A convenient and safe synthesis of 4,5-disubstituted-2-oxo-1,3-dioxolenes

Devi Prasad Sahu
Chemical Technology Division, Central Drug Research Institute Lucknow 226 001

Received 23 November 2000; accepted (revised) 3 December 2001

Employing bis(trichloromethyl)carbonate (BTC), a safe and crystalline substitute of phosgene, 4,5-disubstituted-2-oxo-1,3-dioxolenes 3 have been synthesized by cyclocarbonylation of α-hydroxyketones 1 in 47-67% yield.

4,5-Disubstituted-2-oxo-1,3-dioxolenes or vinylene carbonates 3 have several synthetic applications. The 4,5-diaryl-2-oxo-1,3-dioxolene 3e-g have been employed as an amino protecting reagent of amino acids during the peptide synthesis. 4,5-Dimethyl-2-oxo-1,3-dioxolene 3a has been used in the manufacture of Lenampicillin hydrochloride, a prodrug of Ampicillin. 1,3-dioxolene 3 has been employed as dienophile as well as dipolarophile in cycloaddition reactions. Some of the vinylene carbonates are used in the manufacture of specialty polymers used in injection moulding.

The 2-oxo-1,3-dioxolenes 3 are synthesized by cyclocarbonylation of appropriate α-hydroxyketones 1 with phosgene in the presence of a base. As phosgene was highly toxic, its replacement with a safer substitute is highly desirable, especially, in the large-scale preparation of 2-oxo-1, 3-dioxolenes. Bis (trichloromethyl)carbonate (BTC), a crystalline solid obtained by exhaustive photo-chlorination of diethyl carbonate has been used as a cheap and safe substitute of phosgene in chlorination, carbonylation, dehydration, and oxidation reactions. The exponential growth in the synthetic applications of BTC as phosgene substitute during last decade has been recently reviewed.10 As a part of our11,12 on going program to explore synthetic uses of BTC and need of 4,5-dimethyl-1,3-dioxolen-2-one 3a, an intermediate required in the production of Lenamicillin hydrochloride prompted us to explore the synthesis of 3,5-disubstituted-1, 3-dioxolen-2-ones employing BTC and the results are presented in this note (Scheme I).

The symmetrical α-hydroxyketones 1 are prepared following the literature methods.1,15 BTC in the presence of a base dissociates stepwise and forms three equivalents of phosgene. Thus α-hydroxy ketones 1 on treatment with BTC and BHC in the presence of dimethylaniline in an appropriate solvent at 0°C, afford α-chloroformyloxy ketones 2.

Phosgene formed in situ from BTC instantaneously reacts with 1 and its non-accumulation in the reaction medium precludes its detection in the vicinity of the reaction vessel. Theoretically 1/3 equivalents of BTC was required per an equivalent of 1, higher proportion of BTC up to 1/2 equivalent was employed for its complete conversion to 2. Though 2 can be isolated and characterized by its IR spectra (absorbance at

Scheme I

† CDRI Communication No. 6093
NOTES

1780 and 1720 cm\(^{-1}\) it can be conveniently cyclized directly to 3 without isolation and purification. The cyclization of 2 to 3 was affected by heating. The temperature at which 2 has to be heated to furnish 3 depends upon the nature of the substituents. With alkyl substituents in 2 it has to be heated in neat at 160° (Method 1) to afford 3. Compound 2 with aryl, alkyl substituents on heating in refluxing xylene cyclizes to 3 (Method 2). Further 2 with aromatic substituents the cyclization to 3 was facilitated by refluxing the solution in toluene (Method 3). Obviously, formation of diaryl-2-oxodioxolenes requires lower activation energy than the dialkyl-2-oxodioxolenes. All the 2-oxodioxolenes synthesized have comparable IR, NMR and mass spectral data with those reported in the literature.

In conclusion, employing BTC, a convenient and safe synthesis of vinylene carbonate from \(\alpha\)-hydroxyketones has been demonstrated.

Experimental Section

The \(\alpha\)-hydroxyketones 1 was prepared following literature method\(^{13, 14}\). BTC was prepared from diethyl carbonate by exhaustive photochlorination\(^5\). The 4,5-disubstituent dioxolenes were prepared as follows.

**Method A.** To a stirred mixture of \(\alpha\)-hydroxyketone 1 (10 mmoles) and N,N-dimethylaniline (15 mmoles) in 30 mL of dichloromethane, a solution of BTC (7.5 mmoles) in DCM was added dropwise over a period of 1/2 hr at 0°C. The resulting solution was stirred at ambient temp. for 2 hr. The solvent was distilled out and the resulting oily residue was heated in an oil bath at 160°C for 4 hr. The oily product distilled under vaccum or recrystallized to obtain 2-oxo-1, 3-dioxolenes.

3a\(^{12}\): yield 42%, m.p. 79-82°C; 3b \(^{13}\): yield 51%, b. p. 108-112°C/1 torr.

**Method B.** To a stirred mixture of \(\alpha\)-hydroxyketone (10 mmoles) and N, N-dimethylaniline (15 mmoles) in 15 mol of xylene, a solution of BTC (7.5 mmoles) in 15 mL of xylene, was added dropwise at 0°C. The solution was warmed to room temperature, and then heated to reflux for 5 hr and cooled to ambient temp. The xylene solution was successively washed with 1N HCl, 5% NaHCO\(_3\) solution, dried and evaporated. The residual solid was recrystallized from appropriate solvent.

3c\(^{12}\): yield 55%, m.p. 82-83°C; 3d\(^{1}\): yield 48%, m.p. 80-82°C.

**Method C.** The experimental procedure followed is same as described in Method B except that dry toluene instead of xylene was employed as diluent. The product was isolated by recrystallisation from absolute alcohol.

3e\(^{1}\): yield 61%, m.p.75-78°C; 3f\(^{14}\): yield 65%, m.p. 117-19°C; 3g\(^{14}\): yield 66%, m.p. 175-77°C.

References