Reaction of Chlorosulphonyl Isocyanate with Cyclic Dienes. Evidence for a True Dipole in 2+2 Addition

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Summary The first reactions of chlorosulphonyl isocyanate with cyclohexadienes involve primary addition to yield *N*-chlorosulphonyl β-lactams followed by secondary and tertiary dipolar rearrangements; evidence for the intermediacy of a true dipole in β-lactam formation is presented.

The reactions of acyclic dienes with chlorosulphonyl isocyanate (CSI) have recently been the subject of considerable study[1,2] and have been viewed[1] as ${}_{\pi}2_s + {}_{\pi}2_a$ cycloadditions yielding *N*-chlorosulphonyl β-lactams which may open to dipolar intermediates thereby providing access to 1,4-addition products. However, the only apparent example of addition to a cyclic diene is provided by the formation of a stable *N*-chlorosulphonyl β-lactam from cyclo-octa-1,3-diene.[3]

On reaction of CSI with cyclohexa-1,3-diene in CH_2Cl_2 at room temperature, the isocyanate i.r. band was completely replaced within 5 min by a peak at 1809 cm^{-1}. Cooling of the reaction mixture and treatment with benzenethiol–pyridine at low temperature followed by work-up and chromatography on neutral alumina gave β-lactam (**2b**)† (70%), m.p. 70·5—71·5°, ν_{max} (CH_2Cl_2) 3410 and 1755 cm^{-1}.

When a similar mixture was left at 25° for 30 h, the 1809 cm^{-1} peak was completely replaced by absorption at 1588 cm^{-1}. Evaporation gave a quantitative yield of (**3**),† m.p. 83—84° (decomp.).

Alternatively, if the reaction was performed in $CHCl_3$ and the mixture heated under reflux, (**2a**) and (**3**) underwent consecutive heterolytic cleavage and after 17 h the only CO absorption was at 1750 cm^{-1}. After filtration and evaporation, crude (**4a**) (91%) remained which was converted by hydrolysis at pH 7 into lactam (**4b**),† m.p. 124·5—125°, ν_{max} (CH_2Cl_2) 3430 and 1690 cm^{-1} (33% after chromatography and sublimation).

When cyclo-octa-1,3,5-triene was heated to reflux with CSI in CCl_4, the products were (**8a**) and (**10a**) implicating bicyclo[4,2,0]octa-2,4-diene, and so samples containing up to 60% of bicyclo-octadiene and 40% of cyclo-octatriene were prepared.[4]

Reaction of bicyclo-octadiene with CSI in CCl_4 at room temperature, was monitored by i.r. spectroscopy and gave, within 1 h, (**6a**) ν_{max} (CCl_4) 1815 cm^{-1} [isolated in 41% yield as (**6b**),†‡ m.p. 118—119·5°, ν_{max} (CH_2Cl_2) 3410 and 1756 cm^{-1}, after low-temperature work-up with benzenethiol–pyridine], and (**7**),† ν_{max} (CCl_4) 1595 cm^{-1}, isolated pure (37%) by cooling the reaction mixture at −20°C overnight.

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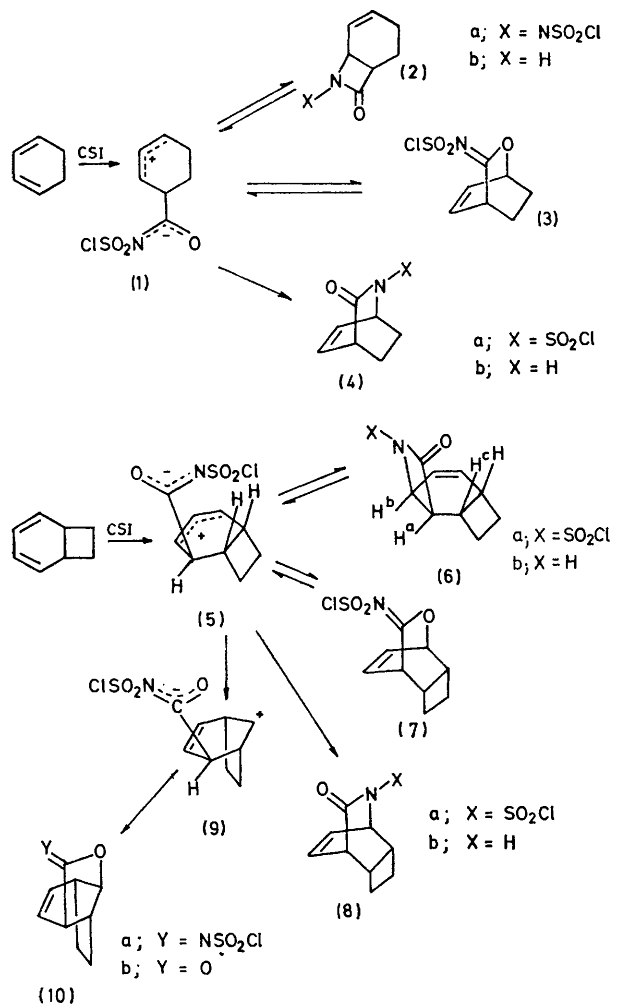
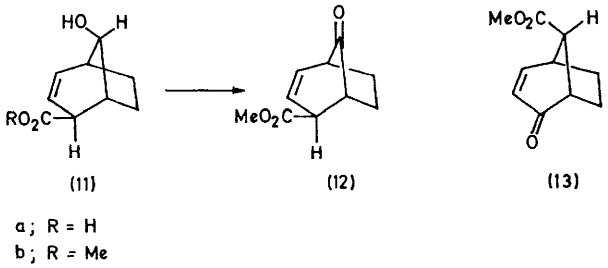
† Proposed structures are fully substantiated by n.m.r. spectroscopy including double-resonance studies, mass spectra, and elemental analysis where stability allowed.

‡ The stereochemistry was confirmed by observation of the signal from H^a as a doublet at δ 3·19 p.p.m. ($J_{a,b}$ 5 Hz); $J_{a,c}$ is zero since the dihedral angle is close to 90°.





If the reaction mixture was left at room temperature, absorption slowly appeared at 1612 and 1750 cm^{-1} corresponding respectively to (**10a**) and (**8a**) which were the only products after 5 days. Fractional crystallisation yielded 25% of (**10a**),† m.p. 133—135°, ν_{max} (CH_2Cl_2) 1612 cm^{-1}. The mother liquors contained (**8a**) which was hydrolysed at pH 7 to yield, after recrystallisation from acetone, 30% of (**8b**),† m.p. 172—173°, ν_{max} (CH_2Cl_2) 3440 and 1680 cm^{-1}.

The structure of the unusual imino-lactone (**10a**) was confirmed by acid hydrolysis to lactone (**10b**), ν_{max} (film) 1780 cm^{-1} (50%). The aqueous remains from the hydrolysis provided the hydroxy-acid (**11a**) which was converted with diazomethane into the ester (**11b**). Sarett oxidation gave keto-ester (**12**),† ν_{max} (CCl_4) 1763 and 1739 cm^{-1} (75%). The observation of a strained 5-ring carbonyl group [as opposed to an αβ-unsaturated carbonyl group in (**13**)] confirmed the mode of attachment of the lactone fragment.

That *N*-chlorosulphonyl β-lactam (**6a**) is accessible *via* the dipolar (**5**) was shown by i.r. spectroscopy of a solution of the unstable imino-lactone (**7**) in CH_2Cl_2. Within 1 h the apppearance of a peak at 1813 cm^{-1} demonstrated the production of a small amount of (**6a**) whose concentration remained constant until (**7**) had been completely converted into (**8a**) and (**10a**) when it fell to zero. The resultant ratio of (**8a**) to (**10a**) was 45:55 (n.m.r. spectroscopy). In nitromethane, the conversion occurred more rapidly and the proportion of (**10a**) increased to 63%.

The reaction of CSI with cyclohexa-1,3-diene thus provides a unique example of 1,2-addition followed by formation of the product of 1,4-cyclisation through oxygen and finally, 1,4-cyclisation through nitrogen where, under appropriate conditions, each isomer may be isolated in high yield. Bicyclo[4,2,0]octa-2,4-diene exhibits parallel behaviour with the incursion of an additional final product (**10a**) derived from a 1,2-shift (**5**) → (**9**) followed by cyclisation through oxygen.

We cannot eliminate the possibility of a concerted or near concerted cycloaddition[1,5] as a first step but, in the light of the present results, 1,4-dipoles such as (**1**) and (**5**) still merit consideration as primary intermediates giving 1,2-addition products under kinetic control and 1,4-adducts under thermodynamic control.

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[1] E. J. Moriconi and W. C. Meyer, *J. Org. Chem.*, 1971, **36**, 2841 and references cited therein.

[2] R. J. P. Barends, W. N. Speckamp and H. O. Huisman, *Tetrahedron Letters*, 1970, 5301.

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

[4] A. C. Cope and F. A. Hochstein, *J. Amer. Chem. Soc.*, 1950, **72**, 2515. The triene took no part in the reaction provided a non-polar solvent was used (*e.g.* CCl_4); indeed isolation of the pure triene may be conveniently achieved after removal of the bicyclic form from the tautomeric mixture with CSI.

[5] The addition of CSI to diphenylmethylenecyclopropane has recently been viewed as concerted; T. J. Barton and R. J. Rogido, *Tetrahedron Letters*, 1972, 3901, as has the addition to 2-cyclopropylpropene; T. J. Barton and R. J. Rogido, *J.C.S. Chem. Comm.*, 1972, 878. Our own unpublished results from a series of 1-substituted-1-cyclopropylethylenes show a considerable dependence of the rate of β-lactam formation on the ability of the 1-substituent to stabilise a positive charge at C-1.