Tetrahedron Letters, Vol. 34, No. 3, pp. 395-398, 1993
Printed in Great Britain

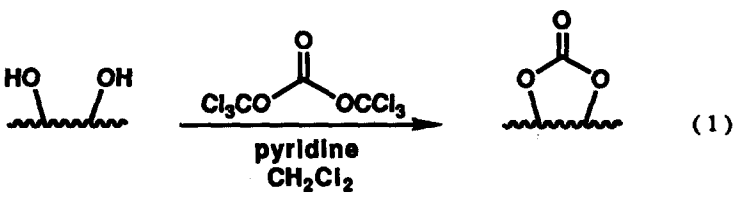
0040-4039/93 $5.00 + .00
Pergamon Press Ltd

# A Safe and Efficient Method For Conversion of 1,2- and 1,3-Diols to Cyclic Carbonates Utilizing Triphosgene

**Robert M. Burk*** **and Michael B. Roof**
Department of Chemical Sciences, Allergan Inc.
2525 Dupont Drive, Irvine, California 92715

*Abstract: Reaction of triphosgene in the presence of pyridine with a variety of diols including hindered tertiary and 1,3-cyclic diols provided high yields of the corresponding cyclic carbonates.*

Proper choice of protecting groups is critical in the synthesis[1] and derivatization[2] of prostaglandins. During the course of our research it was necessary to protect 1,3-dihydroxyprostanoid intermediates with a base labile protecting group. An obvious choice was a cyclic boronate which has previously been used in protection of prostaglandins as 9,11-cyclic boronates[3] when selective functionalization of the 15-hydroxyl group was desired. However, cyclic boronates are highly susceptible to hydrolysis and therefore can not be conveniently handled in multiple chemical sequences. For this reason we decided upon use of a cyclic carbonate but were surprised to discover that no general methodology existed for this transformation. Although there are numerous documented procedures for conversion of 1,2-diols and 1,3-acyclic diols to cyclic carbonates using phosgene, *p*-nitrophenyl chloroformate, trichloroacetyl chloride, 1,1-carbonyldiimidazole or carbon monoxide our attempted employment of these procedures[4] with 1,3-cyclic diols were either unsuccessful or very low yielding. In this note we wish to describe the use of triphosgene in a highly efficient method for protection of diols, especially 1,3-dihydroxycyclopentanes, as cyclic carbonates (Eq. 1).




(1)

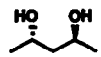
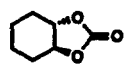
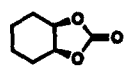
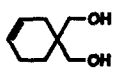
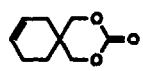
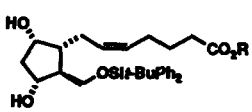
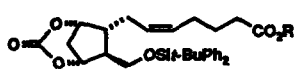
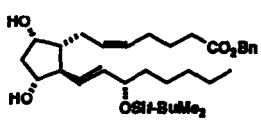
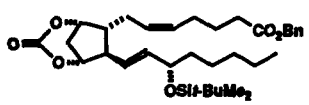
Recently, Eckert[5] reported the use of triphosgene as a safe, stable phosgene replacement and examples of its use in various chloroformylation, chlorination, carbonylation and dehydration reactions. Interestingly, to date the chemical utility of triphosgene[6] remains relatively unexploited as it has only been reported in the preparation of N-carboxy-α-amino acid anhydrides,[7] synthesis of β,γ and δ-lactams,[8] and chlorination of benzylic or allylic alcohols.[9] Similar application of triphosgene to our systems as described in the above reports ($R_3N$, THF or EtOAc or benzene, 23 → 50 °C) resulted in either no carbonylation or competing chlorination at the hydroxy positions. However, subsequent experimentation at lower temperatures, which eliminated chlorination side reactions, led to the following general procedure for carbonylation of diols as illustrated in Table 1.

In a typical small scale experiment a solution of triphosgene (0.5 equiv) in $CH_2Cl_2$ (1.0 mL) was added dropwise to a solution of pyridine (6.0 equiv) and the diol (0.5 mmol) in $CH_2Cl_2$ (1.5 mL) cooled to -70 °C. Once addition was complete the reaction was then allowed to warm to room temperature on its own accord. The resultant homogenous solution was quenched with saturated aqueous ammonium chloride and the aqueous portion was separated and extracted with $CH_2Cl_2$. The organic extract was washed with 1N HCl, saturated aqueous $NaHCO_3$, brine, dried ($Na_2SO_4$), filtered and concentrated *in vacuo*. Products were purified by flash column chromatography on silica gel.

In conclusion, we have provided a new, general procedure for protection of 1,3-dihydroxycyclopentanes as cyclic carbonates. The reported methodology can also serve as an alternative for carbonate protection of various diols including hindered 1,3-acyclic and 1,2-cyclic diols. We anticipate further applications of triphosgene use in the protection of this functionality in the future.

**Acknowledgment:** The authors acknowledge the encouragement and support of Dr. Michael E. Garst.

**Table 1. Synthesis of Cyclic Carbonates With Triphosgene[a]**

| Entry | Diols | Carbonates | Yield(%)[b] |
|---|---|---|---|
| 1. |  |  | 87 |
| 2. |  |  | 92 |
| 3. |  |  | 84 |
| 4. |  |  | 99 |
| 5. |  |  | 83 |
| 6. |  R=$CH_3$ |  | 85 |
| 7. | R=$CH_2CH_2SiMe_3$ | | 93[c] |
| 8. |  |  | 94 |

[a]All reactions were conducted under $N_2$ atmosphere.
[b]Yield of pure products after silica gel chromatography and characterization by their $^1H$ NMR, $^{13}C$ NMR, IR and mass spectra.
[c]Yield for multigram scale reaction carried out using 10 equiv pyridine and 0.5 equiv triphosgene in $CH_2Cl_2$ (0.08 M).

**References and Notes:**


1. For comprehensive reviews on prostaglandin synthesis, please see: (a) Corey, E. J. and Cheng, X. -M. *The Logic of Chemical Synthesis*; John Wiley and Sons, Inc.:New York, 1989; Chapter 11; (b) *New Synthetic Routes to Prostaglandins and Thromboxanes*, Roberts, S. M. and Scheinmann, F. Eds.; Academic Press: London, 1982; (c) Bindra, J. S. and Bindra, R. *Prostaglandin Synthesis*, Academic Press: London, 1977; (d) Mitra, A. *The Synthesis of Prostaglandins*, John Wiley and Sons, Inc.: New York, 1977.

2. For recent examples and leading references: (a) Collins, P. W.; Kramer, S. W.; Gasiecki, A. F.; Weier, R. M.; Jones, P. H.; Gullikson, G. W.; Bianchi, R. G.; Bauer, R. F. *J. Med. Chem.* **1987**, *30*, 193; (b) Collins, P. W.; Gasiecki, A. F.; Jones, P. H.; Bauer, R. F.; Gullikson, G. W.; Woods, E. M.; Bianchi, R. G.; *Ibid.* **1986**, *29*, 1195; (c) Bundy, G. L.; Morton, D. R.; Peterson, D. C.; Nishizawa, E. E.; Miller, W. L. *Ibid.* **1983**, *26*, 790; (d) Schaaf, T. K.; Johnson, M. R.; Constantine, J. W.; Bindra, J. S.; Hess, H. -J.; Elger, W. *Ibid.* **1983**, *26*, 328; (e) Hayashi, M.; Arai, Y.; Wakatsuka, H.; Kawamura, M.; Konishi, Y.; Tsuda, T.; Matsumoto, K. *Ibid.* **1980**, *23*, 525; (f) Hayashi, M.; Miyake, H.; Kori, S.; Tanouchi, T.; Wakatsuka, H.; Arai, Y.; Yamoto, T.; Kajiwara, I.; Konishi, Y.; Tsuda, T.; Matsumoto, K. *Ibid.* **1980**, *23*, 519.

3. See reference 2c and Morozowich, W.; Oesterling, T. O.; Miller, W. L.; Lawson, C. F.; Cornette, J. C.; Weeks, J. R.; Douglas, S. L. *J. Pharm. Sci.* **1979**, *68*, 949.

4. Greene, T. W. and Wuts, P. G. M. *Protective Groups in Organic Synthesis*; John Wiley and Sons, Inc.: New York, 1991.

5. Eckert, H. and Forster, B. *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 894.

6. Triphosgene was recently reported in the preparation of the reagent di(2-pyridyl) carbonate: Ghosh, A. K.; Duong, T. T.; McKee, S. P. *Tetrahedron Lett.* **1991**, *32*, 4251.

7. (a) Wilder, R. and Mobashery, S. *J. Org. Chem.* **1992**, *57*, 2755; (b) Daly, W. H. and Poche, D. *Tetrahedron Lett.* **1988**, *29*, 5859.

8. Gill, G. B.; Pattenden, G.; Reynolds, S. J. *Tetrahedron Lett.* **1989**, *30*, 3229.

9. Goren, Z.; Heeg, M. J.; Mobashery, S. *J. Org. Chem.* **1991**, *56*, 7186.


(Received in USA 11 September 1992)