Organic Process Research & Development **1997**, *1,* 240–246

Lecture Transcripts

Industrial Scale Synthesis of Thiophosgene and Its Derivatives

J. Ian Grayson

Fine Organics Ltd., Seal Sands, Middlesbrough, TS2 1UB, UK

Abstract:

Thiophosgene is manufactured on a mulittonne scale, using the continuous chlorination of carbon disulfide under aqueous conditions to prepare the key intermediate perchloromethyl mercaptan. The development of this process is described, and the uses of thiophosgene in the manufacture of chlorothioformates and isothiocyanates are reviewed.

Thiophosgene is a dense red-orange liquid which fumes in air. It has a very distinctive and highly persistent choking odour and is toxic and a severe irritant to the eyes and mucous membranes. However, its toxicity is considerably lower than that of phosgene, and the strong odour quickly advertises its presence. There is no occupational exposure limit listed for thiophosgene, but the intermediate trichloromethanesulfenyl chloride (perchloromethyl mercaptan, PCMM) has an occupational exposure limit of 0.1 ppm. Thiophosgene was first definitively prepared by Rathke[1] in 1870 from carbon disulfide and chlorine, and the method was later improved by Klason,[2] who used zinc reduction of perchloromethyl mercaptan to isolate distillable amounts of thiophosgene.

Early syntheses of thiophosgene gave the product in small amounts together with carbon tetrachloride and carbon disulfide, from which it was not readily separable by distillation. The direct reactions of sulfur and carbon tetrachloride, carbon and sulfur monochloride, or chlorine and methyl thiocyanate give only low yields of thiophosgene, and most practical syntheses involve the manufacture and dechlorination of perchloromethyl mercaptan.

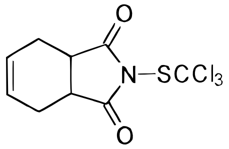
Because of the complex routes to its preparation, and particularly because of the strong obnoxious odour and lachrymatory nature of the product and its precursors, thiophosgene has not been as widely used as phosgene in organic synthesis. It does, however, have a wide range of applications in synthesis, both as a thiocarbonyl building block and in heterocycle synthesis.[3] Thiophosgene is more stable than phosgene towards hydrolysis (by a factor of *ca.* 200[4]) and is best stored as a neat liquid or as a solution in an inert solvent, preferably under a layer of water or hydrochloric acid.

Manufacture of Perchloromethyl Mercaptan

The wide use of thiocarbonyl compounds in agrochemicals and pharmaceuticals, for example in thiocarbamate fungicides, and the requirement for toll manufacture of complex isothiocyanates and chlorothioformates as high-value intermediates for these compounds led us to investigate the industrial scale synthesis of thiophosgene. The previous unavailability of thiophosgene has led to the development of alternative routes to molecules which could be readily synthesised via thiophosgene. These alternative routes have often involved forcing conditions and are particularly unsuitable for the complex, highly functionalised molecules which are found in modern agrochemicals and pharmaceuticals.

As all the technically useful methods for the manufacture of thiophosgene proceed via the PCMM intermediate, the first hurdle was to develop a safe and efficient synthesis of this compound. Fine Organics already has wide experience of the handling of both bulk chlorine and carbon disulfide. The reduction of PCMM to thiophosgene is well documented[3] and, apart from the containment of the starting material and product, was not expected to present technical problems.

PCMM has been prepared on an industrial scale, and there are many patents on improvements to the manufacturing process.[5] It is an important intermediate in its own right as a precursor to the agrochemical fungicide captan (**1**).



(**1**)

The traditional route to the manufacture of PCMM is via the addition of chlorine into carbon disulfide in the presence of iodine. This is the method originally used by Rathke and is described in *Organic Syntheses*[6] (eq 1).

$$CS_2 + 3Cl_2 \rightarrow Cl_3CSCl + SCl_2$$

$$2CS_2 + 5Cl_2 \rightarrow 2Cl_3CSCl + S_2Cl_2 \qquad (1)$$

$$CS_2 + 3Cl_2 \rightarrow CCl_4 + S_2Cl_2$$

---

[1] Rathke, B. *Ber. Dtsch. Chem. Ges.* **1870**, *3*, 858.
[2] Klason, P. *Ber. Dtsch. Chem. Ges.* **1887**, *20*, 2376.
[3] Reviews: Tilles, H. In *The Chemistry of Sulfur Compounds*; Kharasch, N., Meyers, C. Y., Eds.; Pergamon: New York, 1966; Vol. 2, p 311. Sharma, S. *Synthesis* **1978**, 803.
[4] Böhme, H. *Ber. Dtsch. Chem. Ges.* **1941**, *74*, 248.
[5] Review: Sosnovsky, G. *Chem. Rev.* **1958**, *58*, 509.
[6] Dyson, G. M. *Organic Syntheses*; Wiley: New York, 1932; Collect. Vol. I, p 506.

S1083-6160(97)00002-9 CCC: $14.00

The perchloromethyl mercaptan is accompanied by large amounts of sulfur monochloride and sulfur dichloride. Sulfur monochloride cannot be separated from PCMM by distillation because of their similar boiling points, so improvements have concentrated on increasing the amount of sulfur dichloride formed relative to sulfur monochloride and reducing the quantities of other by-products, e.g., carbon tetrachloride. The original catalyst used was iodine,[2] but other catalysts have been used with good results, such as charcoal, diketones, phosphates or phosphites, and soluble lead carboxylates.[7] For example, carbon disulfide and chlorine can be combined directly by passing over charcoal in a tube reactor.[8] In the alternative workup method, as in the *Organic Syntheses* process, the sulfur monochloride can be destroyed by a steam distillation of the product, but this produces large quantities of sulfur which are difficult to remove from the apparatus (eq 2).

$$2S_2Cl_2 + 2H_2O \rightarrow SO_2 + 3S + 4HCl \qquad (2)$$

To avoid the problems of the sulfur chloride by-products, PCMM can be prepared by the chlorination of carbon disulfide in aqueous hydrochloric acid, sometimes also in the presence of sulfuric acid.[9] Interestingly, higher concentrations of acid favour the formation of PCMM: increasing the initial hydrochloric acid concentration from 0% up to 20% w/w increased the yield of PCMM from 65% up to 86%, while reducing the chlorination time and the amount of distillation residues. The sulfur by-products from this process are converted to sulfuric acid under the reaction conditions, simplifying the isolation of the product (eq 3).

$$CS_2 + 5Cl_2 + 4H_2O \rightarrow Cl_3CSCl + 3H_2SO_4 + 6HCl \qquad (3)$$

In this method the build-up of concentrated acid solutions is avoided by continuous addition of water during the chlorination. However, it is also possible to run at high acid concentrations, so as to recover the HCl from the aqueous phase by distillation.[10] The process lends itself to continuous operation, and there have been several patents on the design of a continuous or semicontinuous process for this aqueous route.[11]

Development of Batch and Continuous Processes for PCMM

The initial development of PCMM production at Fine Organics was as a batch pilot scale process, using the aqueous route. Chlorine was added to a mixture of carbon disulfide and aqueous hydrochloric acid in a glass-lined reactor, either under a slight positive pressure or bubbled through a dip pipe. In both cases, the reaction time was excessive. When the reaction was scaled up to 2000 L equipment, the total chlorination time was usually 3−4 days. At completion of reaction, close to the theoretical 5 equiv of chlorine had been consumed. The rate of reaction was monitored by measuring the break-through of chlorine into the reaction headspace, and the reaction was stopped either when GC analysis showed less than 5% carbon disulfide remaining or when the chlorine level was measured at >1% in the head space. Overchlorination leads to formation of high levels of carbon tetrachloride (eq 4).

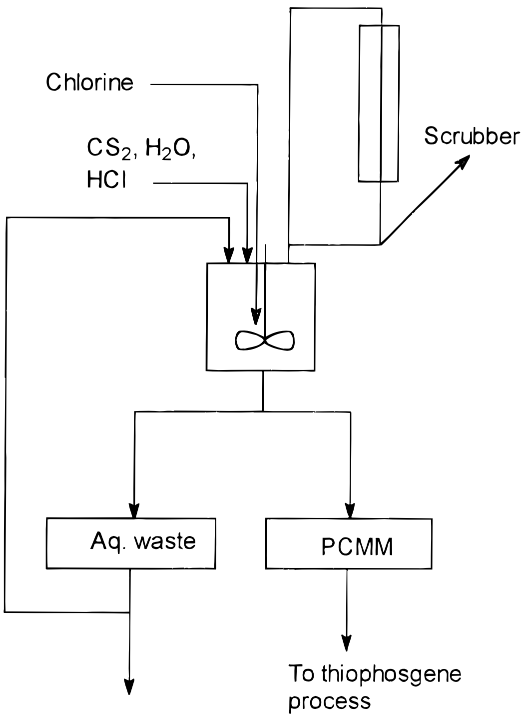


Figure 1. **Batch manufacture of PCMM.**

$$Cl_3CSCl + 3Cl_2 + 4H_2O \rightarrow CCl_4 + H_2SO_4 + 6HCl \qquad (4)$$

It was found that the initial hydrochloric acid charge was only necessary on a start-up batch; for subsequent batches a portion of the aqueous acid waste could be recycled. An outline of the batch process is shown in Figure 1.

The conversion of chlorine to PCMM was up to 90%. The PCMM had a purity of 85−90% (GC area), with up to 5−10% of each of carbon disulfide and carbon tetrachloride and a small amount of high-boiling material. The low-boiling impurities can be removed by vacuum stripping of the crude PCMM; distillation of the product itself is unnecessary and leads to some decomposition. DSC measurements on PCMM showed small exothermic events at 134 and 216 °C with a total energy of 50 J/g. The heat of reaction was calculated as $\Delta H =$ ca. -700 kJ/mol of PCMM, which presented no problem for heat removal on the batch scale with these reaction times.

Safety tests were performed on the chlorination mixture to determine whether there was any explosion risk from carbon disulfide in a chlorine atmosphere. Literature precedent shows that many organic compounds exhibit very wide explosion limits in a chlorine atmosphere, comparable with the explosion limits in pure oxygen.[12] The explosion limits in air for carbon disulfide are 1.3−50% v/v, and the minimum ignition energy is 0.01 mJ. Tests showed that

---

(7) Zupancic, B. G. *Synthesis* **1975**, 169. Greco, C. C.; Walsh, E. N. US Patent 4 092 357, 1978.

(8) Mägerlein, H.; Meyer, G.; Rupp, H.-D. *Synthesis* **1971**, 478. Rupp, H.-D.; Meyer, G.; Zengel, H.-G.; Mägerlein, H. German Patent 2 154 305, 1971.

(9) Masat, J.; Zbirovsky, M. Br. Patent 1 108 484, 1965.

(10) Bhutani, S. K. US Patent 3 993 693, 1976.

(11) Vamo, J.; Vrzyula, D.; Aujesky, L.; Becka, J. Czechoslovak Patent 134 692, 1969. Spolana n.p. German Patent 2 156 329, 1972.

(12) Mal'tseva, A. S.; Roslovskii, A. I.; Frolov, Y .E. *Mendeleev Chem. J. (Engl. Transl.)* **1974**, *19*, 81; *Zh. Vses. Khim. O-va. im. D. I. Mendeleeva* **1974**, *19*, 542. Dokter, T. *J. Hazard. Mater.* **1985**, *10*, 73.

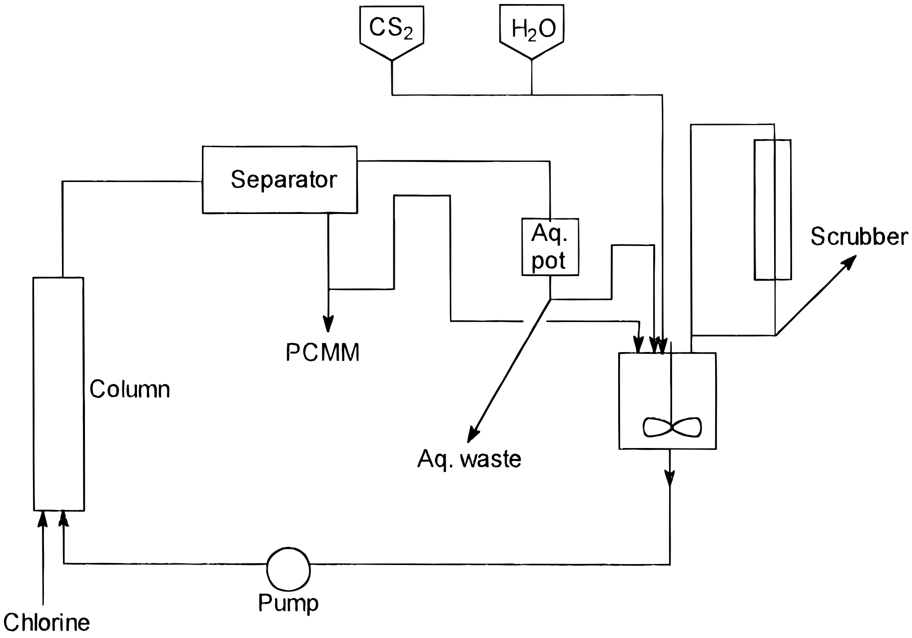


Figure 2. **Pilot plant loop reactor for PCMM.**

instantaneous mixing of chlorine and carbon disulfide did not lead to any autoignition, and that mixtures of chlorine and carbon disulfide could not be ignited with an electric spark (within the range 5−25 °C). Mixing was found to produce an immediate exotherm, corresponding to the reaction to give PCMM. In fact, the reaction is so fast that no chlorine is detected in the system in laboratory or pilot plant batch runs until the carbon disulfide concentration is very low. There is therefore no appreciable accumulation of chlorine in the process.

The disadvantages of the batch process were (1) a high inventory of highly flammable carbon disulfide for a considerable time during the process; (2) long chlorination times, with slow absorption of the chlorine into the two-phase system in a standard stirred reactor, and a slow delivery rate for the gaseous chlorine addition; (3) the fact that the changing acidity of the process as more hydrochloric and sulfuric acids are generated can affect the ratio of PCMM to by-products such as carbon tetrachloride and high-boiling polysulfide compounds. This can be controlled by the addition of extra water during the process along with the chlorine, but this measure reduces the overall batch size.

A continuous process, on the other hand, would give a faster throughput in order to meet the requirements for a multitonne capacity for the thiophosgene downstream products, while maintaining lower inventories of both carbon disulfide and chlorine.

The first semicontinuous plant was constructed using an existing 450 L pilot plant vessel as a hold vessel and heat exchanger. This was connected via a pump to a 150 mm × 3 m glass column packed with glass rings (Figure 2). Carbondisulfide and water were charged to the reactor, and chlorine was introduced at the base of the column. The liquid stream from the head of the column was fed to a horizontal glass separator, from which both phases could be either separated off or returned to the loop. Once equilibrium was established, the aqueous and organic layers were removed so as to keep the loop contents constant.

Table 1. **Product composition from the pilot plant loop reactor**

molar excess of CS_2 over theory, %	GC area % PCMM	CS_2	CCl_4	others
10	92	5	2	<1
33	83	14	2	<1
50	75	23	2	<1

The system was primed with water, hydrochloric acid, and a PCMM/CS_2 mixture representative of the product stream expected (ca. 80% PCMM). This was circulated around the loop, and the chlorine addition was started. At regular intervals, aliquots of ca. 10 kg of carbon disulfide and 50 L of water were charged, and approximately 10 L of the organic layer and 75 L of the aqueous layer were removed from the separator, in order to maintain a constant loop volume. The chlorine was generally added at such a rate as to maintain a 33% molar excess of carbon disulfide over the stoichiometric amount.

Under these conditions, the pilot system gave almost complete chlorine consumption at up to 40 kg of chlorine/h. In comparison the batch process, using the larger scale equipment, could only run at a chlorine addition rate of 10−15 kg/h. The heat of reaction was calculated from the jacket inlet and outlet temperatures to correspond with the theoretical amount, taking into account the lower heats of dissolution of HCl and H_2SO_4 at the high concentrations present in the aqueous phase.

The pilot process was run with different ratios of chlorine to CS_2, giving product compositions as shown in Table 1. The observed ratio of PCMM to CS_2 in the product corresponded well with the calculated theoretical excess of CS_2. However, with a 10% molar excess of CS_2, the system could only be run at 15 kg of chlorine/h without breakthrough of chlorine at the top of the column. There was no improvement in product purity when running with more than the standard 33% molar excess of CS_2.

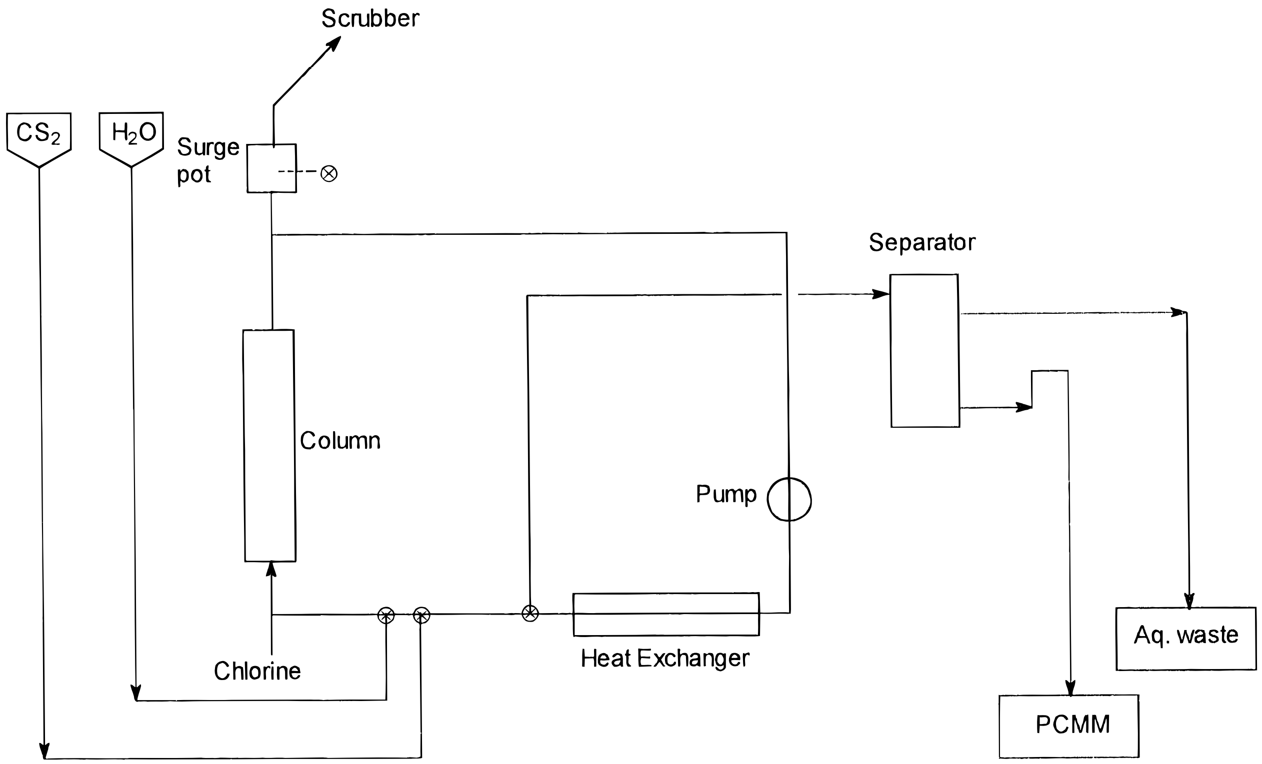


Figure 3. **Main plant loop reactor for PCMM.**

On the basis of laboratory results and the pilot plant trial, the design parameters for the full scale production plant were determined, the chief requirement being a maximum capacity six to eight times that of the pilot plant. The plant is designed to be fully continuous, with carbon disulfide and water continually metered into the loop before the column, and chlorine injected into the base of a halar-lined steel column, packed with PTFE (Figure 3). The heat of reaction is removed by a heat exchanger at the base of the loop, followed by a variable take-off of both phases to a separator tank. From this, the aqueous and organic phases are continually drained to the aqueous effluent receiver and the PCMM hold tank, respectively. The level of material in the loop is governed by PLC control of the liquid feed and take-off valves, coupled with monitoring of the level in a surge pot above the column. The separator take-off is controlled by lutes, backed up by conductivity level detectors. The plant is designed to run with a slightly higher carbon disulfide excess than in the pilot plant. Chlorine breakthrough is monitored by a chlorine meter in the surge pot above the column.

The PCMM continuous plant is located within a separate enclosure inside the production building. The enclosure is kept at a negative pressure with respect to the rest of the building via an environmental scrubber system (sodium hypochlorite). All feed control operations can be carried out from the PLC console in the plant control room, so that frequent entry to the enclosure is not required. The enclosure air and the head space in the loop are continually monitored for chlorine, and a high level will shut down chlorine supply to the system. Similarly a high oxygen level in any part of the process will shut down the system.

After commissioning of the plant, when the design flow rates were achieved, the GC wt % assay of the product mixture was found to be

product	wt %
PCMM	82−86
CS_2	10−12
CCl_4	2−4
others	<1

and the measured acid strength in the effluent was 11−12 mol/kg. This was in accordance with the theoretical model of the process chemistry. In particular, lower levels of impurities were found compared with the batch process, because of the control of the reactant composition and of the acid strength in the reaction column. The carbon disulfide excess is carried through the thiophosgene process unchanged and is removed during solvent stripping at a later stage.

Once commissioned, the stability of the continuous plant was very satisfactory. Small changes of rates of addition or take-off did not affect performance, and because of the loop volume, even a change of 25% in the water, CS_2, or chlorine feed rates would take 1−2 h to produce a processing problem. At high chlorine, low CS_2, or low water feeds, the aqueous effluent becomes more acidic, and eventually the aqueous layer would begin to lose HCl gas, causing pressure surges in the loop. Additionally, at high chlorine or low CS_2 rates, there is an increase in the levels of CCl_4 formed. High levels of CCl_4 in the product may also be an indication of corrosion or feed contamination with iron, as CCl_4 can be formed directly from CS_2 under these conditions (eq 5).

$$CS_2 + 3Cl_2 \xrightarrow{Fe} CCl_4 + S_2Cl_2 \qquad (5)$$

At low chlorine feed rates, or high water feed rates, the acid strength in the loop drops. Below ca. 5 mol/kg of acid, high-boiling impurities form, which can precipitate and block the separator. The nature of the high-boiling components is not clear, but they are probably composed of species such as **2** or **3**.

$Cl_3C{-}(S)_n{-}CCl_3$ **2** $Cl_3C{-}SO_2Cl$ **3**

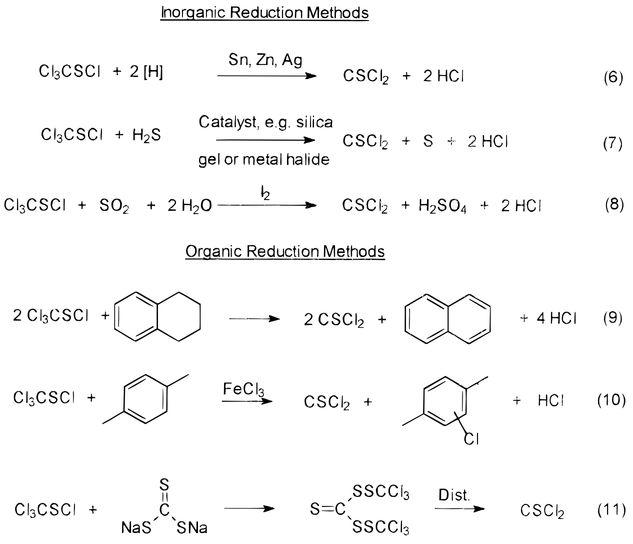
The introduction of the continuous process for PCMM at Fine Organics has been very successful, and the plant now operates for periods of several months at a time between shut-downs, with a constant throughput of PCMM equivalent to a yield of 75−85% based on chlorine. This continuous plant supplies the full scale batch plant for thiophosgene and its downstream derivatives, some of which are produced on a multitonne scale.

Reduction of Perchloromethyl Mercaptan to Thiophosgene

Methods of reduction of PCMM to thiophosgene can be divided into those using inorganic and those using organic reducing agents. The earliest methods used dissolving metal reagents such as silver, tin, and zinc in acidic solution (eq 6).[2,6] These have proved unreliable with respect to yield and scale-up potential, being dependent on the rate of addition of PCMM and the particle size of the metal used.[13] Other examples of inorganic reagents which have been used are hydrogen sulfide over silica gel, metal sulfides, or metal chlorides (eq 7).[14] An apparatus for continuous operation of this reduction process using a column packed with silica gel and operated at 115 °C has been described.[15] Hydrogenation of PCMM over a quartz catalyst at 350 °C also gives thiophosgene.[16] The reduction can also be run in an aqueous solution using sulfur dioxide (or an inorganic sulfite or bisulfite) and an iodine catalyst (eq 8).[17]

As an alternative to the use of inorganic reducing agents, which often require the disposal of metal-containing waste streams, organic reducing agents have been developed. An example of this type of reaction is the slow addition of PCMM to tetralin at 200 °C. This gives thiophosgene, which is flash distilled and then fractionated from unreacted starting material (eq 9). The naphthalene formed remains as a heel in the distillation vessel.[18] In another method the reduction can be performed in refluxing xylene with a ferric chloride catalyst[19] (eq 10). Sodium trithiocarbonate has also been employed as a reducing agent[20] (eq 11).

The different methods all have their own advantages, and at Fine Organics we investigated various methods on a pilot plant scale. An important factor when using the crude PCMM from the continuous process is that the reduction process is unaffected by the varying levels of carbon disulfide or carbon tetrachloride in the crude product. We have finally adopted a process which allows the preparation and direct use of thiophosgene in a hydrocarbon or chlorinated hydrocarbon solvent, as appropriate for the downstream use of the product.



Manufacture and Use of Thiophosgene on an Industrial Scale

The concept for the manufacture and use of thiophosgene is based on the continuous chlorination process for PCMM, followed by the batch conversion of this intermediate into thiophosgene and then into downstream products in the same plant. This removes the need for storage of large amounts of either PCMM or thiophosgene and permits the maximum use of the PCMM plant.

The operation of the full scale plant is shown in Figure 4, which represents the manufacture of a liquid chlorothioformate or isothiocyanate. A similar set of operations is used to manufacture solid chlorothioformates or isothiocyanates. In each case, a batch of PCMM, sufficient to react completely with the amine or phenol, is transferred from the holding vessel into V 1, where it is converted into thiophosgene. The conversion of the active content of PCMM to thiophosgene is >99%. After extraction, the thiophosgene is reacted directly with the amine or phenol in a water/solvent two-phase mixture in V 2. The usual solvents are chlorinated hydrocarbons. As base, sodium hydroxide, carbonate, or bicarbonate is used, depending on the stability of other functional groups in the molecule. A phase transfer catalyst can also be used to increase the amount of the chlorothioformate or isothiocyanate formed and decrease the amount of the dithiocarbonate or thiourea impurities. The isolation of the product is either by direct distillation or by crystallisation in V 3 using a displacement solvent followed by filtration.

In order to achieve clean conversion of thiophosgene to the downstream products, it is important to maintain a slight excess of thiophosgene over substrate (usually ca. 10%) and a low reaction temperature (usually 0−10 °C). In some cases, particularly where a strong base is used, additional base and thiophosgene are required to obtain complete conversion, as the thiophosgene is hydrolysed under

---

(13) Frankland, P. F.; Garner, F. H.; Challenger, F.; Webster, D. *J. Soc. Chem. Ind.* **1920**, *39*, 313.
(14) Rupp, H.-D.; Meyer, G.; Mägerlein, H. German Patent 2 138174, 1973. Rupp, H.-D.; Meyer, G.; Mägerlein, H. German Patent 2 138 175, 1973. Meyer, G.; Mägerlein, H.; Rupp, H.-D. German Patent 2 326 396, 1974.
(15) Mägerlein, H.; Meyer, G.; Rupp, H.-D. *Synthesis* **1974**, 26.
(16) Tietze, E.; Schmidt, F. German Patent 873 836, 1953.
(17) Horak, J.; Zbirovsky, M. *Ind. Chim. Belge* **1967**, *32*, 94. Zbirovsky, M.; Horak, J. Czechoslovak Patent 103 963, 1962.
(18) Tietze, E.; Peterson, S. German Patent 853 162, 1952.
(19) Orwoll, E. F. US Patent 2 668 853, 1954.
(20) Fischer, F.; Gottfried, R. *Z. Chem.* **1964**, *4*, 189.

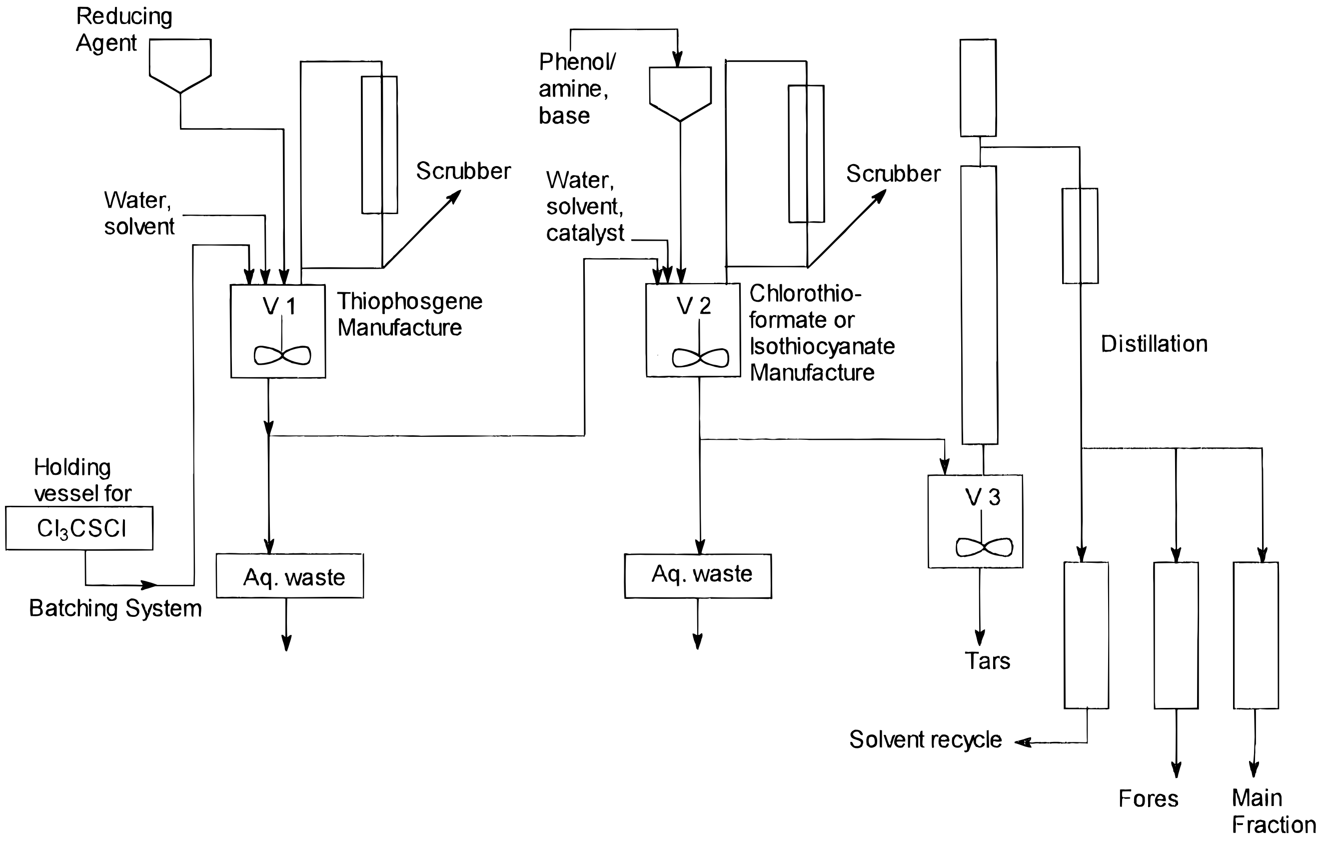


Figure 4. **Manufacture of thiophosgene and a liquid chlorothioformate or isothiocyanate.**

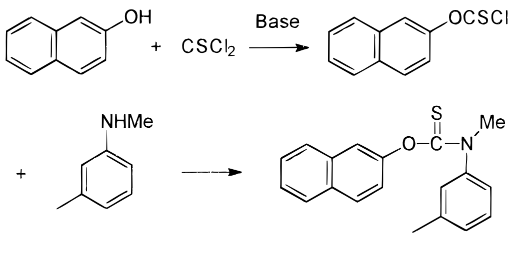
basic conditions in competition with the addition reaction. Thiophosgene is, however, stable in water under acid conditions.

While the preparation of PCMM is carried out in an enclosed area, the downstream stages are all performed in standard glass-lined vessels in a multipurpose plant. There is no exposure to thiophosgene during processing as this stage is not isolated. Any samples required for analysis are taken in an extracted cubicle around V 1. The odour problems are much less with the downstream products than with thiophosgene, and handling of these products does not present such a problem. All stages are performed under a nitrogen atmosphere, as thiophosgene can react with atmospheric oxygen to give phosgene. Exposure to air during processing is the most usual way for the thiocarbonyl derivatives to be contaminated by the corresponding carbonyl compounds during manufacture. An unusual property of thiophosgene is oxychemiluminescence. This is the atmospheric oxidation to phosgene, which is accompanied by the emission of light. This effect, which is common to several classes of reactive sulfur compounds,[21] was observed at Fine Organics during the development of the process.

All process off-gases are led to a train of scrubbing towers containing sodium hydroxide solution and then, together with the exhausts from vacuum pumps, to a final alkaline scrubber. The aqueous waste streams are neutralised where necessary with sodium hydroxide before disposal. These practices reduce the thiophosgene and other related substances, as judged by environmental odour, to nondetectable levels.

Uses of Thiophosgene

The principal uses of thiophosgene are, as outlined above, in the manufacture of chlorothioformates and isothiocyanates. For chlorothioformates there is no other practical synthetic route. The chlorothioformates are thermally stable but water/base sensitive oils or crystalline solids, and their main use is in the manufacture of thiocarbamate fungicides, as for example in the preparation of tolnaftate (**4**).[22]



TOLNAFTATE (**4**)

Isothiocyanates can be manufactured by other methods, such as the addition of an amine to carbon disulfide and the decomposition of the intermediate dithiocarbamate formed.[23] While these methods are suitable for simple aliphatic and aromatic isothiocyanates, the forcing conditions often employed (e.g., strong heating and use of hydrogen peroxide) are incompatible with functionalised isothiocyanates used as agrochemical or pharmaceutical intermediates. For the conversion of high-value aliphatic or aromatic amines to

---

(21) Delépine, M. *C. R. Hebd. Seances Acad. Sci.* **1922**, *174*, 1291.

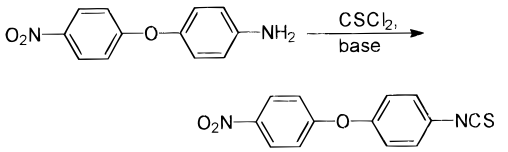
(22) Miyazaki, K.; et al. US Patent 3 334 126, 1967.

(23) Dains, F. B.; Brewster, R. Q.; Olander, C. P. *Organic Syntheses*; Wiley: New York, 1932; Collect. Vol I, p 447. Moore, M. L.; Crossley, F. S. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. III, p 599. Giesselmann, G.; Günther, K. European Patent Appl. 446 420, 1991.

isothiocyanates, thiophosgene offers the advantages of high yields and low levels of by-products (e.g., thioureas). Two examples are given for an aliphatic (**5**)[24] and an aromatic (**6**)[25] isothiocyanate.

$$EtOOC{-}CH_2{-}NH_2 \cdot HCl \xrightarrow[\text{base}]{CSCl_2,} EtOOC{-}CH_2{-}NCS$$

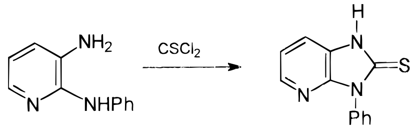
(**5**)



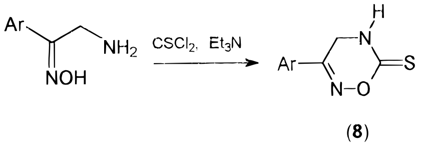
NITROSCANATE (antihelmintic)

(**6**)

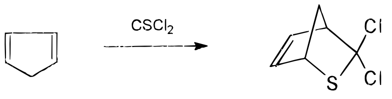
Thiophosgene will also add to bifunctional compounds, to give a variety of sulfur-containing heterocycles, such as **7** and **8**,[26] and can also form sulfur heterocycles, e.g., **9**, via the Diels−Alder reaction.[27] Some of these sulfur heterocycles (**10** and **11**) are being developed as herbicides.



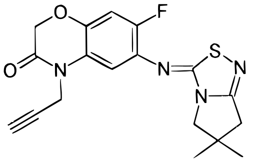
(**7**)



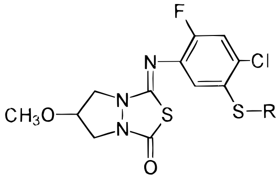
(**8**)



(**9**)



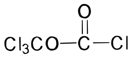
SCHERING (**10**)



CIBA-GEIGY (**11**)

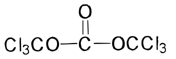
Thiocarbonyl Diimidazole

While phosgene is not easily transportable and is generally manufactured on site, it can be handled and shipped as the stable derivatives diphosgene (trichloromethyl chloroformate, **12**) and triphosgene [bis(trichloromethyl) carbonate, **13**]. For thiophosgene, these options are not available, as the thiophosgene dimer exists as a cyclic, unstable form (**14**).[28]



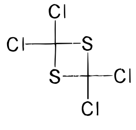
$$Cl_3CO{-}\overset{O}{\overset{\|}{C}}{-}Cl$$

Diphosgene (**12**)



$$Cl_3CO{-}\overset{O}{\overset{\|}{C}}{-}OCCl_3$$

Triphosgene (**13**)

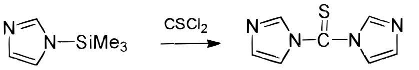


Thiophosgene dimer

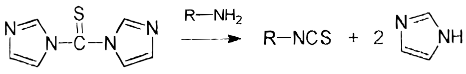
(**14**)

For pharmaceutical or agrochemical manufacturers, who wish to retain control over the insertion of a thiocarbonyl group into an intermediate, thiocarbonyl diimidazole (TCDI) is available as a stable, solid equivalent of thiophosgene, which is offered by Fine Organics without any transport restrictions, and can be used in many cases as a replacement for thiophosgene, for example in the synthesis of isothiocyanates and thioureas.

TCDI is a yellow solid of melting point 103 °C, which can be prepared from thiophosgene and imidazole or more conveniently from (trimethylsilyl)imidazole (eq 12).[29] The latter reaction has the advantage of producing only volatile side products, as it is otherwise difficult to free the TCDI from residual imidazole. TCDI contains very low levels of the carbonyl equivalent, CDI, and can therefore be used to cleanly introduce the thiocarbonyl function. It is significantly more stable towards hydrolysis than CDI, but can slowly decompose on exposure to air or water to give COS and imidazole.

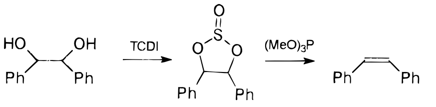


(12)

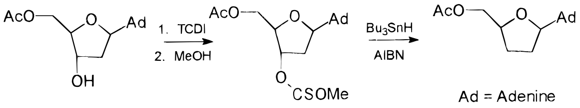


(13)

As well as being a useful substitute for thiophosgene in the manufacture of complex isothiocyanates (eq 13), TCDI has been used as an olefination reagent (the Corey−Winter olefination), forming a thionocarbonate with 1,2-diols, which can be reductively cleaved with trimethyl phosphite (eq 14).[30] In addition, thiocarbonyl diimidazole has been used as part of a free-radical deoxygenation sequence in the preparation of dideoxyadenosines (eq 15).[31]



(14)



(15)

In summary, thiophosgene is a versatile organic intermediate, which is manufactured and used at Fine Organics in multitonne quantities. In addition, thiocarbonyl diimidazole is available as a stable solid thiophosgene equivalent for use in synthesis.

Received for review October 17, 1996.⊗

OP970002C

---

(24) Floch L.; Kovac, S. *Collect. Czech. Chem. Commun.* **1975**, *40*, 2845.
(25) Agripat S. A. French Patent 1 491 477, 1967.
(26) Clark, R. L.; Pessolano, A. A.; Shen, T.-Y. German Patent 2 623 469, 1976.
(27) Middleton, W. J. *J. Org. Chem.* **1965**, *30*, 1390.
(28) Jones, J. I.; Kynaston, W.; Hales, J. L. *J. Chem. Soc.* **1957**, 614.
(29) Staab, H. A.; Walther, G. *Justus Liebigs Ann. Chem.* **1962**, *657*, 98. Pullukat, T. J.; Urry, G. *Tetrahedron Lett.* **1967**, 1953.
(30) Corey, E. J.; Winter, R. A. E. *J. Am. Chem. Soc.* **1963**, *85*, 2677.
(31) Priske, E. J.; Martin, J. C. *Synth. Commun.* **1985**, *15*, 401.

⊗ Abstract published in *Advance ACS Abstracts*, February 15, 1997.