Control Over Cyclisation Pathways in the Reaction of Chlorosulphonyl Isocyanate with Olefins

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Summary A β-lactam derivative has been intercepted in the reaction of CSI with camphene at −60° and at higher temperatures the products are shown to be derived *via* heterolysis, rearrangement and cyclisation through nitrogen or oxygen in the ambident anion with no proton transfer; the behaviour of α-fenchene under identical conditions is compared and contrasted and solvent control over secondary cyclisations is described.

The reaction of chlorosulphonyl isocyanate (CSI) with simple olefins to produce (2+2) cycloaddition products (*N*-chlorosulphonyl β-lactams) and unsaturated amides (by proton transfer) is generally considered to proceed *via* dipolar intermediates.[1,2] In the reaction with camphene[3] lactam (**5a**) was formed *via* Wagner–Meerwein rearrangement, the first of a number of demonstrations of the ability of the uniparticulate electrophile[4] CSI to generate and trap carbonium ions in systems where cationic rearrangement or competitive cyclisation[5] is possible. A second product was thought to arise by transfer of an α-carbonyl proton and was assigned structure (**7a**).[3]

In the present work, addition of CSI to camphene in $CDCl_3$ or CH_2Cl_2 at −60° provided an essentially quantitative yield of (**3a**) [as shown by n.m.r. and i.r. spectra, ν_{max} (CH_2Cl_2) 1818 cm^{-1}] whose transformation to secondary products was so rapid above 0° that it was not observed under the conditions employed by Graf.[6] For structural proof, the reaction mixture was cooled from −60° to −78 °C and diluted very slowly with cold acetone; benzenethiol (2 equiv.) followed by pyridine (1·5 equiv.) in acetone was then added. After stirring as the temperature rose to 0°, addition of water, and extraction, the sole product (75% yield after chromatography on florisil) was (**3b**),‡ m.p. 201—202°, ν_{max} (CH_2Cl_2) 3408 and 1760 cm^{-1}, which formed a dihydrouracil derivative,[1]‡ m.p. 177—180°. A number of thermally labile *N*-chlorosulphonyl β-lactams have been

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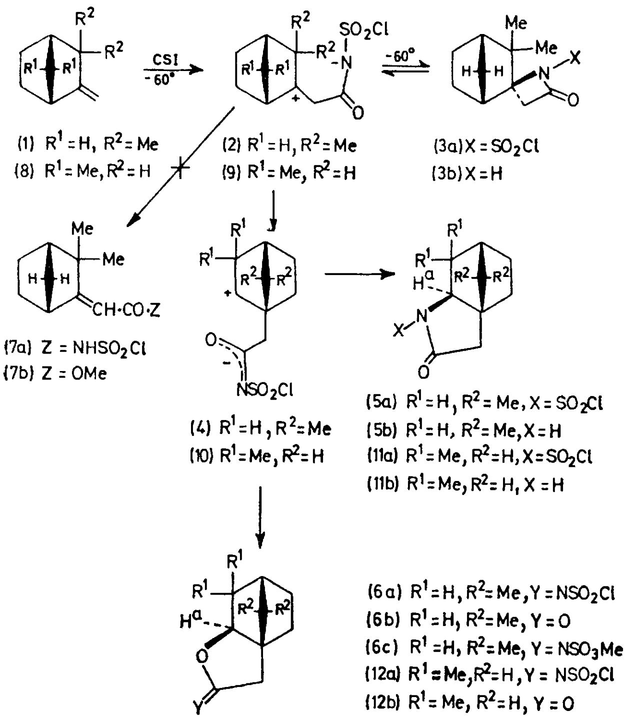
‡ Satisfactory spectroscopic and analytical data were obtained.

intercepted similarly[7a] even in cases where only a small stationary concentration is involved.[7b]



Thermal rearrangement of (**3a**) was conveniently followed by low-temperature n.m.r. spectroscopy and led to the two secondary products described by Graf.[3] The more soluble component, m.p. 122—123°, ν_{max} ($CHCl_3$) 1768 cm^{-1} was (**5a**)‡ but the structure of the less soluble component, m.p. 133—134°, ν_{max} ($CHCl_3$) 1606 cm^{-1} is reassigned as (**6a**) on the basis of its i.r. spectrum ($>C=N{\cdot}SO_2Cl$) and the signal due to H^a in the n.m.r. spectrum: δ 4·75 (dd, J 4 and 8 Hz due to unequal coupling to the protons R^1) together with its ready acid hydrolysis to lactone (**6b**),‡ ν_{max} ($CHCl_3$) 1774 cm^{-1} and conversion into (**6c**), ν_{max} (Nujol) 1668 cm^{-1} on treatment with MeOH and Et_3N. Reaction of (**6a**) with MeOH alone does yield the ester (**7b**)[3,8] but this provides little support for structure (**7a**) in view of the ease of rearrangement of these systems.

In the logical extension to α-fenchene (**8**), CSI was rapidly consumed at −60° but attempts to observe or isolate a β-lactam intermediate failed. The 7-methyl group in (**9**) evidently inhibits the approach of the bulky *N*-chlorosulphonyl group and prevents *exo*-2+2 addition. Wagner–Meerwein rearrangement takes over completely yielding (**11a**)‡ ν_{max} (CH_2Cl_2) 1772 cm^{-1} and (**12a**), ν_{max} (CH_2Cl_2) 1608 cm^{-1}, even at −60° (n.m.r.). Compound (**11a**) was purified by fractional crystallisation, m.p. 131—132°, but imino-lactone (**12a**) resisted purification and was characterised as the lactone (**12b**),‡ ν_{max} (liquid) 1779 cm^{-1}. The signal for H^a in (**11**) and (**12**) now appears as a doublet, J 1—1·5 Hz (the result of coupling to the *anti*-7 proton) confirming the adjacent position of the two methyl groups.

The observation of ready rearrangement in the α-fenchene reaction clearly implicates a dipolar intermediate (**9**). Since camphene reacts with CSI at the same low temperature, the formation of (**3a**) may be seen as the product of kinetically controlled cyclisation of (**2**) with formation of (**5a**) and (**6a**) as the result of thermodynamic control.[9]

Cyclisation through oxygen is now accepted as a normal pathway in the reaction of CSI with conjugated trienes and dienes[10] and the process need no longer be looked upon as unusual[11] in reactions with mono-olefins provided a suitable rearrangement pathway provides access to 5-membered or larger rings.

Table. *Effect of solvent on the ratio of cyclisation products in reaction with CSI.*[a]

Solvent	Camphene Ratio (**5a**) : (**6a**)	α-Fenchene Ratio (**11a**) : (**12a**)
Hexane	75 : 25	77 : 23
CH_2Cl_2	50 : 50	67 : 33
MeCN	16 : 84	33 : 67
$MeNO_2$	13 : 87	33 : 67

[a] Ratios were measured by n.m.r. spectroscopy. The products were stable under the reaction conditions in each case. Reaction temperature variations have an additional, but small, effect on the ratios.

The dramatic control exerted by solvent over the course of the cyclisation to yield rearranged products (Table) has not previously been observed in such a secondary step. The effect of increasing solvent polarity has hitherto been confined to promotion of the rate of the primary step in olefin–CSI reactions.[2]

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[1] R. Graf, *Angew. Chem. Internat. Edn.*, 1968, **7**, 172.

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

[5] L. A. Paquette, S. Kirschner, and J. R. Malpass, *J. Amer. Chem. Soc.*, 1969, **91**, 3970.

[6] The Hoechst group[2] have observed a transient carbonyl peak at 1818 cm^{-1} ascribed to (**3a**) but have not characterized (**3**).

[7] J. R. Malpass (a) unpublished, (b) succeeding communication.

[8] Prepared independently according to the method of G. Langlois, *Ann. Chimie.*, 1919, **12**, 193.

[9] In a very recent paper, a case of initial β-lactam formation has been interpreted as a concerted $_{\pi}2_s + {}_{\pi}2_a$ cycloaddition; T. J. Barton and R. J. Rogido, *Tetrahedron Letters*, 1972, 3901.

[10] Succeeding communications and references cited therein.

[11] T. W. Doyle and T. T. Conway, *Tetrahedron Letters*, 1969, 1889; E. Dunkelblum, *ibid.*, 1972, 1551.