Chlorosulfonyl Isocyanate

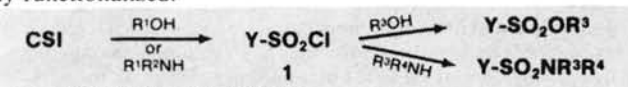
A Lively Heterocumulene!

Chlorosulfonyl isocyanate (CSI) is probably the most chemically reactive isocyanate known, yet it itself is stable at temperatures up to 300°C. It was first reported by Graf[1] 25

$ClSO_2NCO$ **(CSI)**

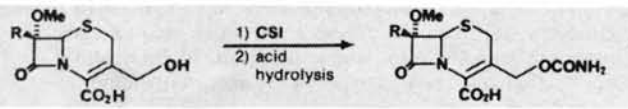
years ago and has been the subject of several reviews.[2] This exciting reagent has enabled a variety of useful and often novel transformations, some of which are described below.

CSI undergoes the expected nucleophilic additions by alcohols and amines to produce the respective *N*-chlorosulfonyl carbamates and ureas (**1**), which may be subsequently functionalized.

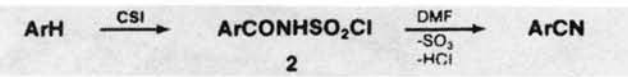


Y = R^1OCONH- or R^1R^2NCONH-

The reactivity of **CSI** with alcohols is so great that alcohols can be derivatized in the presence of other functional groups. Work by Christensen[3] on synthetic cephalosporins provides an example.

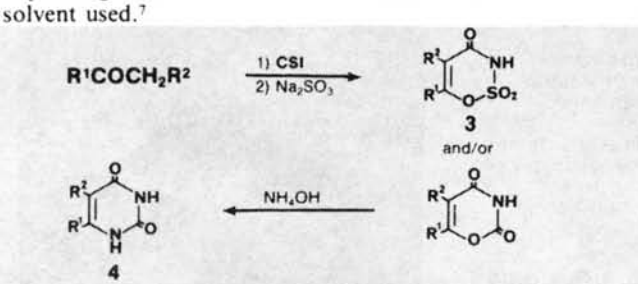


Aromatic compounds that readily undergo electrophilic substitution (*e.g.*, anthracene and 1,3-dimethoxybenzene) react with **CSI** to produce the *N*-chlorosulfonyl carboxamides **2**, which can be subsequently converted to the corresponding *nitriles* in 70-90% overall yields by treatment with DMF.[4]

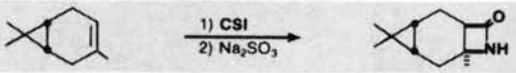


A related sequence converts carboxylic acids[4] and enolizable ketones[5] to nitriles in 60-90% overall yields.

A variation of the latter method provides either the potential "third generation" sweeteners[6] **3** or substituted uracils **4**, depending on the nature of the ketone substituents and the solvent used.[7]

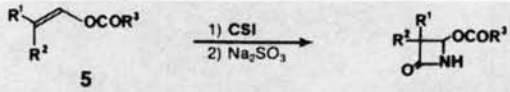


The ability of **CSI** to undergo cycloaddition to multiple bonds adds another dimension to its usefulness. The most extensively studied case is the net [2 + 2] cycloaddition of **CSI** to olefins, leading to β-lactams in moderate to high yields.[8] These additions are highly regio- and stereospecific, as the following example[9] illustrates:



The use of sodium sulfite is a mild, convenient and apparently general method[10] for reducing the initially formed *N*-chlorosulfonyl β-lactams to the corresponding N-unsubstituted compounds.

Heterosubstituted β-lactams, comprising the fundamental nucleus of the penicillin and cephalosporin antibiotics, may be prepared by the reaction of **CSI** with vinyl esters (**5**).[11] The acyloxy substituent of the resulting lactam is readily displaced by a variety of nucleophiles (*e.g.*, RCO_2^-, RSO_2^-, N_3^-, RO^-, and RS^-) in good to excellent yields, leaving the 4-membered ring intact.



In view of the *cis* addition of **CSI** to olefins and the facile hydrolytic cleavage of β-lactams, this versatile reagent also provides a convenient route to *erythro*- and *threo*-β-aminoacids.[12]

Use of the uniparticulate electrophilic character of **CSI** as a *mechanistic probe* has been amply demonstrated by Paquette in his studies of molecules such as bullvalene[13] and barrelene.[14]

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References: **(1)** Ger. Offen. 928,896 (1952); *Chem. Zbl.*, 11687 (1955). **(2)** W.A. Szabo, *Aldrichimica Acta*, **10**, 23 (1977); J.K. Rasmussen and A. Hassner, *Chem. Rev.*, **76**, 389 (1976), and references 1-3 cited therein. **(3)** Ger. Offen. 2,264,651 (1974); *Chem. Abstr.*, **81**, 120653*j* (1974). **(4)** G. Lohaus, *Chem. Ber.*, **100**, 2719 (1967). **(5)** J.K. Rasmussen and A. Hassner, *Synthesis*, 682 (1973). **(6)** K. Clauss and H. Jensen, *Angew. Chem., Int. Ed. Engl.*, **12**, 869 (1973). **(7)** J.K. Rasmussen and A. Hassner, *J. Org. Chem.*, **38**, 2114 (1973). **(8)** See, for example, N.S. Isaacs, *Chem. Soc. Rev.*, **5**, 181 (1976). **(9)** T. Sasaki, S. Eguchi, and H. Yamada, *J. Org. Chem.*, **38**, 679 (1973). **(10)** T. Durst and M.J. O'Sullivan, *ibid.*, **35**, 2043 (1970). **(11)** K. Clauss, D. Grimm, and G. Prossel, *Justus Liebigs Ann. Chem.*, 539 (1974). **(12)** A.I. Meyers, "Heterocycles in Organic Synthesis," John Wiley & Sons, Inc., New York, N.Y., 1974, pp 285-286. **(13)** L.A. Paquette, S. Kirschner, and J.R. Malpass, *J. Amer. Chem. Soc.*, **92**, 4330 (1970). **(14)** L.A. Paquette and W.E. Volz, *ibid.*, **98**, 2910 (1976).

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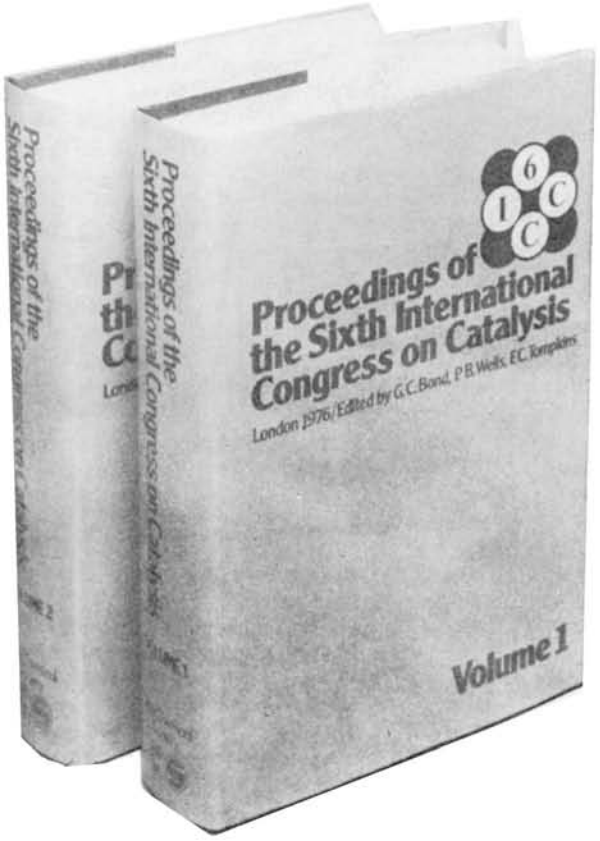

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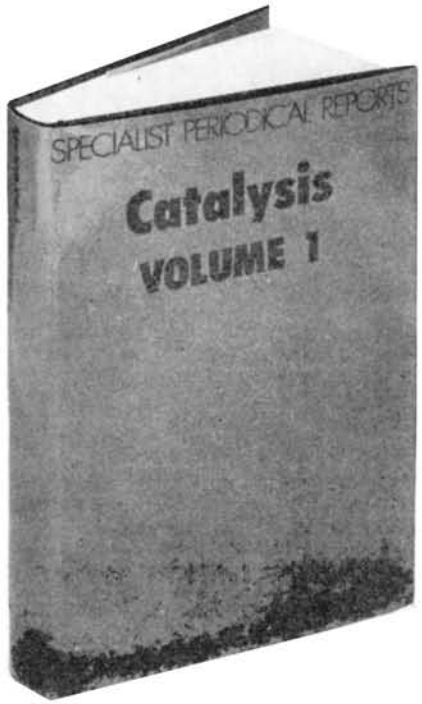

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