Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

The Addition of Phosgene to 2,3-Butanedione: A Facile Synthetic Entry into the 4,5-Dichloro-1,3-dioxolan-2-one Family

Joseph A. King Jr. [a]
[a] General Electric Corporate Research and Development, P. O. Box 8, Schenectady, New York, 12301

To cite this article: Joseph A. King Jr. (1993) The Addition of Phosgene to 2,3-Butanedione: A Facile Synthetic Entry into the 4,5-Dichloro-1,3-dioxolan-2-one Family, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 23:6, 847-853

To link to this article: http://dx.doi.org/10.1080/00397919308009845

SYNTHETIC COMMUNICATIONS, 23(6), 847-853 (1993)

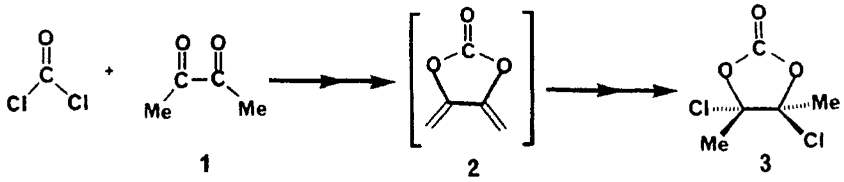
THE ADDITION OF PHOSGENE TO 2,3-BUTANEDIONE: A FACILE SYNTHETIC ENTRY INTO THE 4,5-DICHLORO-1,3-DIOXOLAN-2-ONE FAMILY

Joseph A. King Jr.

General Electric Corporate Research and Development
P. O. Box 8, Schenectady, New York, 12301

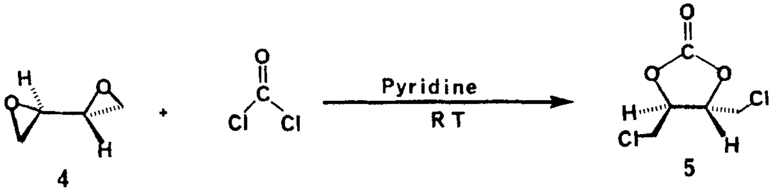
Abstract: The addition of phosgene to 1,2-Diketones at room temperature constitutes a facile entry into the 1,3-dioxolan-2-one family.

Recent pharmaceutical and medicinal interest has been shown in the chemistry of halogenated dioxolanones as intermediates in the synthesis of β-lactam antibiotics and carcinostatics.[1] Halogenated dioxolanones have been used as novel polymer precursors and for mechanistic studies, as well.[2] Previous synthetic procedures have relied on the direct halogenation (chlorination) of the requisite pre-formed dioxolanone.[3] We report here a simple, one-pot, direct addition of phosgene to 1,2-diones to produce 4,5-dichloro-1,3-dioxolan-2-ones; hence, the use of chlorine, a more virulent and corrosive reagent than phosgene, is avoided.



Scheme 1

The reaction of 2,3-butanedione (**1**) with phosgene in the presence of pyridine, produces *trans*-4,5-dichloro-4,5-dimethyl-1,3-dioxolan-2-one (**3**) in good yield (**Scheme 1**). To a stirred, cooled (4°C, ice-water bath) solution of 2,3-butanedione (16 g; 0.192 moles) and pyridine (7.6 g; 0.096 moles) in 400 ml of methylene chloride, was added 200 ml of a methylene chloride solution of phosgene (18.96 g; 0.192 moles). The addition time was 15 minutes. No temperature rise was observed to occur during the addition. A flocculent, light yellow precipitate formed as the phosgene was added to the cold reaction solution.[4] This heterogeneous solution was stirred for an additional 16 hours. During this time, the precipitate redissolved yielding a reddish-brown solution. Both the formation of **3** and the consumption of the starting material (**1**) can be followed by gas chromatography. When the reaction was complete, the solution volume was reduced to 100 ml by rotary evaporation, and then diluted with 400 ml of pentane. The organic layer was washed with water (2 x 500 ml), saturated brine solution (2 x 500 ml), and then dried over $MgSO_4$. The solvent was removed by rotary evaporation, and the resulting solid brown residue sublimed at 85°C (0.5mmHg) to yield 20.52 g (58.7%) of **3** as colorless needles; by subliming the material at 55°C (20mmHg) large clear prisms are obtained (m.p. 87.5-88°C).[5] The yield of isolated material could be improved to 82% by: (i) adding two equivalents of pyridinium hydrochloride to the starting solution and (ii) using fractional distillation to concentrate the mother liquor after drying with the $MgSO_4$.



Scheme 2

The regioselectivity of the HCl addition to form **3** was confirmed by the independent synthesis of the other possible regio-adduct of high symmetry (**5**). The addition of phosgene to (±) 1,3-butadiene diepoxide (**4**, **Scheme 2**) produced compound **5** in 75% isolated yield.[6] The symmetry of the phosgene addition to the diepoxide could be deduced from the ^{13}C-NMR spectra (3 signals). A comparison of the two compounds' (**3** and **5**) chemical shift data, the number of resonance peaks observed and their spin multiplicity, demonstrated the regiochemical preference for the formation of **3** in the initial reaction of phosgene with 2,3-butanedione. The stereochemical relationship of the two chlorines (or methyl groups) to one another could not be deduced using NMR techniques. As a result, a single crystal structure determination was undertaken. The rotation photographs demonstrated patterns which indicated a polycrystalline nature in the presence of single crystals.[7] The material (**3**) produced crystals of sufficient quality to confirm the gross molecular configuration, but suffered from several modes of disorder which made accurate bond data suspect.[8] The two chlorine atoms were determined to be trans to one another.

The reaction is believed to proceed via the intermediacy of 4,5-dimethylene-1,3-dioxolan-2-one (**2**); compound **2** is known to be highly reactive towards addition across its double bonds.[3c,9] The pyridine functions as a base catalyst (proton abstractor) which is regenerated upon reprotonation of

2.[10] Furthermore, the proposed mechanism is consistent with our observation that the yields of **3** are improved by the addition of anhydrous pyridinium hydrochloride to the initial reaction solution; the side reactions of **2** are suppressed by the competitive addition of the HCl to the double bonds. Mechanisms involving the activation of carbonyl groups by the direct nucleophilic addition of chloride ion are known as well.[11] Insufficient mechanistic work has been performed to exclude this latter possible mechanism.

The phosgene addition reaction was extended to 1,2-cyclohexadione (46% yield). Oxalyl chloride, ethyl oxalate, and benzil were found to be unreactive under these reaction conditions. The lack of reactivity of these latter three compounds lends further support for the proposed intermediacy of structures such as **2** along the reaction pathway. Furthermore, the contrast between the products from α-diketones and the homologous β-diketones is interesting. The reaction of 2,4-pentanedione produces only 4-methyl-6-methylene-1,3-dioxen-2-one (78% isolated) under our conditions; no halide containing species were observed.

Acknowledgment: The author wishes to thank Garold L. Bryant, Jr. for the acquisition of the x-ray data.

References

1. (a) Jp 60/100571 A2 [85/100471], 4 Jun 1985, 8pp: Kyoto Pharmaceutial Indistries, Ltd. (b) Can CA 1110385 A2, 6 Oct 1981, 50pp: BASF A.-G.. (c) Ger. Offen DE 2625539, 22 Dec 1977, 27pp: BASF A.-G.. (d) Bellus, D., Martin, P., Sauter, H.-P., and Winkler, T. Helv. Chim. Acta., *63*, 1130 (1980).

2. (a) Feast, J. W. and Harper, K. Br. Polym. J., *18 (3)*, 161 (1986). (b) Weinstein, B. and Orton, E. US 4525540 A, 25 Jun 1985, 6pp. (c) Feast, J. W. and Harper, K. J. Mol. Catal., *28*, 293 (1985). (d) Hinshaw, J. C. J. Chem. Soc., Chem. Commun., 630 (1971). (e) Katzhendler, J., Ringel, I., Goldblum, A., Gibson, D., and Tashma, Z. J. Chem. Soc., Perkin Trans. II, 1729 (1989).

3. (a) Ried, W. and Bedlinger, O. Chem. -Ztg., *108* (1), 15 (1984). (b) Bellus, D., Fischer, H.-P., Greuter, H., and Martin, P. Helv. Chim. Acta, *61 (5)*, 1784 (1978). (c) Scharf, H.-D. and Plum, H. Justus Liebig Ann. Chem., *1*, 27, (1977). (d) U.S. 3455954, 15 Jul. 1969, 3pp: 3M Company. (e) Scharf, H.-D, Droste, W., and Liebig, R. Angew. Chem. Internat. Edit. 7, 215 (1968). (f) Ried, W., Belhinger, O., and Bats, J. W. Chem. Ber., *116*, 3794 (1983).

4. This precipitate was found to be a diadduct of pyridine with phosgene. Although hydrolytically sensitive, this diadduct can be used as a convenient solid replacement for phosgene: King, J. A. Jr., Donahue, P. E., and Smith, J. E. J. Org. Chem. *53*, 6145 (1988).

5. Anal. calcd. for $C_5H_6Cl_2O_3$: C, 32.46; H, 3.27; Cl, 38.33. Found: C, 32.24; H, 3.13; Cl, 38.5. IR (CCl_4): ν = 1904, 1865 (c=o), 1805, 1240, 1000, 720 cm^{-1}. ^{1}H-NMR (90 MHz, $DCCl_3$) δ 2.20. ^{13}C-NMR (300 MHz, $DCCl_3$) δ149.17, 105.72, 26.48. FDMS 184 (M^+); HRMS (for ^{35}Cl) calcd. for $C_5H_6O_3Cl_2$: 183.9694. Found: 183.9694.

6. (±) 1,3-Butadiene diepoxide (4; 3.076 g, 0.0357 moles), the dipyridine adduct of phosgene (9.615 g, 0.0357 moles), and a mixed ether/methylene

chloride solvent (70 ml, 5:2 by volume) were combined in a 300 ml Fischer-Porter reactor vessel. The vessel was sealed, stirred for 16 hours at RT, and then heated at 50°C for 3 h. The solvent was removed by rotary evaporation and the resulting residue dissolved in ether (100 ml). The ether was washed with water (3 × 100 ml), saturated brine solution (2 × 75 ml), and then dried over Na_2SO_4. The ether was removed and the residue distilled under vacuum (125-130°C; 0.1mmHg) to yield 4.93 g (75%) of a clear liquid which solidifies on standing: m.p. 81.5-82°C. IR (CH_2Cl_2) ν = 1820 (c=o), 1165, 1070 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$) δ 4.84 (dd, J = 2.9, 4.6 Hz, 1H), 3.84 (dd, J = 4.6, 14.6 Hz, 1H), 3.76 (dd, J = 2.9, 14.6 Hz, 1H). ^{13}C-NMR (300 MHz, $CDCl_3$) δ 152.9, 76.8, 43.6. Anal. calcd. for $C_5H_6Cl_2O_3$: C, 32.46; H, 3.27; Cl, 38.33. Found: C, 32.19; H, 3.20; Cl, 38.47.

7. A total of ten crystals were examined. Some of the crystals were observed to be only polycrystalline in nature.

8. The material was found to change over time on exposure to x-ray irradiation even at low temperature (-140°C). The lattice was found to be tetragonal, and the space group $P4_2/nmc$ (#137) with 4 molecules in the unit cell (8 assymmetric units). Lattice parameters: a = 7.341(2)Å, c = 14.3375(9)Å. The determined R-value was 7.42% with an R_W = 9.70%.

9. Scharf, H.-D., Plum, H., Fleischhauer, J., and Schleker, W. Chem. Ber. *112*, 862 (1979).

10. The addition of protonated onium salts to reactive π-systems has been examined previously: (a) Jung, M. E. and Buszek, K. R. J. Am. Chem. Soc.

110, 3965 (1988). (b) McCulloch, A. W. and McInnes, A. G. Can. J. Chem. *52*, 3569 (1974) (c) Herkes, F. E. and Simmons, H. E. J. Org. Chem. *38*, 2845 (1973). These systems examined protonated onium salt that contained non-nucleophilic counterions.

11. (a) Coghlan, M. J. and Caley, B. A. Tetrahedron Lett. *30*, 2033 (1989). (b) Bowman, M. P. and Olofson, R. A. J. Org. Chem. *55*, 2240 (1990). (c) Olofson, R. A. Pure & Appl. Chem. *60*, 1715 (1988).

(Received in USA 9 October, 1992)