrogen. In most cases, the reactions were followed by monitoring i.r. spectra; significant features of the spectrum of the reaction mixture are given in parentheses at the appropriate point in the text. N.m.r. studies on reactions, mentioned in the text, were performed by adding CSI (0.3—0.5 mmol) *via* a microsyringe to a solution of an equimolar amount of the substrate in deuteriochloroform (*ca.* 0.5 ml) in an n.m.r. tube and monitoring the n.m.r. spectrum.

Reactions of Chlorosulphonyl Isocyanate with Cyclopentadiene.—Cyclopentadiene (b.p. 41—42°) was freshly prepared by thermolysis of cyclopentadiene dimer for each reaction and stored at −78 °C until required to prevent dimerisation.

(*a*) A solution of cyclopentadiene (Ia) (1.5 g, 22.7 mmol) in dichloromethane (3 ml) was added to a solution of CSI (1.75 ml, 20.5 mmol) in dichloromethane (30 ml) at ambient temperature over 10 min. After a further 15 min the vigorously stirred mixture [$\nu_{max.}$ 1 818 (major) and 2 250 (minor) cm^{-1}] was treated with a solution of anhydrous sodium sulphite (6 g) in water (25 ml). After 30 min the organic layer was separated and the aqueous layer was extracted with dichloromethane (2 × 15 ml). The combined organic layer and extracts were dried and evaporated yielding *6-azabicyclo*[3.2.0]*hept-3-en-7-one* (IIIa) (889 mg, 40%) as a pale yellow oil which on distillation afforded a colourless oil (755 mg, 34%), b.p. 90—95° at 0.2 mmHg; $\nu_{max.}$ 3 410 (NH) and 1 755 cm^{-1} (CO); *m/e* 109 (M^+), 80, 78, 66(b), 65, and 43 (Found: C, 64.3; H, 6.6; N, 12.5.* C_6H_7NO requires C, 66.0; H, 6.5; N, 12.8%).

(*b*) A solution of cyclopentadiene (Ia) (3.0 g, 45.4 mmol) in dichloromethane (5 ml) was added to a solution of CSI (3.53 ml, 41.3 mmol) in dichloromethane (125 ml) at ambient temperature over 30 min, and the mixture ($\nu_{max.}$ 1 818 cm^{-1}) was stirred for 5 h at ambient temperature. The resulting deep red solution [$\nu_{max.}$ 1 790 and 1 775 (major), and 1 818 and 1 695 (minor) cm^{-1}] was treated with a solution of anhydrous sodium sulphite (12 g) in water (50 ml) for 30 min at ambient temperature and worked up in the normal way (above) yielding a yellow oil (2.3 g), which was separated by chromatography on alumina (activity II; 50 g). Elution with methanol–ether yielded the β-lactam (IIIa) (258 mg, 5.5%) as a yellow oil, a 1 : 1 mixture

* Analysis consistently agreed with theory + *ca.* 3.5% water.

of (IIIa) and (VIIa) (115 mg, 2%) as a yellow oil, and 2-azabicyclo[2.2.1]hept-5-en-3-one (VIIa) (1.281 g, 27.5%) * as white crystals, m.p. 54—56° (from acetone–ether) (lit.,[10] 54—55°); $\nu_{max.}$ 3 430 (NH) and 1 715 cm^{-1} (CO); *m/e* 109 (M^+), 78, 66(b), 65, and 43. (Found: C, 66.1; H, 6.6; N, 12.8. Calc. for C_6H_7NO: C, 66.0; H, 6.5; N, 12.8%).

3-Ethoxy-2-azabicyclo[2.2.1]*hepta-2,5-diene* (XVIII).— A solution of the lactam (VIIa) (100 mg, 0.92 mmol) in dichloromethane (1 ml) was added to a stirred solution of triethyloxonium tetrafluoroborate (250 mg, 1.3 mmol) in dichloromethane (5 ml) under dry nitrogen at ambient temperature. After 1 h the mixture was stirred with aqueous 50% potassium carbonate (4 ml) for 15 min. After filtration through Celite to break up the emulsion, the organic layer was separated, dried, and evaporated yielding 3-ethoxy-2-azabicyclo[2.2.1]hepta-2,5-diene (XVIII) (110 mg, 80%), as an oil which rapidly darkened and resinified at ambient temperature; $\nu_{max.}$ (CCl_4) 1 620 (C:N), 1 325, and 1 263 cm^{-1}; δ(CCl_4) 6.86 (1 H, ddd, *J* 5.5, 2.7, and 0.7 Hz), 6.64 (1 H, ddd, *J* 5.5, 3.1, and 1.4 Hz), 4.63 (1 H, m), 4.05 (2 H, m),† 3.32 (1 H, m), 2.21 (1 H, dt, *J* 6.6 and 1.65 Hz), 1.95 (1 H, dt, *J* 6.6 and 1.0 Hz), and 1.27 (3 H, t, *J* 7.0 Hz); *m/e* 137 (M^+) 109, 108, 71, 66(b), and 65.

2-Azabicyclo[2.2.1]*hept-5-ene* (XVI).—A mixture of lithium aluminium hydride (150 mg, 3.95 mmol) and the lactam (VIIa) (200 mg, 1.83 mmol) in ether (15 ml) was refluxed under dry nitrogen for 4 h. Ether saturated with water was then added cautiously to destroy the excess of lithium aluminium hydride, the mixture was filtered, and the filtrate was dried and evaporated yielding *2-azabicyclo*[2.2.1]*hept-5-ene* (XVI) (140 mg, 80%) as an oil, $\nu_{max.}$ (film) 3 380br, 3 060, 2 990, 2 950, 2 880, and 1 335 cm^{-1}; δ(CCl_4) 6.0 (2 H, m), 3.77 (1 H, m), 3.2—2.8 (2 H, m), 2.1 (1 H, s, disappeared on shaking with D_2O), 1.9 (1 H, d, *J* 8 Hz), and 1.25 (2 H, s with fine splitting); *m/e* 95 (M^+), 94, 78, 66(b), and 65.

The amine (XVI) was converted into the hydrochloride salt by bubbling hydrogen chloride into a solution of the amine (114 mg, 1.2 mmol) in ether (5 ml) until no more precipitate was produced. The solution was then evaporated yielding *2-azabicyclo*[2.2.1]*hept-5-ene hydrochloride* (110 mg, 70%) as white hygroscopic crystals, m.p. 90—95° (decomp.) (from ethanol–ether); $\nu_{max.}$ 3 100—2 400br and 1 590 cm^{-1}; δ 9.7br (1 H), 8.7br (1 H), 6.5 (1 H, m), 6.3 (1 H, m), 4.63 (1 H, m), 3.23 (2 H, m), 2.6 (1 H, m), and 1.8 (2 H, m) (Found: C, 53.3; H, 7.7; N, 10.25.‡ $C_6H_{10}ClN$ requires C, 54.75; H, 7.7; N, 10.6%).

Catalytic Hydrogenation of the Lactam (VIIa).—A solution of the lactam (VIIa) (500 mg, 4.6 mmol) in ethyl acetate (15 ml) was hydrogenated at atmospheric pressure for 100 h at ambient temperature over 10% palladium–charcoal (20 mg). The catalyst was filtered off and the solution evaporated yielding 2-azabicyclo[2.2.1]heptan-3-one (XIV) (502 mg, 99%) as a pasty white solid which rapidly deliquesced on exposure to air; $\nu_{max.}$ 3 430 (NH) and 1 700 cm^{-1} (CO); δ 7.2br (1 H), 3.83 (1 H, m), 2.67 (1 H, m), and 2.1—1.2 (6 H, m); *m/e* 111 (M^+), 96, 83, 82, 68, 67(b), 55, and 43.

Reduction of 2-Azabicyclo[2.2.1]*heptan-3-one* (XIV).—The lactam (XIV) (200 mg, 1.8 mmol) was reduced with lithium aluminium hydride (150 mg, 3.95 mmol) in ether (15 ml) as described for the lactam (VIIa). The free amine (XVII) was not isolated but was converted *in situ* into the hydrochloride [as described for the amine (XVI)] yielding *2-azabicyclo*[2.2.1]*heptane hydrochloride* (215 mg, 89%) as white deliquescent crystals, m.p. 206—210° (decomp.) (from ethanol–ether); $\nu_{max.}$ 3 100—2 400br and 1 595 cm^{-1}; δ 9.1br (2 H), 4.07 (1 H, m), 3.07 (2 H, m), 2.88 (1 H, m), and 2.5—1.4 (6 H, m) (Found: C, 53.1; H, 9.1; N, 10.2.§ $C_6H_{12}ClN$ requires C, 53.9; H, 9.1; N, 10.5%).

Reactions of Chlorosulphonyl Isocyanate with Cyclohexa-1,3-diene (1b).—(*a*) A solution of cyclohexa-1,3-diene (1b) (2.0 g, 23.8 mmol) in dichloromethane (10 ml) was added to a solution of CSI (1.73 ml, 20.0 mmol) in dichloromethane (75 ml) at ambient temperature. After 5 min the mixture [$\nu_{max.}$ 1 810 (major) and 2 250 (minor) cm^{-1}] was cooled to −78 °C and acetone (15 ml) and then benzenethiol (4.5 ml, 43 mmol) were added dropwise; pyridine (3.0 ml, 40 mmol) was then added dropwise and the mixture was allowed to warm to 0 °C; water (10 ml) was then added. The mixture was stirred for 30 min at ambient temperature, the organic layer was separated, and the aqueous layer was extracted with dichloromethane (3 × 20 ml). The combined organic layer and extracts were dried and evaporated yielding a mixture of the β-lactam (IIIb) and diphenyl disulphide as a pale yellow solid which was separated by chromatography on alumina (activity I; 70 g). The diphenyl disulphide was removed by elution with light petroleum and ether. Elution with methanol–ether afforded *7-azabicyclo*[4.2.0]*-oct-4-en-8-one* (IIIb) (1.651 g, 67.5%) as off-white crystals, m.p. 70.5—71.5° (from acetone–ether); $\nu_{max.}$ 3 410 (NH) and 1 755 cm^{-1} (CO); δ 6.92br (1 H), 6.16 (1 H, dd, *J* 10 and 4 Hz), 5.90 (1 H, dd, *J* 10 and 4 Hz), 3.99 (1 H, ddm, *J* 5 and 4 Hz), 3.46 (1 H, m), and 2.3—1.42 (4 H, m) (each signal was broadened by further, poorly resolved, coupling); *m/e* 123 (M^+), 80(b), 79, 78, 77, and 43 (Found: C, 68.3; H, 7.35; N, 11.1. C_7H_9NO requires C, 68.3; H, 7.4; N, 11.4%).

(*b*) A solution of cyclohexa-1,3-diene (Ib) (2.0 g, 23.8 mmol) in dichloromethane (10 ml) was added to a solution of CSI (1.75 ml, 20.5 mmol) in dichloromethane (50 ml) at ambient temperature over 10 min. After 30 h at ambient temperature the mixture ($\nu_{max.}$ 1 588 cm^{-1}) was evaporated yielding crude *3-chlorosulphonylimino-2-oxabicyclo*[2.2.2]*-oct-5-ene* (IVb) (4.7 g) as pale yellow crystals containing some residual dichloromethane. Recrystallisation from acetone afforded pure (IVb) (3.12 g, 69%) as white crystals, m.p. 76.5—78°; $\nu_{max.}$ 1 619 and 1 588 cm^{-1} (C=N); δ 6.61 (2 H, m), 5.74 (1 H, m,), 3.90 (1 H, m), and 2.3—1.42 (4 H, m); *m/e* 223/221 (M^+), 195, 193, 186, 158, 143, 141, 122, 107, 106, 105, 101, 99, 80(b), 79, 78, 77, and 74 (Found: C, 38.2; H, 3.5; N, 6.5 $C_7H_8ClNO_3S$ requires C, 37.9; H, 3.6; N, 6.3%).

(*c*) A solution of cyclohexa-1,3-diene (Ib) (3.0 g, 37.5 mmol) in chloroform (5 ml) was added to a solution of CSI (3.05 ml, 35.7 mmol) in chloroform (50 ml) at ambient

* This yield represents a maximum in our hands. In a number of reactions (each followed at regular intervals by i.r. spectroscopy) the optimum point for work-up was found to vary by ±2 h. The highest yield of (VIIa) was obtained by immediate treatment with sulphite solution as soon as the carbonyl absorption due to (Va) reached maximum intensity, even though some absorption at 1 818 cm^{-1} remained. Clearly, interception at too early a stage gave lower yields of (VIIa) together with excessive amounts of (IIIa) but on the other hand, whilst late work-up produced little or no (IIIa), polymerisation reduced the yield of (VIIa). Alternative procedures for removal of the *N*-chlorosulphonyl group (*e.g.* benzenethiol–pyridine at −78 °C) did not convert (Va) into (VIIa) any more efficiently.

† The methylene protons of the ethyl group are diastereotopic.
‡ Analysis consistently agreed with theory + *ca.* 3% water.
§ Analysis consistently agreed with theory + *ca.* 1% water.

temperature over 10 min. After 3.5 h the mixture was refluxed for 17 h.* The resulting red solution ($\nu_{max.}$ 1 750 cm^{-1}) was filtered to remove a small amount of polymeric material (360 mg) and the filtrate was evaporated yielding crude *N*-chlorosulphonyl-2-azabicyclo[2.2.2]oct-5-en-3-one (Vb) as a viscous red oil (6.97 g, 90%); $\nu_{max.}$ 1 753 cm^{-1} (CO); δ 6.7 (2 H, m), 5.43 (1 H, m), 3.7 (1 H, m), and 2.7—1.5 (4 H, m); *m/e* 223/221 (M^+), 186, 158, 143, 141, 122, 106, 80(b), 79, 78, 77, and 64. The product could not be induced to crystallize and was converted into the stable lactam (VIIb).

2-Oxabicyclo[2.2.2]*oct-5-en-3-one* (VIb).—The crude imino-lactone (IVb) (1.1 g, 5.0 mmol) was added to a mixture of acetone (12 ml) and water (8 ml), concentrated hydrochloric acid (6 drops) was added, and the solution was stirred for 30 min at ambient temperature. The solution was then extracted with dichloromethane (4 × 15 ml) and the extracts were combined, dried, and evaporated. The oily product was extracted with light petroleum (b.p. 40—60 °C) (4 × 10 ml) and the extracts were evaporated, leaving *2-oxabicyclo*[2.2.2]*oct-5-en-3-one* (VIb) (0.329 g, 53%) as a clear liquid, $\nu_{max.}$ 1 757 and 1 742 (CO), 1 616 (C=C), 1 365, 1 206, 1 140, 1 047, 1 017, 960, 950, and 817 cm^{-1}; δ 6.47 (2 H,m), 5.13 (1 H, m), 3.36 (1 H, m), and 2.4—1.1 (4 H, m);† *m/e* 124 (M^+), 96.80(b), 79, 78, 77, 68, and 44. A sample for analysis was obtained by distillation on to the cold finger of a small-scale sublimation apparatus at 80 °C and 15 mmHg (Found: C, 67.4; H, 6.5. $C_7H_8O_2$ requires C, 67.7; H, 6.5%).

2-Azabicyclo[2.2.2]*oct-5-en-3-one* (VIIb).—A solution of the crude *N*-chlorosulphonyl lactam (Vb) (1.9 g, 8.6 mmol) in acetone (5 ml), and 2M-sodium hydroxide were added simultaneously drop by drop to a stirred 1 : 1 mixture of acetone and water (20 ml) saturated with sodium chloride; the rates of addition were controlled so as to maintain the reaction mixture at pH 6—7. The mixture was extracted with dichloromethane (4 × 25 ml), and the extract was dried and evaporated, yielding crude *2-azabicyclo*[2.2.2]*oct-5-en-3-one* (VIIb) (0.87 g, 80%) as yellow oily crystals. Chromatography on alumina (activity I; 30 g) (elution ether and ether–methanol) afforded pure (VIIb) (381 mg, 35%) as white crystals, m.p. 124.5—125° (after sublimation at 100 °C and 20 mmHg); $\nu_{max.}$ 3 430 (NH), 1 690 (CO), and 1 613 cm^{-1} (C=C); δ 7.8br (1 H), 6.35 (2 H, m), 4.26 (1 H, m), 3.33 (1 H, m), and 2.13—1.2 (4 H, m); *m/e* 123 (M^+), 95, 80(b), 79, 67, and 43 (Found: C, 68.3; H, 7.3; N, 11.2. C_7H_9NO requires C, 68.3; H, 7.4; N, 11.4%).

Reduction of the Lactam (VIIb).—The lactam (VIIb) (400 mg, 3.25 mmol) was reduced with lithium aluminium hydride (200 mg, 5.25 mmol) in ether (25 ml) as described for the lactam (VIIa) yielding crude 2-azabicyclo[2.2.2]oct-5-ene (XV) (268 mg, 70%) as an oil, $\nu_{max.}$ (film) 3 270 (NH), 3 040, 2 940, 2 860, 1 170, and 1 060 cm^{-1}; δ ($CFCl_3$) 6.23 (2 H, m), 3.33 (1 H, m), 2.87 (1 H, d, *J* 8 Hz), 2.63—2.2 (2 H, m), and 2.0—1.0 (5 H, m; on shaking with D_2O became 4 H, m); *m/e* 109 (M^+), 95, 94, 80(b), 79, 78, 77, 64, and 57. The amine (XV) (170 mg, 1.56 mmol) was converted into the hydrochloride as described for the amine (XVI), yielding *2-azabicyclo*[2.2.2]*oct-5-ene hydrochloride* (185 mg, 82%) as white crystals, m.p. 235—238° (decomp.) (from ethanol–ether); $\nu_{max.}$ 3 080—2 400br and 1 590 cm^{-1}; δ 9.8br (2 H), 6.4 (2 H, m), 4.23 (1 H, m), 3.4—2.2 (4 H, m), and 2.0—1.2 (3 H, m) (Found: C, 57.3; H, 8.3; N, 9.6. $C_7H_{12}ClN$ requires C, 57.7; H, 8.3; N, 9.6%).

Reactions of Chlorosulphonyl Isocyanate with Cyclohepta-1,3-diene (Ic).—(*a*) CSI (0.43 ml, 5.0 mmol) was added to a solution of the diene (Ic) (0.5 g, 5.3 mmol) in dichloromethane (15 ml) at ambient temperature. After 1 h the mixture [$\nu_{max.}$ 1 820 (major) and 2 250 (minor) cm^{-1}] was treated with a solution of anhydrous sodium sulphite (2 g) in water (10 ml) for 30 min and worked up in the usual manner yielding *8-azabicyclo*[5.2.0]*non-5-en-9-one* (IIIc) (260 mg, 38%) as white crystals, m.p. 71—74° (from dichloromethane–ether); $\nu_{max.}$ 3 405 (NH) and 1 753 cm^{-1} (CO); δ 6.8br (1 H), 5.53 (2 H, s), 4.4 (1 H, d, *J* 5 Hz), 3.2 (1 H, m), and 2.5—1.2 (6 H, m); *m/e* 137 (M^+), 122, 94(b), 93, 91, 80, 79, 78, 77, 67, 66, 65, and 43 (Found: C, 69.8; H, 8.1; N, 10.3. $C_8H_{11}NO$ requires C, 70.0; H, 8.1; N, 10.2%).

(*b*) CSI (0.43 ml, 5.0 mmol) was added to a solution of the diene (Ic) (0.5 g, 5.3 mmol) in dichloromethane (15 ml) at ambient temperature, and the mixture was warmed to 30 °C. After 25 h the mixture ($\nu_{max.}$ 1 580 cm^{-1}) was evaporated yielding crude *7-chlorosulphonylimino-6-oxabicyclo*[3.2.2]*non-8-ene* (IVc) (1.2 g, 100%) as pink crystals. Recrystallisation from dichloromethane–ether afforded white crystals, m.p. 87—89°; $\nu_{max.}$ 1 580 (C=N), 1 407, 1 365, and 840 cm^{-1}; δ 6.37 (2 H, m), 5.43 (1 H, m), 3.45 (1 H, m), and 1.8 (6 H, m); *m/e* 237/235 (M^+), 200, 136, 119, 94, 93, 91, 81, 79, 78, 77, and 64 (Found: C, 40.8; H, 4.2; N, 5.9. $C_8H_{10}ClNO_3S$ requires C, 40.8; H, 4.3; N, 5.9%).

6-Oxabicyclo[3.2.2]*non-8-en-7-one* (VIc).—The crude imino-lactone (IVc) (0.206 g, 0.87 mmol) was stirred in a mixture of acetone (5 ml) and water (5 ml), and concentrated hydrochloric acid (6 drops) was added. The solution was stirred for 30 min at ambient temperature then extracted with dichloromethane (3 × 5 ml). The combined extracts were dried, filtered, and evaporated to give the crude lactone (VIc) (0.114 g, 94%). The oily product was extracted with light petroleum (b.p. 40—60 °C) several times. The combined extracts were evaporated to leave a waxy solid (93 mg, 77%). Recrystallisation from light petroleum (b.p. 60—80 °C) and sublimation (90 °C and 15 mmHg) gave *6-oxabicyclo*[3.2.2]*non-8-en-7-one* (VIc), m.p. 94—97°; $\nu_{max.}$ 1 742 (CO), 1 635 (C=C), 1 383, 1 222, 1 184, 1 163, 1 125, 1 067, 1 028, 1 014, and 988 cm^{-1}; δ 6.23 (2 H, m), 4.84 (1 H, m), 3.11 (1 H, m), and 1.72br (6 H, s); † *m/e* 138 (M^+), 111, 110, 109, 94, 81, 79(b), 77, and 66 (Found: C, 69.8; H, 7.3. $C_8H_{10}O_2$ requires C, 69.5; H, 7.3%).

Rearrangement of 7-Chlorosulphonylimino-6-oxabicyclo[3.2.2]*non-8-ene* (IVc).—CSI (0.43 ml, 5.0 mmol) was added to a solution of the diene (Ic) (0.5 g, 5.3 mmol) in nitromethane (15 ml) at ambient temperature. The mixture ($\nu_{max.}$ 1 820 cm^{-1}) was stirred at ambient temperature for 24 h and then evaporated, yielding crude (IVc) (1.2 g, 100%) as pale yellow crystals. The product was dissolved in nitromethane (20 ml) and heated to 80 °C for 5 days. The resulting solution [$\nu_{max.}$ 2 210 (major), 1 720 (major),

* The rearrangement of the *N*-chlorosulphonyl imino-lactone (IVb) could be achieved more quickly and at lower temperatures by the use of more polar solvents. However, whilst reaction was complete within 4 h at 40 °C in nitromethane, the yield of (Vb) was only 55% (n.m.r.). In acetonitrile under the same conditions, the yield of (Vb) was under 20% (n.m.r.) and a peak in the i.r. spectrum at 1 720 cm^{-1} suggested the formation of *N*-chlorosulphonyl amides by proton transfer.

† Spin decoupling studies did not allow complete analysis of the n.m.r. spectrum but confirmed coupling between each methine proton and the olefinic and methylene protons on either side; this, together with the lack of significant coupling between the two methine protons or between olefinic and methylene protons, confirmed the assigned oxabicyclic structure.

and 1 580 (minor) cm^{-1}] was treated with a solution of anhydrous sodium sulphite (2 g) in water (10 ml) for 30 min, and worked up in the usual way yielding an orange oil (300 mg), which was separated by chromatography on silica (10 g). Elution with ether yielded *cyclohepta*-1,3-*diene carbonitrile* (Xc) (195 mg, 33%) as a pale yellow oil. Preparative g.l.c. (160°) afforded a colourless oil, which rapidly turned yellow on exposure to light at ambient temperature, $\nu_{max.}$ (film) 3 020, 2 930, 2 210 (CN), and 1 600 cm^{-1} (C=C); δ 6.4 (1 H, d, J 7 Hz), 6.1 (1 H, dt, J 12 and 4 Hz), 5.7 (1 H, dd, J 7 and 12 Hz), 2.43 (4 H, m), and 1.9 (2 H, m); $\lambda_{max.}$ (EtOH) 272.5 nm (ε 11 900); *m/e* 119 (M^+), 118, 117, 116, 104, 103, 93, 92, 91(b), 77, 67, 61, and 39 (Found: C, 78.0; H, 7.3; N, 11.45. C_8H_9N requires C, 80.6; H, 7.6; N, 11.75%). Elution with 5% methanol–ether afforded a small fraction (45 mg) which was purified by preparative t.l.c. (alumina; 5% methanol–ether) yielding *cyclohepta*-1,3-*dienecarboxamide* (IXc) (22 mg, 3%) as oily crystals, m.p. 70—75° (after sublimation at 100 °C and 0.5 mmHg); $\nu_{max.}$ 3 505 and 3 405 (NH_2), 1 665, 1 630, and 1 355 cm^{-1}; δ 6.61 (1 H, d, J 7 Hz), 6.5—5.7 (4 H, m), 2.5 (4 H, m), and 1.87 (2 H, quint, J 5.5 Hz); $\lambda_{max.}$ (EtOH) 274 nm (ε 8 600); *m/e* 137 (M^+, b), 136, 135, 122, 121, 119, 109, 93, 92, 91, 79, 78, 77, 74, and 59.

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