Pergamon

Tetrahedron Letters, Vol. 35, No. 11, pp. 1755-1758, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0130-P

FLUOROALKOXYPHOSPHONIUM YLIDS. EPIMERIZATION AND TRANSFORMATIONS.

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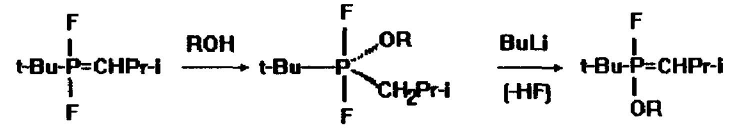
ABSTRACT:Dehydrofluorination of alkoxydifluorophosphoranes 2, containing chiral alkoxygroup, by organometallic bases passes under conditions of kinetic control to afford diastereomeres of ylid 3 in the proportion 1:1. In the presence of lithium salts the epimerization of 3 leads to the formation of the most thermodynamic stable diastereomere. Hydrolysis and reaction of 3 with alcohols affords phosphinates 6, reaction with acids provides fluorophosphinates 7.

Phosphorus ylids, containing halogen atoms at the phosphorus atom (P-halogenoylids), have attracted considerable interest in the last few years.[1,2] To continue systematic studies of the P-halogenoylids we have synthesized non-stabilized P-fluoroylids 3 possessing interesting chemical and stereochemical properties. This type of phosphorus ylids is new, because only non-fluorine containing P-alkoxyphosphonium ylids stabilized by electron-withdrawing groups at the α-carbon atom have been earlier described [3]



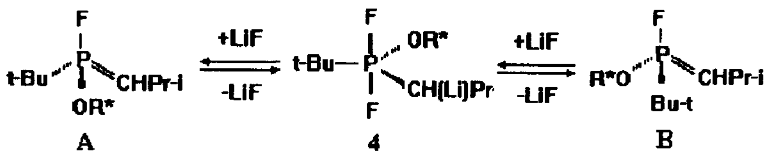
1 2a-c 3a-c

RO= EtO- (a), (-)-$Et_2NCH_2CH(Me)O$- (b), (-)-1,2:5,6-O-dicyclohexylideneglukofuranosyl (c)

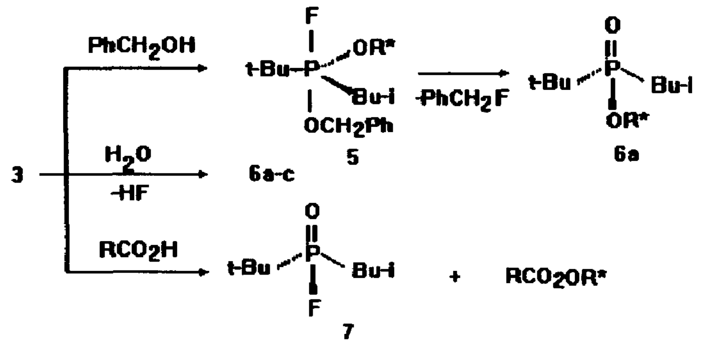
Ylids 3 were obtained by dehydrofluorination of corresponding alkoxydifluorophosphoranes 2. The latter compounds were prepared by addition of alcohol to P,P-difluoroylids 1 in ether at 0-+20°C in very high yields.[4] The alkoxydifluorophosphoranes 2b,c do not have a chiral phosphorus centre and thus are not diastereomeric.[5] The ^{31}P NMR spectra reveals the presence of the only one signal in up field, triplet with coupling constant, $^1J_{PF}$~790 Hz, in accordance with pentacoordinate state of the phosphorus atom At the same time the fluorine atoms of the alkoxydifluorophosphoranes 2b,c are chemically nonequivalent because of influence of chiral equatorial alkoxy-groups. [6] The signals ^{19}F of the compounds 2b,c are doubled and represent two double doublets with the coupling constant of the two axial fluorine atoms $^2J_{FF}$ 40 Hz. Hence one can suppose that the dehydrofluorination of difluorophosphoranes 2 by organometallic bases would be accompanied by asymmetrical induction to afford preferably one of ylid diastereoisomeres **A** or **B**.

The treatment of difluorophosphoranes **2** with the butyllithium in hexane or in ether-hexane solution below 0°C gives P-fluoroylids **3a-c** containing alkoxygroups at the phosphorus atom in very good yields. [7] The careful study of reaction mixtures by means of ^{31}P-$\{^1H\}$ and ^{19}F-NMR spectra have showed that soon after the dehydrofluorination of alkoxydifluorophosphoranes **2b,c** the diastereomeres of ylids **3b** and **3d** are formed in the ratio 1:1. However then, in the presence of lithium salts found in the solution, the diastereomere proportion changes gradually to become equal 4:1 **(3b)** and 95:5 (**3c)** in 12-16 hours at 20 C. The isolation of ylids from reaction mixture and their purification avoids the epimerization. In this case the proportion of diastereoisomeres **A** and **B** does not change.

The epimerization of the ylids **3b,c** can be explained by the next mechanism. The dehydrofluorination of difluorophosphoranes **2** proceeds very fast, evidently under conditions of kinetic control. Owing to the diastereomeres **A** and **B** are formed in the ratio 1:1. After that ylids **3** add reversibly to the multiple P=C bond lithium halogenides to form intermediates **4**, containing achiral pentacoordinate phosphorus atom which as a result of the equilibrium with forms **A** and **B** are converted slowly to the most thermodynamic stable diastereomer



The structure of the ylids **3a-c** is confirmed by ^1H, ^{19}F and ^{31}P NMR spectra. The ^{19} F NMR spectra of the ylids show a doublet of signals centered at - 70 ppm with a very large constant, $^1J_{FP}$ 1100 Hz. The ^1H NMR spectra disclose the presence of a doublets centered at 87-90 ppm with the same constant $^1J_{PF}$ that corresponds to the phosphonium character of the phosphorus atom of the high polar P=C bond.In contrast to the previously described P-alkoxyphosphonium ylids, the compounds **3** are stable and at usual conditions do not undergo the ylid-phosphonate rearrangement. They can be purified by distillation in vacuum. At the same time the ylids **3** are very reactive. The ylids **3** readily add alcohols to afford dialkoxyfluorophosphoranes **5**, which are stable under 0° C and can be registered by means of ^{31}P NMR spectra. δ_P -14 ppm, doublet, $^1J_{FP}$ 900 Hz. At elevation of the temperature to +20°C dialkoxyfluorophosphoranes **5** eliminate alkyl fluorides to form phosphinates **6**. [8] This reaction is perspective as the method for exchange of OH-group into C-F group. [9] The hydrolysis of P-fluoroylids **3** leads also to the formation of the phosphinates **5** obtained as a mixture of two diastereomeres in the ratio 5 : 1 **(6b)** and 10 : 1 **(6c)**, which were separated by column chromatography. The hydrolysis of **3** passes with the change of the optical rotation sign. Ylids **3** are desalkylated by acids RCO_2H (R=Ph, CH_3 , CF_3) to transform into the fluorophosphinate **7** [8]



Acknowledgements: Financial support for this work from National Committee on Science and Technology of Ukraine is gratefully acknowledged.

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6. **2a**: Yield 80%, B. P. 67° C (12 mm Hg), δ_{P},ppm: -40.3, dd, J_{PF} 789 Hz, J_{PF} 41.4 Hz; -40.6, dd, J_{PF}

787 Hz, J_{FF} 40.6 Hz, δ_P, ppm. : -14.07, t, J_{PF} 788 Hz.[10]

2b: Yield 80%, B.P. 76-82 C (0.04mm Hg), δ_F, ppm : -40.3, dd, J_{PF} 788 Hz,: J_{FF} 41.4 Hz; -40.6, dd, J_{PF} 787 Hz, J_{PF} 40.6 Hz. δ_P, ppm.: -14.1, t, J_{PF} 788 Hz. $[\alpha]_D$ +12.4 (hexane).

2c: Yield 95%, δ_F, ppm: -40.3, dd, J_{PF} 789 Hz, J_{PF} 41.4 Hz; -40.6, d, J_{PF} 787 Hz, J_{FF} 40.6 Hz. δ_P, ppm: -11.48, d, J_{PF} 788 Hz. $[\alpha]_D$ -6.75 ° (hexane).

7. **3a**: Yield 60%, B.P. 75 C (10mm Hg). δ_F, ppm: -70.07, d J_{PF} 1090 Hz. δ_P, ppm: 91.4, d, J_{PF} 1080 Hz.
   3b: Yield 60%. B.P. 75 C (0.08mm Hg). δ_F, ppm: -70.8, d; -71.9, d J_{PF} 1075 Hz. δ_P, ppm: 87.5, d and 88.8, d, J_{PF} 1078 Hz.
   3c: Yield 60%. δ_F, ppm: -70.1, d, J_{PF} 1100 Hz. δ_P, ppm: 86.4, d and 87.7, d, J_{PF} 1089 Hz. $[\alpha]_D$ +0.5 ° (hexane)

8. **6a**: Yield 85%, B.P. 95° C (10mm Hg). δ_P, ppm: 60.8.
   6b: Purified by column chromatography with silica gel, eluent is chloroform-methanol in the proportion 5:1. Yield 60%, B.P. 109 C (12mm Hg), δ_P, ppm: 60.23 and 59.9.
   6c: Purified by column chromatography with silica gel, eluent is chloroform- methanol in the proportion 10:1. Yield 60%. δ_P, ppm; 62.84 and 64.73. $[\alpha]_D$ -6 (hexane).
   7: Yield 85%, B.P. 132° C (15 mm Hg). δ_F, ppm: -88.1, d J_{PF} 1035 Hz. δ_P, ppm; 78.4, d, J_{PF} 1041 Hz.

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10. ^1H, ^{19}F, ^{31}P NMR spectra were recorded on a Varian VXR-300 spectrometer at 300; 281.7; 126.16 MHz. ^{19}F NMR and ^{31}P NMR spectra are referenced at internal $CFCl_3$ and external 85% H H_3PO_4 respectively. The new compounds were characterized by elemental analysis.

(*Received in UK* 25 *August* 1993; *revised* 11 *January* 1994; *accepted* 14 *January* 1994)