The interaction of 4-ethoxy-1,1,1-trifluoro-3-buten-2-one with triethyl phosphite

I.I. Gerus [a],*, M.G. Gorbunova [a], V.P. Kukhar [a], R. Schmutzler [b]

[a] *Institute of Bioorganic and Petrochemistry, Ukrainian Academy of Sciences, Murmanskaya 1, 253660 Kiev, Ukraine*
[b] *Institut für Anorganische und Analytische Chemie der Technischen Universität, Postfach (TU) 3329, D-38023 Braunschweig, Germany*

Abstract

4-Ethoxy-1,1,1-trifluoro-3-buten-2-one reacts with triethyl phosphite on heating to give a [4 + 2] cycloaddition product 2,2,2-triethoxy-2,3-dihydro-3-ethoxy-5-trifluoromethyl-1,2λ^5-oxaphospholene. Its hydrolysis yields, ultimately, a 2-oxo-2-hydroxy-2,3-dihydro-3-hydroxy-5-trifluoromethyl-1,2λ^5-oxaphospholen. © 1998 Elsevier Science S.A. All rights reserved.

1. Introduction

Previously, we have reported β-ethoxyvinyl trifluoromethyl ketone (1) as a convenient and readily accessible reagent in the synthesis of different trifluoromethyl-containing heterocycles [1–3] and dyes [4]. β-Ethoxyvinyl trifluoromethyl ketone has also been proposed as a new reagent for the protection of amino groups in peptide synthesis [5]. All these examples of the application of 1 are based on the initial attack of nucleophilic agents on the β-carbon atom of the vinyl fragment, involving the participation of the carbonyl group (in the case of heterocycles).

In the literature, there are only a few examples of the participation of compound 1 as a heterodiene in cycloaddition reactions: [4 + 1] cycloaddition to cyclohexyl isocyanide [6] and [4 + 2] cycloaddition to alkylvinyl ethers [7].

We have studied another [4 + 1] cycloaddition reaction of compound 1: its interaction with triethyl phosphite.

2. Results and discussion

We have found that the enone 1 reacts with triethyl phosphite in boiling benzene over 6 h to form the cyclic compound 2,2,2-triethoxy-2,3-dihydro-3-ethoxy-5-trifluoromethyl-1,2λ^5-oxaphospholene (2).
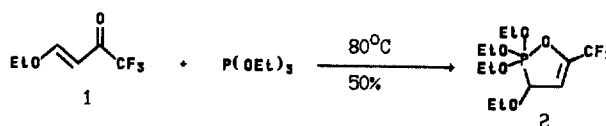

Compound 2 was isolated from the reaction mixture after double distillation in vacuo. According to ^{31}P NMR spectral data, the reaction mixture contained nearly equal quantities of 2 and PO(OEt)$_3$. The mechanism of formation of PO(OEt)$_3$ during this reaction is not clear, but it may result from the removal of oxygen from the enone 1.

Compound 2 is a colourless liquid. In the ^{19}F NMR spectrum, there is only one signal: a singlet due to the trifluoromethyl group. The ^{31}P NMR resonance is complicated: a doublet of doublets of multiplets at -32.7 ppm. This is caused by the coupling of phosphorus with protons 3 and 4 of the ring ($J = 65$ Hz and 35 Hz respectively) and with six protons of the methylene groups. This is in accordance with literature data; for example, 2,2,2-trialkoxy-2,3-dihydro-3-hydroxy-3,5-bis(trifluoromethyl)-1,2λ^5-oxaphospholenes show phosphorus signals at nearly -35 ppm with coupling constants $J(^4HP) = 35–37$ Hz [8]. According to the ^{1}H NMR spectrum, protons 3 and 4 interact with the cis coupling constant 7 Hz. The ^{13}C NMR spectrum of 2 is highly informative, providing ready confirmation of the structure and showing that the coupling to phosphorus extends throughout the ring (see Section 3).

We have found that 2 hydrolyses in the presence of a small amount of water to give a mixture of products. We have studied the hydrolysis of 2 by ^{31}P NMR spectroscopy which

* Corresponding author.

suggests stepwise hydrolysis. In the ^{31}P NMR spectrum of a solution of 2 in wet ether, the signal at -32 ppm disappears, and is replaced by a signal at 16.3 ppm, a doublet of multiplets (J(HP) ~ 50 Hz). The large number of lines in this multiplet indicate the proximity of the two ethoxy groups bonded to phosphorus. We suggest that this signal is probably due to the phosphorus atom of the acyclic intermediate 3, because of its instability: after the removal of ether in vacuo, the ^{31}P NMR spectrum of the residue in benzene changes drastically; the signal at 16.3 ppm disappears and two signals at 36.9 and 34.5 ppm of nearly equal intensity appear. The signal at 34.5 ppm is a doublet of doublets of triplets (J(P^{3}H) ~ 42 Hz, J(P^{4}H) ~ 32 Hz, J(POCH$_2$) ~ 8 Hz). The signal probably corresponds to the phosphorus atom in the cyclic intermediate 4 which contains only one ethoxy group at phosphorus. The signal at 36.9 ppm is a doublet of doublets (J(^{3}HP) ~ 45 Hz, J(^{4}HP) ~ 32 Hz). The signal probably corresponds to the phosphorus atom in intermediate 5 with a hydroxy group at phosphorus. None of the suggested products could be isolated.
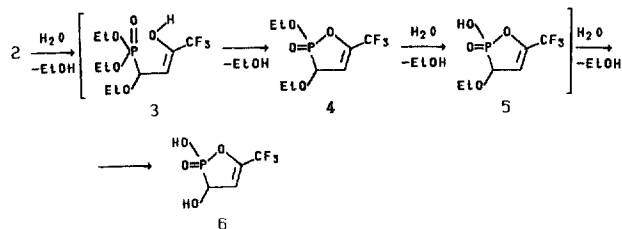
Compound 6 was isolated after the addition of a 1 N solution of HCl to 2, which quickly resulted in the elimination of all ethoxy groups and in the formation of the crystalline compound 6 with low melting point.

The structure of 6 was confirmed by ^{1}H, ^{13}C, ^{19}F and ^{31}P NMR spectroscopy and by elemental analysis. The δ(^{1}H) values of the two ring protons (in positions 3 and 4) are similar: 6.56 and 6.47 ppm. When the ^{1}H NMR spectrum was recorded in various solvents at 200 MHz, a complicated multiplet was observed. A well-resolved spectrum was observed at 500 MHz. It was found that the coupling constants of protons 3 and 4 with phosphorus and with each other were very similar: 21.1, 17.4 and 17.3 Hz respectively. We assume that the proton signal with J(HP) $= 21.1$ Hz can be assigned to the proton in position 3 of the ring. In the ^{13}C NMR spectrum of 3, the δ(^{13}C) values of this compound almost coincide with those of 2. The data of the APT experiment [9] also confirm the structure of 6.

3. Experimental details

^{1}H, ^{13}C, ^{19}F and ^{31}P NMR spectra were recorded on Bruker WP-200 and Varian Gemini-200 instruments. The ^{1}H NMR spectrum of 6 was obtained on a Bruker AMX-500 instrument. Chemical shifts (δ) are given in parts per million relative to tetramethylsilane (TMS) for ^{1}H and ^{13}C, H$_3$PO$_4$ for ^{31}P and CCl$_3$F for ^{19}F.

The enone 1 was synthesized according to the method described in Ref. [10].

3.1. 2,2,2-Triethoxy-2,3-dihydro-3-ethoxy-5-trifluoromethyl-1,2λ^5-oxaphospholene (2)

A mixture of 1 (5 g, 30 mmol) and triethyl phosphite (5 g, 30 mmol) in 20 ml of dry benzene was refluxed under argon for 6 h. The solvent was removed by distillation, and the residue was distilled in vacuo (0.15 mmHg) (argon as a protecting atmosphere). The fraction of b.p. 55–60 °C was refractionated. Yield, 4.8 g (48%); b.p., 58–58.5 °C (0.015 mmHg). NMR: ^{1}H (CDCl$_3$) δ: 6.8 dd (1H, H(3), J(^{3}H^{4}H) $= 7$ Hz, J(^{3}HP) $= 65.4$ Hz), 6.35 dd (1H, H(4), J(^{3}H^{4}H) $= 7$ Hz, J(^{4}HP) $= 34.6$ Hz), 3.9 dq (6H, POCH$_2$, J(HH) $= 7$ Hz, J(HP) $= 7$ Hz), 3.5 m (2H, OCH$_2$), 1.2 m (12H, CH$_3$). ^{13}C (CDCl$_3$) δ: 142.9 d (C(4), J(CP) $= 17.7$ Hz), 134.5 d (C(3), J(CP) $= 217$ Hz), 122.6 qd (CF$_3$, J(CF) $= 289$ Hz, J(CP) $= 6.8$ Hz), 96.2 qd (C(5), J(CF) $= 32.5$ Hz, J(CP) $= 18$ Hz), 62.4 d (POCH$_2$, J(CP) $= 11.2$ Hz), 59.05 s (OCH$_2$), 16.25 d (CH$_3$, J(CP) $= 8.7$ Hz), 15.27 s (CH$_3$). ^{19}F (CDCl$_3$) δ: -80.8 s (CF$_3$). ^{31}P (CDCl$_3$) δ: -32.7 ddm (J(^{3}HP) $= 65.4$ Hz, J(^{4}HP) $= 34.6$ Hz). Found (%): C, 42.81; H, 6.28; F, 16.77. C$_{12}$H$_{22}$F$_3$O$_5$P calculated (%): C, 43.12; H, 6.63; F, 17.05.

3.2. 2-Oxo-2-hydroxy-2,3-dihydro-3-hydroxy-5-trifluoromethyl-1,2λ^5-oxaphospholen (6)

The oxaphospholene 2 (0.67 g, 2 mmol) was added with stirring to a 1 N solution of hydrochloric acid (10 ml). After the mixture had been stirred for 0.5 h, the hydrochloric acid was removed in vacuo and the residue was dried for 10 h at 40 °C and 0.01 mmHg. Yield of 6, 0.37 g (92%). NMR: ^{1}H (500 MHz, D$_2$O) δ: 6.56 dd (1H, H(3), J(^{3}H^{4}H) $= 17.3$ Hz, J(^{3}HP) $= 21.1$ Hz), 6.47 dd (1H, H(4), J(^{3}H^{4}H) $= 17.3$ Hz, J(^{4}HP) $= 17.4$ Hz). ^{13}C (D$_2$O) δ: 138.5 d (C(4), J(CP) $= 5.8$ Hz), 125.0 d (C(3), J(CP) $= 178$ Hz), 120.8 q (CF$_3$, J(CF) $= 288$ Hz), 89.55 qd (C(5), J(CF) $= 32.7$ Hz, J(CP) $= 22$ Hz). ^{19}F (D$_2$O) δ: -85.3 s (CF$_3$). ^{31}P (D$_2$O) δ: 13.8 br. "t" (J(HP) ~ 20 Hz). Found (%): C, 23.08; H, 2.27; F, 27.60; P, 15.53. C$_4$H$_4$F$_3$O$_4$P calculated (%): C, 23.55; H, 1.98; F, 27.93; P, 15.18.

Acknowledgements

References

[1] I.I. Gerus, M.G. Gorbunova, S.I. Vdovenko, Y.L. Yagupolskii, V.P. Kukhar, Zh. Org. Khim. 26 (1990) 1877.

[2] I.I. Gerus, S.I. Vdovenko, M.G. Gorbunova, V.P. Kukhar, *Khim. Heterocycl. Soed.* (1991) 502.

[3] I.I. Gerus, A.V. Kropachev, M.G. Gorbunova, V.P. Kukhar, A.Ya. Ilchenko, *Ukr. Khim. Zh. 59* (1993) 408.

[4] S.V. Pasenok, I.I. Gerus, E.A. Chayka, L.M. Yagupolskii, *Zh. Org. Khim. 25* (1989) 379.

[5] M.G. Gorbunova, I.I. Gerus, S.V. Galushko, V.P. Kukhar, *Synthesis*, (1991) 207.

[6] L.V. Simonyan, E.A. Avetisyan, Z.V. Safronova, *Izv. Akad. Nauk USSR, Ser. Khim.* (1977) 2061.

[7] M. Hojo, R. Masuda, E. Okada, *Synthesis*, (1989) 215.

[8] R. Francke, G.-V. Röschenthaler, *Chem.-Ztg., 113* (1989) 183.

[9] S.L. Patt, J.N. Shoolery, *J. Magn. Reson. 46* (1982) 535.

[10] M. Hojo, R. Masuda, Y. Kokuryo, H. Shioda, S. Matsuo, *Chem. Lett.*, (1976) 499.