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Phosgenations – A Handbook

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Phosgenations – A Handbook

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Contents

Preface

Phosgene is a typical *highly reactive chemical* that has been in use since the early days of the chemical industry. In phosgene, the organic chemist will easily recognize either a building block providing the carbonyl function in many classes of organic compounds or a versatile reagent for carrying out selective chlorocarbonylation, chlorination, dehydration, and carbonylation reactions.

Because of its highly toxic nature, the handling of phosgene *gas*, either on a small scale, as in the laboratory, or on a medium-to-large scale, as in the agrochemical and pharmaceutical industries, *needs special expertise*. In spite of the high rates of nucleophilic phosgene reactions, there is a constant danger in carrying out phosgenation reactions that stems from the need to store phosgene, and the use of phosgene solutions is inevitably associated with hazards relating to the dynamics of external feeding.

A handbook on phosgenation requires a review of the organic chemistry of phosgene, with particular emphasis on the needs of organic chemists who require practical procedures to enable them to use the reagent safely and, in specific cases, to offer alternative methods when phosgene is not easily available.

The substitution of phosgene by alternative reagents is an important subject in the fine chemicals industry, particularly for pharmaceutical and agrochemical syntheses.

Most of the patents relating to phosgenation processes claim not only phosgenation by phosgene gas, but also by the main phosgene substitutes. The term *"the synthesis was performed by using phosgene or its derivatives (oligomers)"* has become not only a patent covering expression, but a true indication of the utility of alternative phosgene equivalents.

The principal aim of the book is to review, select, and order in a practical way the numerous methods known as "phosgenation".

The authors have both gained experience in phosgenation chemistry over several decades.

H.E. writes: – "Thirty years ago, I started my doctoral thesis with a preparation of 2-chloroethyl chloroformate from phosgene on a 600 g scale. My supervisor was Ivar Ugi, an expert in phosgene chemistry, and Ugi's tradition in this field has been continued, particularly in isocyanide chemistry. In 1986, I rediscovered *triphosgene* and realized its potential, in principal, as a substitute for phosgene in

nearly all reactions of the latter. This methodology led to patent applications. For several years, my company "Dr. Eckert GmbH" was the sole producer and distributor of triphosgene on the world market. Some further patents followed on "safety phosgenation" and "tetrachloromethane-free" phosgene. In 2002, the 25th year of Dr. Eckert GmbH, I placed the leadership in the hands of the next generation, in order to give them the opportunity to demonstrate competence and responsibility."

L.C. writes: – "My interest in the preparative chemistry and reactivity of phosgene equivalents started in 1974 during PhD studies on carbonic acid derivatives with regard to technologically important chlorinated alkyl carbonates. The search for a synthetic strategy that would exploit good leaving groups adjacent to carbonyl functions and, thus, equivalent to the chlorine atoms of phosgene led to the rediscovery of triphosgene as a phosgene substitute. One main contribution devoted to the synthesis of this compound concerned the scale-up (10–100 kg) of the solvent-free method for its preparation, and the coupled "cyclic phosgenation process" starting from dimethyl carbonate, methanol, and chlorine. I studied the multi membered cyclic transition-state mechanism of nucleophilic substitution (alcoholysis and aminolysis) of chlorinated carbonates and isocyanates, and found several medium-scale applications in the synthesis of active pharmaceutical ingredients (APIs). Recently, several studies on the catalytic and safe decomposition of triphosgene have been published."

Our feeling, according to our long experience in the development of practical routes employing phosgene or phosgene equivalents, is that the '*palette*' of phosgenation reactions will grow more and more. Our task in writing this book has thus been to present the appropriate methods for carrying out reactions and for the preparation of reagents.

July 2003
Livius Cotarca Heiner Eckert

1
Contradictions

Phosgene is a substance of great contradictions.

On the one hand, **phosgene** is central to the chemistry of pharmaceuticals, polyurethanes, and polycarbonates; a huge market sector generating 8 million tons of products with an immense market value has been established. **Phosgene** is also useful in recently developed production processes for the manufacture of high purity *diamonds* [1] and of the nutritive sweetener *aspartame* [2] (see Section 4.3.5.4), as well as in highly innovative nanotechnology research as a *"fuel"* for the first *"molecular motor"* [3] (see Section 5.5). On the other hand, for some people **phosgene** is the incarnation of evil, primarily stemming from its use as a warfare agent in World War I [4], but it has also gained a fearsome reputation through its role in chlorine chemistry and as a highly reactive chemical.

Central to the concerns about the use of **phosgene** is its high toxicity, which has led to a TLV of 0.1 ppm (for a definition of TLV, see Section 3.4), and people fear the gas enormously. There is another highly volatile chemical with the same TLV of 0.1 ppm, namely *acrolein* (vapor pressure 29,000 Pa at 20 °C; for comparisons see Table 3.3, Section 3.3), which is generated in substantial amounts in everyday life at barbecue parties by roasting foods; people do not pay attention to it at all, even though the health hazards are similar to those associated with phosgene, such as potential lung edema after several hours.

Some procedures/processes have been developed to produce isocyanates by *phosgene-free* routes (see Section 4.3.1), citing the avoidance of dangerous **phosgene** for reasons of safety. In this connection, it is remarkable that the toxicities of alkyl isocyanates, such as *methyl isocyanate* (leaked from the Union Carbide plant in Bhopal/India in the disastrous accident at midnight, 2–3 December, 1984) with a TLV of 0.005 ppm, far exceed that of phosgene (TLV 0.1 ppm). Another way of substituting phosgene involves reacting rather low-energy molecules, such as ureas, at high temperatures (see Section 6.2.2.2). Such heat-powered reactions are mostly unselective and favor side reactions and the formation of by-products, thus increasing waste. Moreover, the excess thermal energy contributes to the greenhouse effect, and thus these reactions are *environmentally* unfavorable.

The net result of these contradictory factors is that for all phosgenation reactions, by which we mean all reactions that can be achieved by the use of **phosgene**, all relevant intrinsic (*yield*, *reactivity*, *handling*, *work-up*) and extrinsic (*safety*,

toxicity, *environmental impact*) criteria (see Chapter 6) have to be weighed against each other, and the best methods and reagents for the desired transformation should be worked out or developed, free of ideological indoctrination. This may or may not point to the use of phosgene itself.

The aim of this book is to present the state-of-the-art on phosgenation chemistry, including all its *phosgene equivalents and substitutes* (some 70 are dealt with in this book), resulting in many novel reactions and processes for improved methods to obtain "phosgenation" products (see Chapters 4 and 5).

A second concern of this book is to show the modern trend of producing **phosgene** *captively*, and *on demand*, thereby minimizing storage (see Section 2.1.2), as well as the efforts to combine safe equivalents with the sometimes superior properties of phosgene in so-called *safety phosgenation*, which involves no storage of phosgene. The **phosgene** is generated *on demand* and immediately consumed, and so the quantity actually present in the reaction system is minimized (see Sections 2.2.2.1 and 7.1.2).

A third, forward-looking concern of this book is the presentation of examples of processes that meet the requirements of *"green chemistry"*, which are often syntheses using carbon dioxide, such as the production of **dimethyl carbonate** from methanol (see Section 4.3.3.8). The other class of reactions in this branch of chemistry are smart catalytic reactions, through which the generally high activation energies of phosgenation reactions can be lowered, thus saving energy. Further considerations on trend-setting will be mentioned in Chapter 9 – Outlook.

References

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2 J. S. Tou, B. D. Vineyard, *J. Org. Chem.* **1985**, *50*, 4982–4984.

3 T. R. Kelly, R. A. Silva, H. de Silva, S. Jasmin, Y. Zhao, *J. Am. Chem. Soc.* **2000**, *122*, 6935–6949.

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2
Phosgenation Reagents

Phosgene is a typical highly reactive chemical used since the beginning of the chemical industry. It has been produced on a large scale and used as an intermediate in the dye and polymer (urethane) industries for many years in Europe and the U.S. [1–3]. The compound carries emotional baggage resulting from its use as a warfare agent during World War I.

Among other technologies for the production of fine chemicals, *phosgenation* has attracted much attention. **Phosgene** is currently used to produce *isocyanates* (intermediates for polyurethane resins and pesticides) from amines, *chloroformate esters* and *organic carbonates* from alcohols, *polycarbonates*, *acid chlorides* from carboxylic acids, *nitriles* from carboxamides, *isonitriles* from *N*-formylated compounds, and *heterocyclic compounds* from difunctional substrates. Several *carbamates* and *ureas* have useful biological activities, and some derivatives thereof have proven to be potent HIV-1 protease inhibitors. These applications produce many important intermediate compounds, including some that are employed in the synthesis of peptides [4–6], and in the activation of poly-*N*-[2-hydroxy-1,1-bis(hydroxymethyl)-ethyl]acrylamide gels for affinity chromatography [7]. The production and use of **phosgene** is under close scrutiny in view of the storage and use of large amounts of chlorine and carbon monoxide, the production of large volumes of waste containing chlorinated by-products, and the high risk of storing and transporting a volatile and very toxic compound. Despite these concerns, 5–6 million tons y^{-1} of **phosgene** are produced and used worldwide.

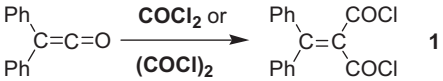
Because of its highly toxic nature, the handling of **phosgene** *gas*, either on a small scale in the laboratory, or on a medium to large scale in the agrochemical and pharmaceutical industries, needs special expertise. The constant danger in carrying out phosgenation reactions also results from the phosgene storage and from the use of solutions, and it is furthermore associated with the dynamics of external feeding. The *in situ* generation of phosgene would offer greater safety because the high rate of nucleophilic phosgene reactions ensures low stationary concentrations and hence safer reaction conditions.

Both the transportation and storage of **phosgene** pose considerable risks. *Phosgenations* are currently undertaken at the production site of the phosgene. Thus, all other reagents and starting materials have to be brought to the **phosgene**. This entails a high degree of planning, with its associated costs and time.

The need to replace phosgene by substitutes not only stems from considerations relating to its high toxicity, but is also due to the fact that its production and use involve chlorine as a raw material and result in the generation of large amounts of halogenated by-products since chlorine is not present in the majority of its end products [8]. A general discussion on the complex criteria for selecting a **phosgenation reagent** is given in Chapter 6.

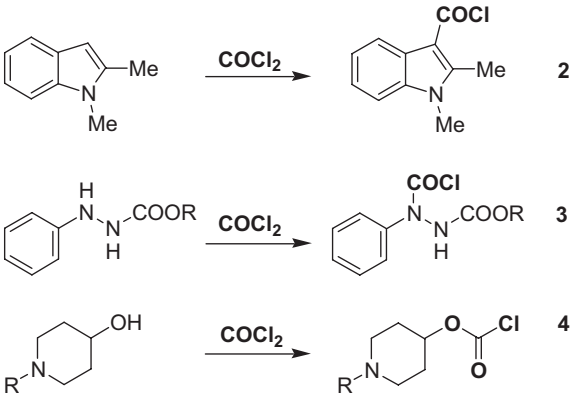
In recent years, **trichloromethyl chloroformate** (**diphosgene**) [4, 9] and **bis-(trichloromethyl) carbonate** (**triphosgene**) [10–15] (for reviews, see [16–20]) have frequently been used in organic synthesis as **phosgene** *sources* [11, 21]. These liquid and crystalline *phosgene equivalents*, respectively, have the advantage of being much easier to handle than the *gaseous* **phosgene**.

A long list of *phosgene substitutes* has been proposed and investigated. **Catechol phosphorus trichloride** reacts with compounds containing C=O, P=O, S=O, RO, PO, and SiO groups to give the corresponding chloro derivatives. **Oxalyl chloride** can be an effective alternative chloroformylating agent to phosgene. The reaction of oxalyl chloride with diphenyl ketene, for example, proceeds under milder conditions than that with phosgene to give the identical organic product **1** [22].

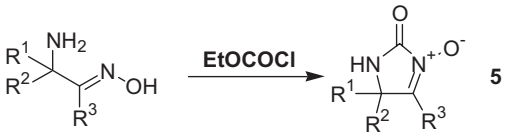


1

Aryl and *alkyl* **chloroformates**, *chlorinated chloroformates* (**diphosgene**), and *chlorinated carbonates* (**triphosgene**) can be used to convert carboxylic acids to the corresponding chlorides. The formation of alkyl chlorides from alcohols using these reagents is also possible. In many cases, however, such derivatives are difficult, or impossible, to prepare, in which case **phosgene** has to be employed. Some examples yielding **2**, **3**, and **4** are given below [23–25].

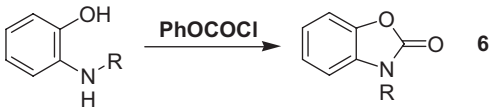


The carbonylating property of **phosgene** can be successfully realized using as substitute reagents lower alkyl chloroformates, such as **ethyl chloroformate**, which is particularly suitable as a ring-closing reagent in the synthesis of imidazoline derivatives **5** [26]; see also Chapter 6.



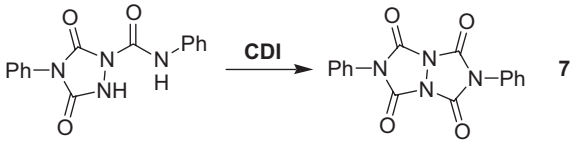
5

Compared to the reaction with **phosgene**, better yields are obtained in this reaction when the R substituents are small alkyl groups, such as methyl or ethyl, although in other cases the reaction was found to be better when phosgene was used. Cyclic carbamic acid derivatives **6** have been similarly prepared using **phenyl chloroformate** [24]; see also Chapter 6.



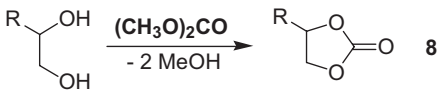
6

1,1-Carbonyldiimidazole (**CDI**) is used as a *phosgene equivalent* for many carbonylations, giving yields of **7** comparable of that achieved with **phosgene** [24]; see also Chapter 6.

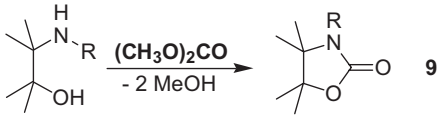


7

Dimethyl carbonate is a recognized substitute for **phosgene** in many carbonylation and ring-closing reactions, affording **8** and **9**, respectively [27].



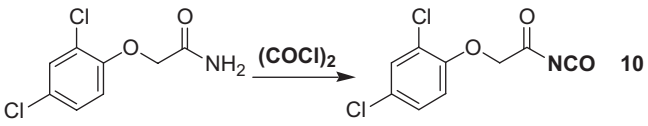
8



9

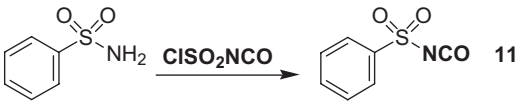
Although there are many alternative routes for the synthesis of isocyanates [24] (see also Chapter 4), none are as simple or as attractive as the carbonylation of primary amines with **phosgene**. This is reflected by the widespread employment of phosgene in the industrial manufacture of isocyanates; the use of **phosgene** continues despite numerous attempts to find suitable alternatives (see Chapter 4). However, **acyl isocyanates** such as **10** cannot normally be prepared by the reaction of **phosgene** with the corresponding carboxylic acid amide, since the phosgene

causes dehydration of the amide group to the corresponding nitrile. In this case, **oxalyl chloride** is effective [24].



10

Chlorosulfonyl isocyanate can be used in place of phosgene to prepare sulfonyl isocyanates **11** [24]; see also Chapter 4.



11

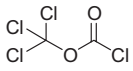
Thionyl chloride, **phosphorus(V) chloride**, and **triphenylphosphine**/**tetrachloromethane** can be used to convert monosubstituted amides into chloro imines. These reagents, as well as **oxalyl chloride**, also transform disubstituted amides into the corresponding imidium chloride salts.

Dehydration is a process for which many phosgene "competitors" have proved useful. **Thionyl chloride**, **phosphorus pentoxide**, **phosphorus oxychloride**, **triphenylphosphine**/**tetrachloromethane**, and **catechol phosphorus trichloride** are the reagents of choice in many dehydration processes.

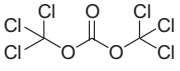
Several methodologies are directed toward the development of mild and safe reagents that can be utilized instead of **phosgene** in organic synthesis [28]. Most of these reagents are themselves prepared from **phosgene**. For example, **bis(4-nitrophenyl)carbonate** [29], **1,1-carbonyl-bis(imidazole)** (**CDI**) [30], **1,1-carbonyl-bis(benzotriazole)** [31], **phenyl chloroformate** [32], and **di-*tert*-butyl dicarbonate**, **$(Boc)_2O$** [33] are prepared from **phosgene**. In a few exceptions, **diphosgene** and **triphosgene** are used instead. In fact, the term **triphosgene** applied to **bis(trichloromethyl) carbonate** is a misnomer, since this compound is not derived from **phosgene** but by exhaustive chlorination of dimethyl carbonate [16]. Scheme 2.1 shows the structures of *phosgene equivalents* and their abbreviations.

There is opinion that employing these reagents is merely a way of circumventing and not of facing and solving the problem of avoiding the use of **phosgene**. However, the question becomes much more complex if process safety is taken into consideration and used as a reagent selection criterion (see Chapter 6). *Phosgenation* is undoubtedly a key step in the synthesis of many pharmaceuticals and agrochemicals. Small- or medium-scale operations require *intrinsic safety*, which must be ensured either by the stabilities of the raw materials (reagents), intermediates, and products, or by hazard minimization during the operation. Consequently, employing *phosgene-free reagents* or *phosgene-like raw materials* with controlled phosgene release during reaction, and the design of safer methods, are important goals with regard to these organic processes.

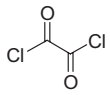
Phosgene



Trichloromethylchloroformate (Diphosgene)



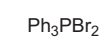
Bis(trichloromethyl)carbonate (**BTC**) (Triphosgene)



Oxalyl chloride

Phosphorus oxybromide

Phosphorus oxychloride



Dibromotriphenyl phosphorane

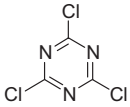
Phosphorus pentoxide

Boron tribromide

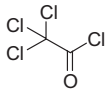
Boron trichloride

Thionyl chloride

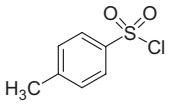
Thionyl bromide



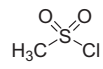
Cyanuric chloride (**CyCl**) 2,4,6-trichloro-1,3,5-triazine



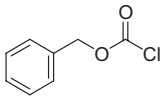
Trichloroacetyl chloride



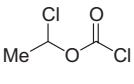
Tosyl chloride (**Tos-Cl**) *p*-Toluenesulfonyl chloride



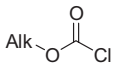
Methanesulfonyl chloride (**Ms-Cl**)



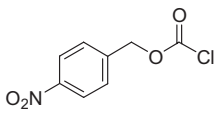
Benzyl chloroformate (**Z-Cl**)



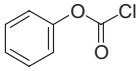
1–Chloroethyl chloroformates



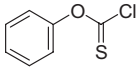
Alkyl (Me,Et) chloroformates



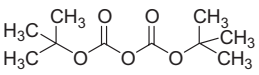
4-Nitrobenzyl chloroformate (**NZ-Cl**)



Phenyl chloroformate

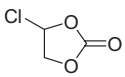


Phenyl chlorothionoformate

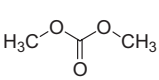


Di-*t*-butyl dicarbonate (**Boc_2O**)

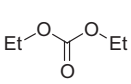
Ethylene carbonate (**EC**)



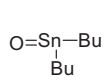
Chloroethylene carbonate



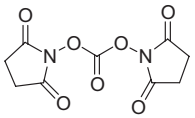
Dimethyl carbonate (**DMC**)



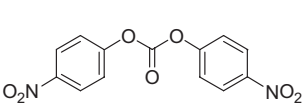
Diethyl carbonate



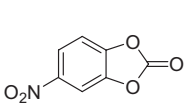
Dibutyltin oxide



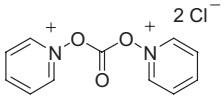
Disuccinimidyl carbonate (**DSC**)



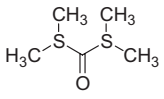
Bis(4-nitrophenyl)carbonate (**DNPC**)



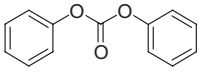
Nitrophenylene carbonate (**NPC**)



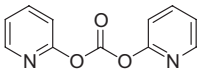
Pyridine N-oxide carbonate



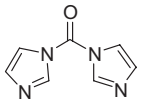
S,S-Dimethyldithio carbonate



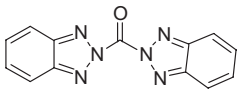
Diphenyl carbonate (**DPhC**)



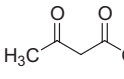
Di-2-pyridyl carbonate (**DPC**)



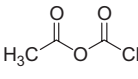
1,1-Carbonyldiimidazole (**CDI**)



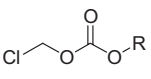
1,1-Carbonylbisbenzotriazole



Ethyl acetoacetate



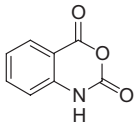
Acetic anhydride



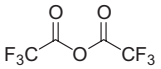
α-Chloroalkyl alkyl carbonates

Diphenylphosphoryl azide

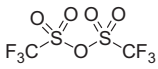
Scheme 2.1. **Phosgene equivalents** and **substitutes**: structures and abbreviations; order according to Table 7.2, Section 7.2.



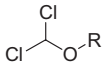
Isatoic anhydride



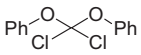
Trifluoroacetic anhydride (**TFAA**)



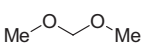
Trifluoromethanesulfonicanhydride (Triflic anhydride) (**Tf_2O**)



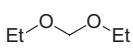
1,1-Dichloromethyl Me or Et ether



Dichlorodiphenoxy methane



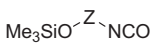
Formaldehyde dimethylacetal (methylal)



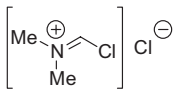
Diethoxymethane

Carbon monoxide

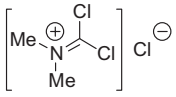
Carbon dioxide



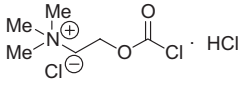
Trimethylsiloxane isocyanates



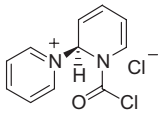
(Chloromethylene) dimethylammonium chloride (**Vilsmeier reagent**)



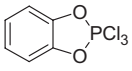
(Dichloromethylene) dimethylammonium chloride (**Viehe's salt**)



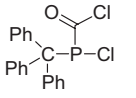
Choline chloroformate hydrochloride



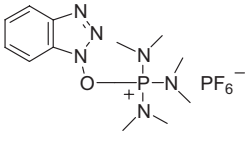
Pyridine-phosgene adduct (**2-DHPP**)



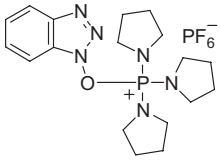
Catechol phosphorus trichloride



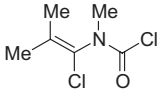
Chlorocarbonyl-chloro-triphenylmethane phosphine



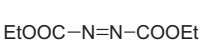
Benzotriazol-1-yloxytris (dimethylamino)-phosphonium hexafluorophosphate (**BOP**)



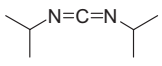
Benzotriazol-1-yloxytripyrrolidino-phosphonium hexafluorophosphate (**PyBOP**)



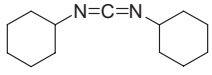
Phosgene-imine adduct



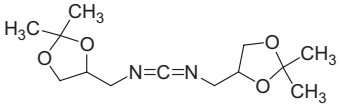
Diethyl azodicarboxylate (**DEAD**)



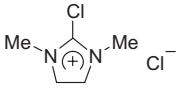
Diisopropylcarbodiimide



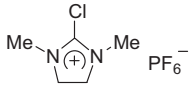
Dicyclohexylcarbodiimide (**DCC**)



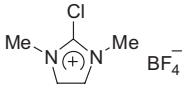
1,3-Bis(2,2-dimethyl-1,3-dioxolan-4-ylmethyl)carbodiimide (**BDDC**)



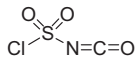
2-Chloro-1,3-dimethyl-imidazolium chloride (**CDC**)



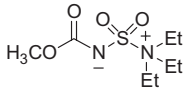
2-Chloro-1,3-dimethyl-imidazolium hexafluorophosphate



2-Chloro-1,3-dimethyl-imidazolium tetrafluoroborate



Chlorosulfonyl isocyanate



(Methoxycarbonylsulfamoyl) triethylammonium-N-betaine (**Burgess reagent**)

Scheme 2.1 *(continued)*

Procedures employing *phosgene equivalents* can also be applied to the large-scale preparations of those carbamates, ureas, or heterocyclic compounds that are difficult to synthesize efficiently by other and safer methods, mainly compounds bearing different functionalities and incorporating chiral carbons in the side chains. In this regard, a first crucial step towards more environmentally friendly approaches to ureas was taken with the use of **bis(4-nitrophenyl)carbonate**, ***S,S*-dimethyldithiocarbonate**, **1,1-carbonyl-bis(imidazole)**, **di-*tert*-butyl dicarbonate**, and **phenyl chloroformate** [28].

The most appealing and promising strategy, however, is the *carbonylation* of amines and/or nitro compounds with **carbon monoxide** over transition metal complexes, which permits the use of safer raw materials. These reactions are catalytic and do not produce large amounts of saline by-products [34, 35].

A further important improvement, which allows the manufacture of **ureas** with concomitant reduction of waste at source (i.e. avoiding the production of large amounts of saline by-products, which represent the main constituent of chemical waste) has been the application of **carbon dioxide**. This strategy combines the use of a non-toxic reagent with the benefit of reducing the emission of **CO_2** in a direct way by fixation of the molecule into other molecules [36–38].

2.1 Phosgene

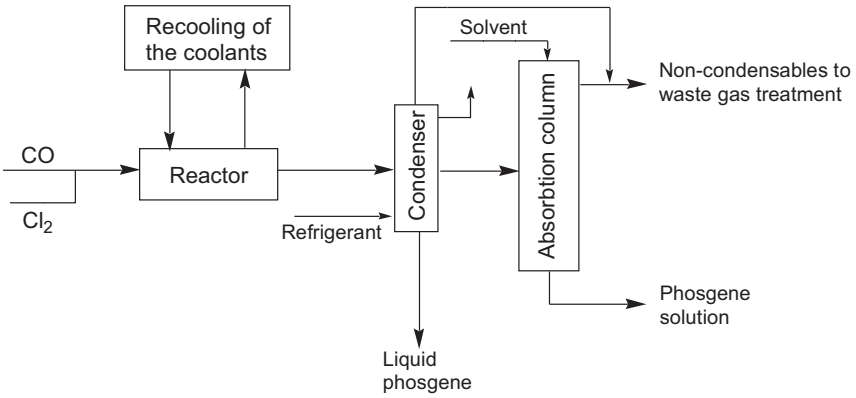
Phosgene (carbonyl dichloride) is a colorless reactive gas with a bp of 8.2 °C, a vapor pressure at 20 °C of 162,000 Pa or 1215 mmHg, and a vapor density of 3.5. Phosgene was first prepared by John Davy in 1812 by the action of light on a mixture of chlorine and carbon monoxide.

The current scale of world phosgene consumption is $5–6 \times 10^6$ tons y^{-1}. The vast majority of phosgene is utilized at its site of production: only very small quantities are shipped. Only *Van De Mark* (now part of *SNPE*), located in Lockport, N.Y., sells **phosgene** on the merchant market. Traditionally, small-scale consumers of **phosgene** had little choice but to buy it from *Van De Mark*. Because of its toxicity, small or zero inventories of **phosgene** are usually maintained, although it is easily liquefied.

Phosgene can be prepared from carbon monoxide, from halogenated hydrocarbons, from carbonaceous materials, from carbon dioxide, carbonyl sulfide or carbon disulfide, and from other oxygenated compounds [39]. The method based on the chlorination of carbon monoxide is by far the most important and has been scaled-up for the commercial manufacture of phosgene.

2.1.1 Conventional Manufacturing Processes

Phosgene is produced commercially by the highly exothermic vapor-phase reaction of anhydrous chlorine gas with high-purity carbon monoxide in the presence of an



Scheme 2.2. Simplified flow chart for the production of **phosgene**.

activated carbon catalyst [1]. The enthalpy of formation is -107.6 kJ mol^{-1}, hence efficient heat removal is required.

$$CO(g) + Cl_2(g) \longrightarrow COCl_2(g)$$

The basic manufacturing process for phosgene has not changed significantly since the 1920s and comprises the preparation and purification of the raw materials, carbon monoxide and chlorine, the metering and mixing of these materials, the reaction of the mixed gases over activated charcoal, and the purification and condensation of the phosgene product. A flow diagram of the process is illustrated below (Scheme 2.2).

The process is normally operated on a continuous basis, employing a high degree of automation. Owing to the toxicity of phosgene, extensive safety features are an integral part of the plant design. The reaction is rapid and nearly quantitative with respect to both raw materials. Traditionally, **phosgene** is produced from large-scale units running at a steady state, and the product requires downstream storage. The plants are provided with a safety absorption system, whereby any surplus **phosgene** is absorbed and destroyed with a circulating caustic solution. This kind of process is only well-suited for large users and it engenders a lot of environmental concerns.

Detailed descriptions of the *basic manufacturing processes* are given in several important references [40–43].

A summary of recently filed patent applications and granted patents regarding **phosgene** preparation is presented in Table 2.1.

Phosgene produced by the traditional processes will typically contain 400–500 ppm by weight tetrachloromethane (the major world producers claim a CCl_4 content of 50–400 ppm). The amount of tetrachloromethane needs to be evaluated on the basis of the total worldwide production of phosgene. In relation to the cumulative effect of recycling *polycarbonates* (the major polymeric material for which phosgene is a raw material), tetrachloromethane has been shown to have both

Tab. 2.1. Recently disclosed processes for the preparation of **phosgene**.

Patent/Application Number	*Authors*	*Owner*	*Main Claims of the Patent*
DE 19916856 A1 23/09/**1999**	H. Eckert, B. Gruber, J. Auerweck	Dr. Eckert GmbH, Hallbergmoos, DE (D-85399)	Phosgene manufactured from CO, Cl_2, and metal (Al, Ga) halide (Cl) catalyst. Low CCl_4 contents of <1 ppm in batch process.
US 5891319 06/04/**1999**	F. J. Freiere, K. B. Keating, E. K. Sakata	DuPont, USA	Electrochemical, low-temperature, uncatalyzed process for the production of carbonyl halides (not specific to phosgene).
WO 9914159, **1999** EP 1017623 B1, **2002** US 6399822 B1, **2002** JP 2001516692, **2001** DE 1974057, **1999** (15/09/**1997**)	H. Eckert, B. Gruber, N. Dirsch	Dr. Eckert GmbH, Hallbergmoos, DE (D-85399)	Method and device for preparing phosgene from diphosgene and/or triphosgene, by reaction on a catalyst comprising compounds with one or several N atoms with a pair of deactivated electrons.
PCT WO 9828227 02/07/**1998**	W. Cicha, L. E. Manzer	DuPont, USA	Process for producing phosgene from CO and Cl_2 using a carbon catalyst having an active metal content of $\geq$1000 ppm.
JP 10120410 A2 12/05/**1998**	S. Nakano	Teijin Chem. Ltd., Japan	Phosgene manufactured in the presence of an activated C catalyst, by the reaction of Cl_2 and CO containing $\leq$6.0 mol% H. Yellowing of the phosgene obtained is prevented by reducing the H content in CO.
PCT WO 9800364 08/01/**1998**	W. Cicha, L. E. Manzer	DuPont, USA	Process for producing phosgene having a low CCl_4 content from CO and Cl_2 at $\leq$300 °C using a silicon carbide catalyst prepared by contacting silicon monoxide with finely divided carbon.
JP 9059012 A 04/03/**1997**	T. Hosomi, T. Takada	Mitsubishi Gas Chem. Co., Japan	Crude phosgene having a CCl_4 content of $<$100 ppm (v/v) is produced from CO and Cl_2 using active carbon as catalyst. The crude phosgene is liquefied at

Tab. 2.1 *(continued)*

Patent/Application Number	*Authors*	*Owner*	*Main Claims of the Patent*
			−40 to +7 °C, and optionally further evaporated at 9–25 °C to obtain purified product. $COCl_2$ of purity >99 wt% and with a CCl_4 content of <10 ppm (*w*/*w*) can be produced by this process. The methane content of the CO used as raw material is preferably <100 ppm.
PCT WO9730932 A1 28/08/**1997**	W. Cicha, L. E. Manzer	DuPont, USA	Process for producing phosgene from CO and Cl_2 using a carbon catalyst having an active metal content of ≤1000 ppm.
EP 796819 A1 24/09/**1997**	N. Kunisi, N. Murai, H. Kusama	Idemitsu Petrochem. Co., Japan	Reaction of CO with Cl_2 by passing both through a catalyst layer comprising active carbon as main component, which is diluted with a material (ceramic and/or metal material) that is largely inert to CO_2 and Cl_2.
WO 9719205 29/05/**1997** DE 19 543 678 28/05/**1997**	F. Gestermann, J. Dobbers, H. Rindfleisch	Bayer A.-G., DE	Process for direct electrochemical gaseous phase $COCl_2$ synthesis using a conducting membrane probe.
US 4764308 16/08/**1988** EP 0134506 B1 22/03/**1989**	H. Sauer, H. F. Porkert, D. Liebsch	Bayer A.-G., DE	Phosgene is produced by reacting Cl_2 and an excess of CO in the presence of activated charcoal in a two-stage process. In the first stage, the chlorine and CO are reacted in a tubular reactor containing activated charcoal at a temperature above 250 °C until 95–98% of the chlorine has reacted. The reaction gases are cooled to 50–120 °C, and then introduced into a second reactor maintained at 5–100 °C, where the

Tab. 2.1 *(continued)*

Patent/Application Number	*Authors*	*Owner*	*Main Claims of the Patent*
			phosgene-forming reaction is completed. The phosgene leaving the second reactor has a residual chlorine content of <50 ppm. The heat generated during phosgene formation is used to produce steam.
US 4231959 04/11/**1980** EP 003530 A1 22/08/**1979**	R. Obrecht	Stauffer Chem. Co., USA	Reaction of Cl_2 and excess CO in the presence of an activated carbon catalyst by recovering unreacted CO and recycling it to the reaction zone (contaminants: <10 wt% each of N_2 and HCl; trace amts. <1 wt% each of O_2 and CCl_4, and <100 ppm Cl_2).

significant ozone depletion and global warming potentials. Therefore, there is an interest in developing phosgene processes in which the amount of tetrachloromethane impurity is minimized.

In the production of *polycarbonates* from dihydroxylic compounds and **phosgene**, tetrachloromethane also causes a yellowing of the material, which is disadvantageous for optical applications of the polymers; a colorless product can only be achieved when the **phosgene** has a CCl_4 content <150 ppm [44].

Thus, the development of a process for producing highly pure phosgene has been one goal of research in this field. On the other hand, extensive industrial research has been dedicated to the quest for new phosgene-free routes to polycarbonates. **Diphenyl carbonate** (**DPhC**) is used as the key reagent for incorporating the carbonate functionality into polycarbonates by the so-called non-phosgene route. One of the difficulties associated with this process, however, is making the **DPhC**. Currently, **DPhC** is made from **dimethyl carbonate** (**DMC**) by transesterification with phenol (see, for example, the *Enichem* process). This reaction is equilibrium-constrained and requires a fairly complicated processing scheme. The **DMC** is in turn prepared by oxidative methylation of carbon monoxide with methanol (as in the *Enichem* process) as a preferred alternative to obviate the need for phosgene.

Several efforts have been made to lower the *tetrachloromethane* content of phosgene to below 150 ppm [44–48]. Examining the patent literature, the major tech-

nical improvements have been focussed on the catalyst; indeed, substitution or modification of the catalyst should have a minimal impact on the existing manufacturing process and should therefore require the least investment.

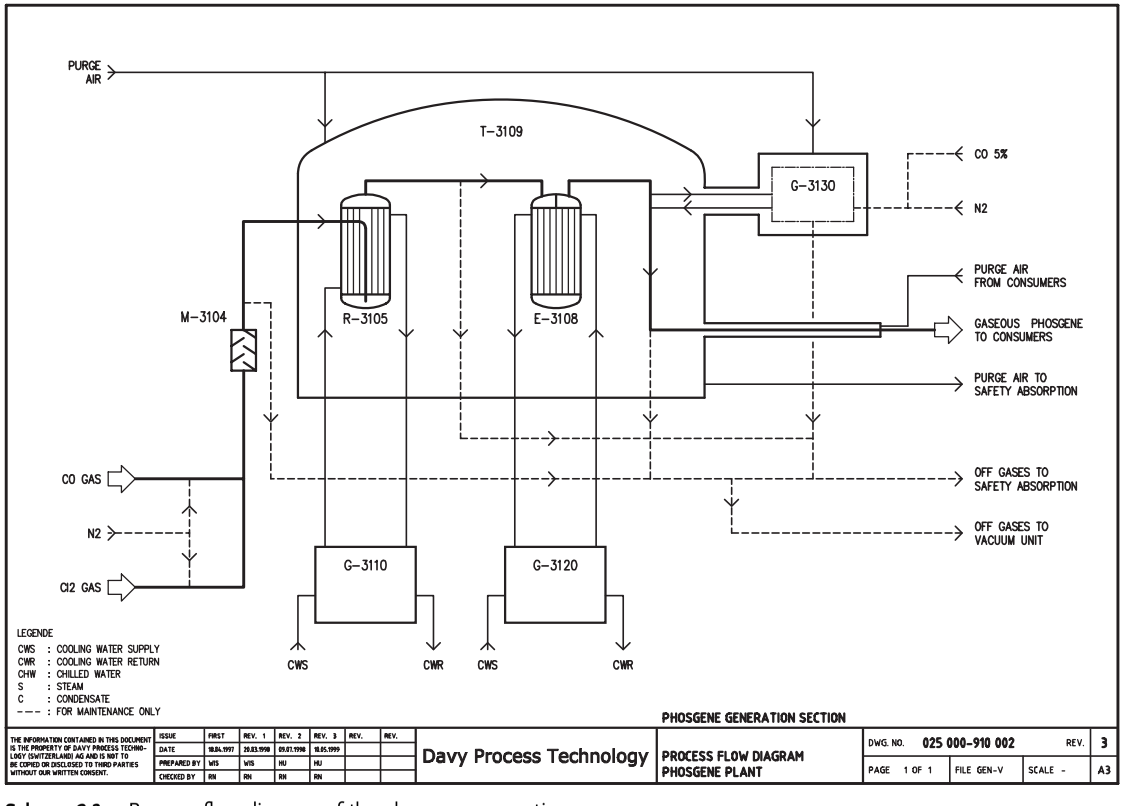
In a recent contribution to this field, a process was reported whereby **phosgene** is manufactured from chlorine and carbon monoxide under catalysis by a Group III metal halide [47]. The key feature of this process is that it uses a *carbon-free catalyst*, principally based on Group III metal (Al or Ga) halides, which avoids the formation of chlorinated carbon products. The carbon-free catalysts were applied in the production of nearly *CCl_4-free* **phosgene**, which contained as little as 1 ppm of the contaminant. The reported reaction times for a batch reaction system using $GaCl_3$ and $GaCl_2$ (3.7 mol%) as catalyst, e.g. 1.5 h and 1 h, respectively, at 1200 kPa, generating **phosgene** in 100% yield, are very promising. *Aluminum chloride* can also be used as catalyst, but reaction times are significantly longer. The reaction temperature is very low (below room temperature to 100 °C) compared to those of traditional process. An elegant feature of the process is that the catalyst is continuously regenerated and activated by resublimation. The process seems to be well-suited for scale-up and may be operated in either continuous or batch mode. The described process has important advantages considering the low level of tetrachloromethane contamination (<1 ppm) of the product, the very mild and highly versatile conditions of operation based on established chemistry, and the ready availability of the high turnover catalyst.

A further Bayer process yields **phosgene** with a CCl_4 content below 150 ppm by reacting carbon monoxide and chlorine in the presence of *elemental carbon* at 30–80 °C at a pressure of 120–400 kPa [44]. Companies such as DuPont [45] and Idemitsu [46] pursue the same approach by treating charcoal catalysts with 0.1–2.3% of active metals, thereby also producing **phosgene** with CCl_4 levels <150 ppm. **Phosgene** manufacture generally takes place in special equipment and plants.

2.1.2
Manufacturing Processes "*On Demand of Consumer*"

Another way of providing consumers on location with **phosgene** *"on demand"* is through the use of *Modular Phosgene Generators*, which are available in several output sizes ranging from 3–10,000 kg h^{-1} from *Davy Process Technology (DPT)*, Switzerland [49]. These *Modular Generators* produce **phosgene** from carbon monoxide and chlorine, and consist of two sections, the intrinsic *phosgene generator* (Scheme 2.3) and a *safety absorption* module (for commercial availability, see Section 7.1.1).

A recent publication [50] details the new *Novartis Crop Protection Inc.* plant (at Monthey, Switzerland) for the manufacture and use of **phosgene** in equipment that is considered *intrinsically safe*. Indeed, the implementation of "dynamic reactors" for the production of phosgene, which manufacture and deliver the phosgene to the users on demand as required, without intermediate storage, has made it possible to strongly reduce the quantities of phosgene contained within the plant. Furthermore, confinement of the phosgene production, supply, and utiliza-



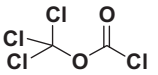
Scheme 2.3. Process flow diagram of the phosgene generation section of a *phosgene generator* from Davy Process Technology (DPT) [49].

tion equipment within a double envelope makes it possible to collect and destroy any leakage of the phosgene in dedicated installations [50].

2.2
Phosgene "Oligomers"

2.2.1
Diphosgene

Trichloromethyl chloroformate (**diphosgene**) **12** is a dense liquid, d_{15} 1.65, bp 128 °C, and vapor pressure at 20 °C of 1370 Pa or 10.3 mmHg (see Chapter 3 and [51]). The compound was used as a warfare agent during World War I and has also been called *Supralite* or *Superpalite*.



12

Kurita systematically investigated the reactivity of **diphosgene** and compared its reactions with those of phosgene [52]. Ugi proposed **diphosgene** as the reagent of choice for the synthesis of isocyanides [53].

Some of the safety hazards associated with phosgene could be circumvented by the general availability of diphosgene [1, 54]. It is readily available from the regular commercial suppliers; for sources, see Section 7.2.

The catalytic decomposition routes of **diphosgene** are extremely interesting. The compound is stable at room temperature, but decomposes to **phosgene** when heated above 300 °C [55–57], or on contact with iron(III) oxide, iron(III) chloride, or aluminum(III) chloride (less active) or activated charcoal (very active) [51].

The kinetics of the thermal decomposition of **diphosgene** has been studied over a temperature range of 260–310 °C and a pressure range of 4–17 mmHg. The reaction has been found to be first order and homogeneous, with catalysis by the glass walls of vessels having only a slight influence [56]. The rate constant is given by the expression: $k_1 = 1.4 \times 10^{13} e^{-14.500/RT}$.

The possible equilibrium between phosgene, carbon monoxide, and chlorine was not found to arise as a result of the reaction, the sole product of decomposition being **phosgene**.

The formation of *N*-carboxy α-amino acid anhydrides with diphosgene is usually unsuccessful without prior decomposition of the diphosgene to phosgene [58]. **Diphosgene** decomposes instantly to give phosgene under catalysis by *active charcoal*, making the method as rapid as the phosgene stock solution method [58] (see Section 4.3.5).

Decomposition to *tetrachloromethane* and *carbon dioxide* occurs on exposure to alumina [51, 55, 57, 60].