Surprising Formation of Chlorinated Butenolides from Dialkyl Acetylenedicarboxylates and Hexachloroacetone in the Presence of Triphenyl Phosphite

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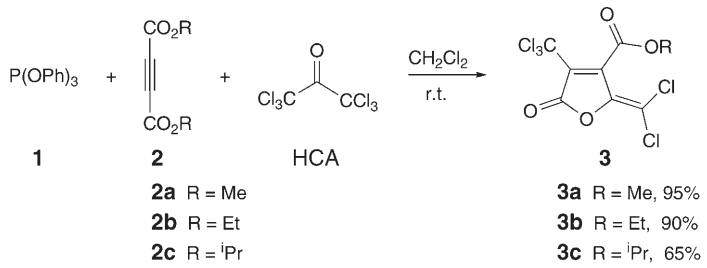
Triphenyl phosphite reacts smoothly with dialkyl acetylenedicarboxylates and hexachloroacetone to produce alkyl 2-(dichloromethylene)-2,5-dihydro-5-oxo-4-(trichloromethyl)furan-3-carboxylates in good yields.

Introduction. – Butenolides, a structural unit in many natural products, are important intermediates in organic synthesis [1]. These compounds are often encountered among fungi [2], bacteria [3], and gorgonians [4] to name a few. Their saturated analogues act as signaling substances in bacteria [5] and enhance spore formation of streptomycetes or induce metabolite production [6].

As part of our current studies on the development of new routes in heterocyclic systems [7], we describe a simple synthesis of chlorinated alkyl 2,5-dihydrofuran-3-carboxylates. Thus, triphenyl phosphite (**1**) reacts with dimethyl acetylenedicarboxylate (**2a**, DMAD) in the presence of hexachloroacetone (HCA; 1,1,1,3,3,3-hexachloropropan-2-one)[1]) in dry CH_2Cl_2 at room temperature to produce methyl 2-(dichloromethylene)-2,5-dihydro-5-oxo-4-(trichloromethyl)furan-3-carboxylate (**3a**) in 95% yield [9] (*Scheme 1*).

Scheme 1



Results and Discussion. – The reaction of the activated acetylenes **2** with HCA in the presence of **1** was complete within a few hours. The ^{1}H- and ^{13}C-NMR spectra of the

[1]) HCA was introduced as a source of positive chlorine [8a] as well as of dichlorocarbene [8b][8c]. It has also been used for the preparation of amides [8d] and of alkyl trichloroacetates [8e].

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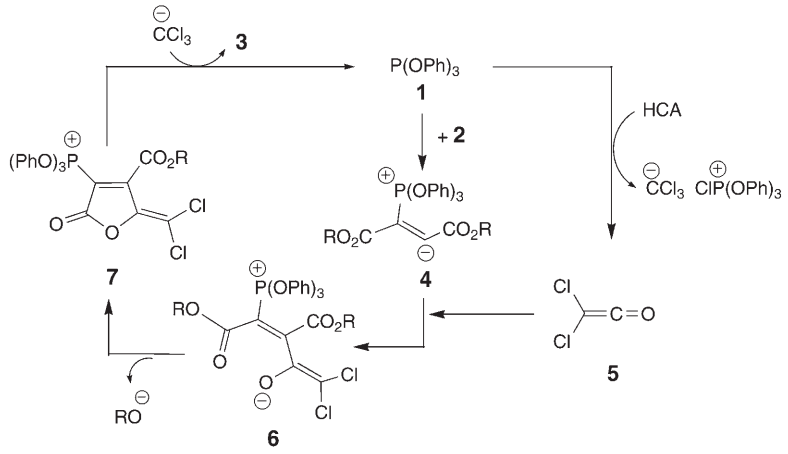
crude reaction mixtures clearly indicated the formation of 2,5-dihydrofuran-3-carboxylates **3a**–**3c** (*Scheme 1*). No other products were detected by NMR spectroscopy. The structures of the products were corroborated by IR, ^{1}H- and ^{13}C-NMR spectroscopy, and elemental analysis. For example, the ^{1}H-NMR spectrum of **3a** in $CDCl_3$ showed a *singlet* for the COOMe group (δ(H) 3.99). The ^{13}C-NMR spectrum of **3a** exhibited eight signals in agreement with the proposed structure. The mass spectrum of **3a** displayed the ^{35}Cl/^{37}Cl isotope pattern of the molecular ion peaks for 5 Cl substituents with the main peak at $m/z = 340$. The ^{1}H- and ^{13}C-NMR spectra of **3b** and **3c** are similar to those for **3a** except for the alkyl moieties, which exhibited characteristic resonances in appropriate regions of the spectrum (see *Exper. Part*).

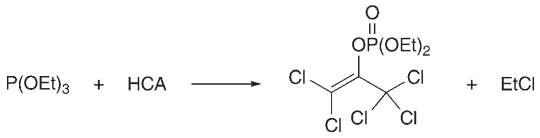
Although the mechanistic details of the above reaction are unknown, a plausible pathway of product formation is formulated in *Scheme 2.* It is conceivable that the initial event is the formation of the 1,3-dipolar intermediate **4** from **1** and the acetylenic ester [9–12], which is subsequently attacked by dichloroketene **5** generated *in situ* from HCA and **1** to produce **6**. The intermediate **6** undergoes a cyclization reaction to generate **7**, which is finally converted to **3** by substitution of triphenyl phosphite with trichloromethanide.

Scheme 2



The reaction between HCA and trialkyl phosphites leads to the formation of enol phosphates, *e.g.*, diethyl 2,2-dichloro-1-(trichloromethyl)ethenyl phosphate [13] (*Scheme 3*), which has been investigated in view of its biological activity as an insect repellent [14]. This dehalogenation reaction, which is an example of the *Perkow* reaction [15], represents a partial reduction of HCA.

Scheme 3



In conclusion, we have described a convenient route to functionalized 2,5-dihydrofuran-3-carboxylates from hexachloroacetone and dialkyl acetylenedicarboxylates **2** in the presence of triphenyl phosphite (**1**). The chlorinated butenolides reported in this work may be considered as potentially useful synthesis intermediates. The advantage of the present procedure is that the reaction is performed under neutral conditions by simple mixing of the starting materials in CH_2Cl_2. The procedure described provides an acceptable one-pot method for the preparation of functionalized butenolides.

Experimental Part

General. Starting materials **1**, **2**, and HCA were obtained from *Fluka* and used without further purification. IR Spectra: *Shimadzu IR-460* spectrophotometer; in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *Bruker DRX-500-Avance* instrument; in $CDCl_3$ at 500.1 and 125.7 MHz, resp.; δ in ppm, J in Hz. EI-MS (70 eV): *Finnigan MAT-8430* mass spectrometer; in m/z. Elemental analyses (C, H, N): *Heraeus CHN-O-Rapid* analyzer.

General Procedure for the Preparation of Compounds **3**. Described as an Example for **3a**. To a stirred soln. of DMAD (= dimethyl but-2-ynedioate; 0.28 g, 2 mmol) and HCA (= 1,1,1,3,3,3-hexachloropropan-2-one; 0.52 g, 2 mmol) in CH_2Cl_2 (10 ml) was added triphenyl phosphite (0.50 ml, 2 mmol) at r.t. The reaction mixture was then stirred for 24 h at r.t. The solvent was removed under reduced pressure, and the viscous residue was subjected to column chromatography (SiO_2; hexane/AcOEt 9:1) to afford the pure title compound.

Methyl 2-(Dichloromethylidene)-2,5-dihydro-5-oxo-4-(trichloromethyl)furan-3-carboxylate (**3a**). Yield: 0.64 g (95%). Pale yellow powder. M.p. 92–95°. IR (KBr): 1773, 1723 (C=O), 1577, 1235. ^1H-NMR: 3.99 (*s*, MeO). ^{13}C-NMR: 55.8 (MeO); 74.9 (CCl_3); 118.7 (CCl_2); 127.7, 142.5, 143.4 (3 C); 160.0, 163.7 (2 C=O). EI-MS: 344 (2, $M^{+\bullet}$), 342 (6, $M^{+\bullet}$), 340 (10, $M^{+\bullet}$), 338 (6, $M^{+\bullet}$), 305 (35), 281 (31), 261 (35), 224 (10), 165 (12), 106 (18), 82 (20), 59 (100), 33 (36). Anal. calc. for $C_8H_3Cl_5O_4$ (340.37): C 28.23, H 0.89; found: C 28.15, H 0.90.

Ethyl 2-(Dichloromethylidene)-2,5-dihydro-5-oxo-4-(trichloromethyl)furan-3-carboxylate (**3b**). Yield: 0.63 g (90%). Pale yellow powder. M.p. 75–77°. IR (KBr): 1763, 1720 (C=O), 1571, 1229. ^1H-NMR: 1.36 (*t*, $J = 7.1$, *Me*CH_2); 4.33 (*q*, $J = 7.1$, Me*CH*$_2$). ^{13}C-NMR: 14.1 (Me); 59.4 (CH_2O); 74.6 (CCl_3); 117.9 (CCl_2); 127.3, 141.9, 142.7 (3 C); 159.4, 162.6 (2 C=O). EI-MS: 358 (1, $M^{+\bullet}$), 356 (4, $M^{+\bullet}$), 354 (6, $M^{+\bullet}$), 352 (4, $M^{+\bullet}$), 319 (24), 122 (14), 73 (100), 59 (10), 45 (20). Anal. calc. for $C_9H_3Cl_5O_4$ (354.40): C 30.50, H 1.42; found: C 30.55, H 1.38.

Isopropyl 2-(Dichloromethylidene)-2,5-dihydro-5-oxo-4-(trichloromethyl)furan-3-carboxylate (**3c**). Yield: 0.47 g (65%). Yellow oil. IR (KBr): 1763, 1716 (C=O), 1604, 1256. ^1H-NMR: 1.39 (*d*, $J = 6.2$, *Me*$_2$CH); 5.12 (*sept.*, $J = 6.2$, Me$_2$*C*H). ^{13}C-NMR: 21.8 (2 Me); 64.7 (CH–O); 75.7 (CCl_3); 117.2 (CCl_2); 128.9, 138.2, 149.5 (3 C); 164.4, 167.4 (2 C=O). EI-MS: 372 (1, $M^{+\bullet}$), 370 (3, $M^{+\bullet}$), 368 (6, $M^{+\bullet}$), 366 (4, $M^{+\bullet}$), 333 (29), 130 (12), 116 (14), 87 (100), 72 (16). Anal. calc. for $C_{10}H_7Cl_5O_4$ (368.42): C 32.60, H 1.91; found: C 32.72, H 1.88.

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