Tetrahedron Letters,Vol.24,No.32,pp 3387-3390,1983 0040-4039/83 $3.00 + .00
Printed in Great Britain

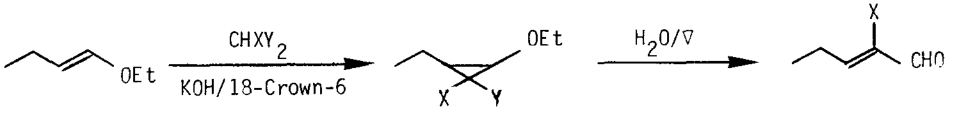
ANOMALOUS FORMATION OF 1,1,4-TRIBROMOHEX-1-EN-3-ONE IN THE WITTIG REACTION OF 2-HALOPENT-2-ENALS WITH DIBROMOMETHYLENE TRIPHENYLPHOSPHORANE

F. Camps, J. Coll, G. Fabriàs, A. Guerrero and M. Riba
Instituto de Química Bio-Orgánica, C.S.I.C.
Jorge Girona Salgado, s/n. Barcelona-34 SPAIN.

Summary: The heretofore unreported Wittig reaction of 2-halopent-2-enals with dibromomethylene triphenylphosphorane yields variable amounts of 1,1,4-tribromohex-1-en-3-one and/or the expected dienes according to the substrate and reaction conditions. A plausible mechanism to rationalize the unforeseen formation of this ketone is discussed.

Wittig reaction of aldehydes with dibromomethylene triphenylphosphorane is a well established procedure for preparation of 1,1-dibromo olefins[1] In relation with an ongoing project in this laboratory, we have studied the previously unreported reaction of this ylide with 2-halopent-2-enals. The results of this work are described in the present communication.

The required aldehydes[2] 2-fluoropent-2-enal (3a), 2-chloropent-2-enal (3b) and 2-bromopent-2-enal (3c), so far not described in the literature, have been prepared by cyclopropanation of 1-ethoxy-1-butene (1), under PTC conditions[3] or in the presence of potassium t-butoxide[4] followed by thermal ring opening reaction of the corresponding 1,1-dihalo-2-ethoxycyclopropanes 2a-c, in moderate overall yields (40-48%).

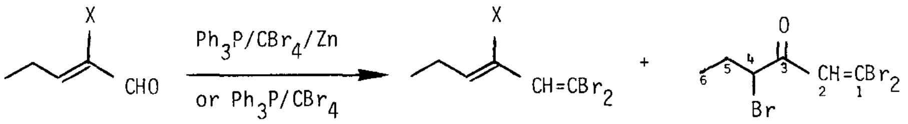


1

2a: X=F, Y=Cl
2b: X=Y=Cl
2c: X=Y=Br

3a: X=F
3b: X=Cl
3c: X=Br

Dibromomethylene triphenylphosphorane was generated using either of the two different experimental conditions: (A) by mixing triphenylphosphine, carbon tetrabromide and zinc dust in a 1:1:1 molar ratio in methylene chloride at 23°C for 24-30 h, or (B) by reacting triphenylphosphine and carbon tetrabromide in a 2:1 molar ratio for 10 min. under the same reaction conditions. Wittig reaction with aldehydes 3a-c was carried out under argon by adding the substrates to the ylide solutions at 0°C and then allowing the reaction mixture to warm up to room temperature. After conventional work-up, variable yields of the highly unstable expected dienes 4a-c along with a by-product, identified as 1,1,4-tribromohex-1-en-3-one (5), were obtained. The results are summarized in Table 1.



3a: X=F
3b: X=Cl
3c: X=Br

4a: X=F
4b: X=Cl
4c: X=Br

5

Characterization of compound 5 was based on its spectroscopic and analytical features: IR ν_{max} (CCl_4) 3010, 1700, 1555 cm^{-1}. ^1H NMR δ (CCl_4) 7.51 (s, 1H, CH=C), 3.98 (dd, J=7 Hz, 1H, CHBr), 1.73 (m, 2H, CH_2), 0.77 ppm (t, J=7 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ 189.35 (s, C-3), 131.24 (d, C-2), 107.78 (s, C-1), 56.21 (d, C-4), 26.15 (t, C-5), 12.32 ppm (q, C-6). Elementary analysis: Calculated for $C_6H_7OBr_3$ C, 21.33; H, 2.09; Br, 71.75; Found C, 21.67; H, 2.10; Br, 71.38. EI-MS m/z 332, 334, 336, 338 ($M^{+\cdot}$, <1%), 304, 306, 308, 310 (<1%), 252, 254, 256 (9.3%), 211, 213, 215 (100%), 183, 185, 187 (9.6%), 104, 106 (8.0%), 41 (24.9%).

NMR assignments were confirmed by single frequency homo- and heterodecoupling experiments. Irradiation of the signal at δ 1.73 in the ^1H NMR spectrum collapsed the doublet of doublets at δ 3.92 and the triplet at δ 0.77 into singlets. Furthermore, when the signal at δ 0.77 was irradiated the complex system centered at δ 1.73 was simplified into a pair of doublet of doublets, due to the diastereotopic character of C-5 hydrogens. Moreover, when the signal at δ 7.27 in the ^1H NMR spectrum was irradiated, the corresponding doublet at δ 131.24 in the ^{13}C NMR spectrum collapsed into a singlet, whereas irradiation of the signal at δ 3.92 in the proton spectrum transformed the doublet at δ 56.21 ppm in the carbon spectrum into a singlet.

Table 1. Wittig reaction of 2-halopent-2-enals with dibromomethylene triphenylphosphorane.

Entry	Aldehyde	Reactants ratio Substrate/Ph_3P/CBr_4/Zn	Reaction time (h)	Yield[a] Diene	Yield[a] Ketone 5
1	3a	1:2:2:2	7	--	30
2	3b	1:2:2:2	40[b]	--	<10[c]
3	3c	1:2:2:2	8	4c (51)	14
4	3d	1:2:2:2	4	4d (45)	--
5	3e	1:2:2:2	2	4e (66)	--
6	3a	1:2:1:0	0.25	4a (53)	12
7	3b	1:2:1:0	0.25	4b (57)	--
8	3c	1:2:1:0	0.3	4c (53)	--

[a] Yields have not been optimized and they refer to the calculated values based on the ^1H NMR spectrum of the crude, unless otherwise stated. Attempted purification of the dienes by distillation or chromatography resulted in decomposition of the product.

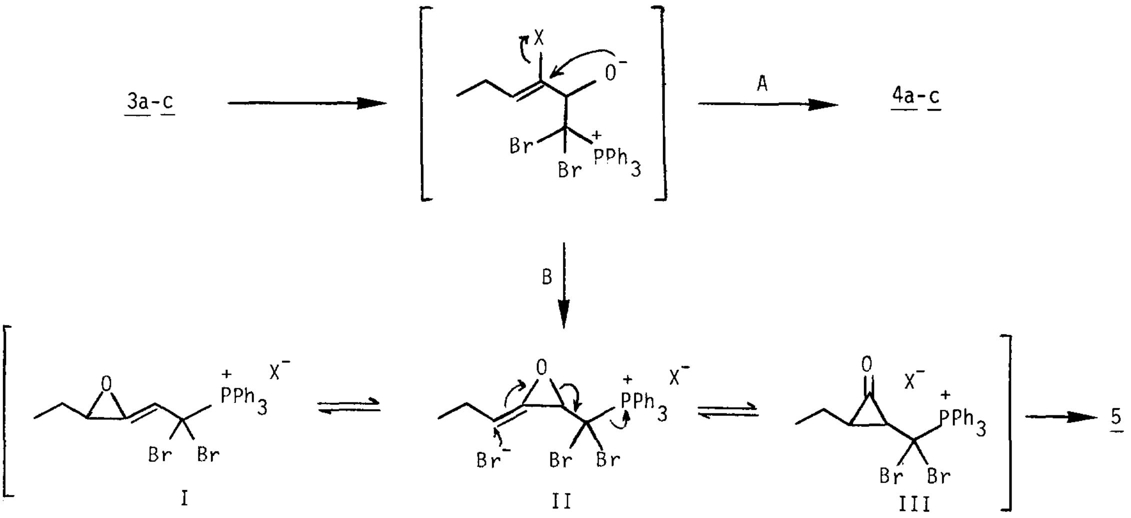
[b] TLC control at different reaction times failed to reveal the presence of diene 4b.

[c] Starting product (52%) was recovered after column chromatography purification.

As shown in Table 1, compound 5 was obtained as the only identified product (30%) when fluoroaldehyde 3a was reacted under A conditions (entry 1), whereas by use of B conditions 53% of the expected diene 4a[5] was obtained along with 12% of ketone 5 (entry 6). Likewise, bromoaldehyde 3c yielded 51% of diene 4c[6] and 14% of ketone 5 in the presence of Zn (entry 3), whereas chloroaldehyde 3b led mostly to the recovery on unreacted material (entry 2). On the other hand, in the absence of Zn (conditions B) aldehydes 3b and 3c gave the normal dienes 4b[7] and 4c in similar yields, with no concomitant formation of the anomalous compound 5 (entries 7-8).

To shed some light on the mechanism of formation of 5, complementary experiments with an α-haloaldehyde (bromoheptanal 3d) and an α,β-unsaturated aldehyde (crotonaldehyde 3e) were carried out under A conditions. The exclusive formation of the expected dienes indicated that the simultaneous presence of halogen and unsaturation in the aldehyde substrate is required for generation of 5. In this context, intermediate formation of an allene oxyde I[9] (pathway B) by intramolecular nucleophilic substitution of the halogen[10] might be postulated as a plausible precursor of compound 5 (Scheme 1).

Allene oxides are known to exist as an equilibrium of the three tautomeric forms $I \rightleftharpoons II \rightleftharpoons III$ and, consequently, they can be expected to undergo reaction at every site of their skeleta.[9] Regiospecific nucleophilic attack at C-4 of form II or at equivalent sites of the other tautomers by a bromide ion, present as $ZnBr_2$ in A conditions, and as $Ph_3\overset{+}{P}Br\ Br^-$ under B conditions, could finally account for the appearance of ketone 5. In agreement with this assumption, we have proved in a separate experiment that the presence of $ZnBr_2$ solution is essential to promote generation of 5, since its removal from the ylide solution, before addition of fluoroaldehyde 3a, afforded exclusively a 1:1 mixture of diene 4a and starting 3a, in which the presence of ketone 5 could not be detected. Furthermore, $ZnBr_2$ has a detrimental effect on the labile dienes, since addition of one equivalent of this Lewis acid to 1,1-dibromo-3-chloro-1,3-hexadiene 3b resulted in complete decomposition of the product after one hour, suggesting that method B is more convenient for preparation of these particular dienes, 3a-c, contrary to the previous recommendation of this Wittig reagent in other cases.[1c]



Scheme 1

Although the postulated mechanism seems to be a plausible one, it does not disclose whether we are dealing with a concerted mechanism or not. In this context further work is in progress.

Acknowledgements

We gratefully acknowledge Comisión Asesora de Investigación Científica y Técnica for financial support (Grant Nº 3296/79) and Consejo Superior de Investigaciones Científicas for a predoctoral fellowship to one of us (G.F.).

References and Notes

1.- (a) R. Rabinowitz and R. Marcus; *J. Am. Chem. Soc.*, **84**, 1312 (1962).
   (b) F. Ramirez, N. B. Desai and N. McKelvie; *J. Am. Chem. Soc.*, **84**, 1745 (1962).
   (c) E. J. Corey and P. L. Fuchs; *Tetrahedron Lett.*, **1972**, 3769.
   (d) L. J. P. Van Amsterdam and J. Lugtenburg; *J. C. S. Chem. Comm.*, **1982**, 946.
   (e) H. J. Bestmann and H. Frey; *Ann. Chem.*, **1980**, 2061.

2.- All new compounds gave satisfactory spectroscopic and analytical data.

3.- Y. Bessière, D. Ngoc-Huê Savary and M. Schlosser; *Helv. Chim. Acta*, **60**, 1739 (1977).

4.- (a) L. A. Last, E. R. Fretz and R. M. Coates; *J. Org. Chem.*, **47**, 3216 (1982).
   (b) P. Amice, L. Blanco and J. M. Conia; *Synthesis*, **1976**, 196.

5.- ^{1}H NMR of **4a** (CCl_4) δ6.79 (d, J=19.8 Hz, 1H, $C\underline{H}=CBr_2$), 5.11 (dt, J=35.4 J'=8.1 Hz, 1H, $C\underline{H}=CF$), 2.10 (b, 2H, $C\underline{H}_2$), 1.02 (t, J=7.5 Hz, 3H, $C\underline{H}_3$).

6.- ^{1}H NMR of **4c** (CCl_4)δ 6.95 (d, J=1.6 Hz, 1H, $C\underline{H}=CBr_2$), 6.20 (dt, J=6.8 J'=1.6 Hz, 1H, $C\underline{H}=CBr$), 2.19 (b, 2H, $C\underline{H}_2$), 1.06 (t, J=7.5 Hz, 3H, $C\underline{H}_3$).

7.- Spectral data of **4b**: ^{1}H NMR (CCl_4) δ6.85 (d, J=1.6 Hz, 1H, $C\underline{H}=CBr_2$), 6.08 (dt, J=6.8 J'=1.6 Hz, 1H, $C\underline{H}=CCl$), 2.28 (b, 2H, $C\underline{H}_2$), 1.06 (t, J=7.5 Hz, 3H, $C\underline{H}_3$). ^{13}C NMR ($CDCl_3$) 134.89 (C-4), 135.26 (C-2), 126.32 (C-3), 97.32 (C-1), 22.34 (C-5), 12.49 ppm (C-6). Values corresponding to C-4 and C-2 signals may be interchanged.

8.- Normal Wittig reaction products have been obtained in the reactions of aldehyde **3a** with *n*-butyl triphenylphosphonium bromide/potassium *t*-butoxide (70% yield) and trimethyl phosphonoacetate/sodium hydride (78% yield).

9.- T. H. Chan and B. S. Ong; *Tetrahedron*, **36**, 2269 (1980).

10.- G. Modena; *Acc. Chem. Res.*, **4**, 73 (1971).

(Received in UK 18 May 1983)