Organic Process Research & Development **1999**, *3,* 377

Letters to the Editor

Comment on "Chemical Safety. Safe Handing of Triphosgene [bis(trichloromethyl)carbonate]"

To the Editor:

A very interesting debate has been promoted on the safe handling and shipping of triphosgene by authored journals (*Chemical and Engineering News*, July 13, 1992, p 4 and February 8, 1993, p 4) some time ago. Very useful advice given by experts in the field at that time have not replaced the lack of qualitative and quantitative data on thermally or chemically induced decomposition of the high chlorine content derivative of carbonic acid.

In the meantime the tremendous growth of phosgeneless methods including triphosgene chemistry during the past decade was surprising, offering to the research laboratories milder and easier controllable conditions for phosgenations.[1]

Recently, some important contributions to the control of triphosgene stability have been brought to the attention of the chemical community. One of these contributions tested as a current method from some years ago in our laboratory is the prepackaged cartridge for intelligent phosgene production based on the triphosgene "depolymerization" using a catalyst containing one or several nitrogen atoms with a pair of deactivated electrons (German Patent DE 19740577 A1, March 18, 1999, *CA 130:211406,* and WO9914159A1, *Method and Device for Preparing Phosgene from Diphosgene and/or Triphosgene*, inventors H. Eckert, B. Gruber, and N. Dirsch).[2] This cartridge to produce phosgene offers optimal safety as limited amounts of phosgene are produced only when needed and on the scale required, from its crystalline precursor, without storage, and then it can be added directly to the reaction vessel where it is to be used.[2]

Studies performed in our laboratory in order to identify and quantify the triphosgene and diphosgene decomposition pathways suggested that there are two limiting cases:

(i) the presence of an excess of a protic nucleophile with oxygen, nitrogen, sulfur, etc. and

(ii) the "less than stoichiometric" molar ratio or in the absence of nucleophilic reagents, and in the presence of a specific catalyst able to stimulate the catalysis by a "naked" chloride anion generated in situ or delivered from outside the reaction system.

In the first case (i) by using common methods (MS, GC, ReactFTIR, NMR, etc.) we were not able to identify phosgene as a reaction species but the formation of much less reactive oxygen or nitrogen derivatives of carbonic acid, e.g., chloroformates, unsymmetrical trichloromethyl carbonates in the case of solvolysis, and trichloromethyl carbamates and ureas in the case of aminolysis, respectively.

Therefore the statement: *"The toxicity of both diphosgene and triphosgene is exactly the same as phosgene since both decompose to phosgene on heating and upon reaction with any nucleophile. Even a trace of moisture leads to formation of phosgene."* (Damle, S. B., *Chemical and Engineering News*, February 8, 1993, p 4) may be reinterpreted today in the light of these experiments and disclosure. There are conditions for nucleophilic reactions of triphosgene where the concentration of gaseous or solute phosgene is definitely below the safety limits imposed by the industrial processes.

In the second case (ii) triphosgene "depolymerization" to gaseous phosgene is a catalytically and temperature controlled process. It can be used as a very safe laboratory source of limited amounts of gaseous phosgene.

The constant danger in carrying out phosgenation reactions also results from the storage of phosgene and the use of solution, and it is undoubtedly associated with the dynamics of external feeding. The in situ generation of phosgene would bring instead much more safety because the high rate of nucleophilic phosgene reactions ensures low stationary concentrations and, hence, safer reaction conditions.

Triphosgene is now produced on a commercial scale at the level of hundreds of tons per year (Aldrich, Fluka, Merck, Lancaster, Ubichem, and Punjab Chemicals). The disclosure of "controlled phosgene production from triphosgene and diphosgene by a solventless catalytic method" and the recently published manufacturing progress (*Speciality Chemicals*, September, 1998, p 281) regarding, in particular, the work-up procedures (which are critical to the stability of the product), will promote this compound on the list of the most interesting building blocks and reagents for fine chemical and pharmaceutical intermediates.

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Received for review May 20, 1999.

OP990045O

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(1) For a review, see Cotarca, L.; Delogu, P.; Nardelli, A.; Sunjic, V. *Synthesis* **1996**, 553.

(2) Triphosgene cartridges are available from Dr. Eckert, GmbH, Munich, Germany, Fax: +49 89 289 13294. Web address: http://Dr-Eckert-GmbH.com.

10.1021/op990045o CCC: $18.00