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Hexacoordinate Phosphates Bearing an Oxaphosphetane Ring: Characterization and Stereomutation

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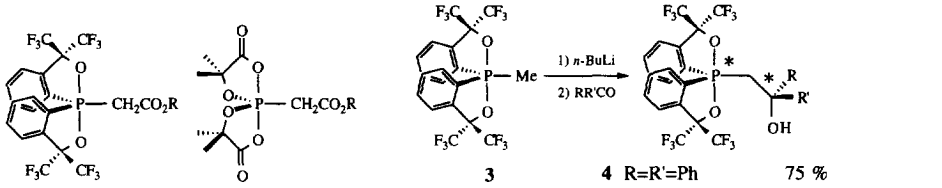
Abstract: The reaction of a β-hydroxyspirophosphorane (**4**) bearing Martin ligands with base was found to give a hexacoordinate phosphate (isomer 1), which eventually isomerized to another phosphate (isomer 2). Kinetic examination of the stereomutation process implied that it involved P–O bond heterolysis as the rate determining step. This was assumed to be followed by pseudorotation and P–O bond formation. © 1997, Elsevier Science Ltd. All rights reserved.

The Wittig reaction and its modifications have enjoyed widespread application in organic synthesis as the choice reactions to incorporate olefinic functionalities into organic compounds.[1] As part of our continuous investigation on hypervalent compounds we have recently found that 10-P-5 phosphoranes **1** bearing Martin ligands could also undergo the Wittig reaction and that with surprisingly high *Z*-selectivity for reagents carrying electron withdrawing groups.[2] Since ordinary Wittig reactions involve pentacoordinate intermediates it follows that the reactions of 10-P-5 phosphoranes would involve hexacoordinate intermediates. During the course of our investigation the ^{31}P NMR observation of hexacoordinate species in a Wittig type reaction involving **2** has been reported.[3] However such intermediates could not be observed for **1**. Therefore in order to observe hexacoordinate species, we have prepared β-hydroxyphosphorane **4**. In the event we have observed the first stereomutation process between isomeric hexacoordinate phosphates bearing an oxaphosphetane ring.[4] We have previously observed similar stereomutation in hexacoordinate antimony[5] and bismuth[6] compounds which bear 5-membered rings. Herein we report our results.[7]



1 **2** **3**

4 R=R'=Ph 75 %
5a R=Ph, R'=CF_3 57 % (combined)
5b R=CF_3, R'=Ph (1:1)

Scheme 1

Synthesis of the compounds was carried out according to Scheme 1. Phosphorane **3** [δ_P ($CDCl_3$) -22.7][8] was deprotonated with *n*-BuLi in THF, followed by treatment with benzophenone, furnishing β-hydroxyphosphorane **4** [δ_P ($CDCl_3$) -20.5].[9] Compound **4** was stable to heating (in diglyme at 130 °C for 24 h) and heating in the presence of base lead to the formation of **3** (DBU in diglyme at 130 °C for 24 h, 100 %; NaH in MeCN at 60 °C for 24 h, ca. 20 %; *t*-BuOK in MeCN at 60 °C for 24 h, ca. 20 %).

The deprotonation of **4** in solution at ambient temperature lead to the quantitative formation of hexacoordinate species **6** as evident from the ca. 100 ppm upfield shift in ^{31}P NMR from that of **4** and the dissymetrization of the ^{19}F NMR signals of the Martin ligands. Interestingly, the initially formed species (**6-isomer-1** [δ_P (CD_3CN) -111.6]) was found to undergo complete stereomutation to another hexacoordinate species (**6-isomer-2** [δ_P (CD_3CN) -121.8]). The stereochemistries of the hexacoordinate isomers could be assigned to those shown in Scheme 2 out of the possible four[10] based upon NMR measurements.[11] Homo-decoupling measurements of each of the protons [δ_H (CD_3CN) 8.12-8.00 and 7.95-7.82] ortho to P in the two Martin ligands in **6-isomer-1** lead to diminishing of the other ortho proton of the opposing Martin ligand, whereas irradiation of each methylene proton [δ_H (CD_3CN) 4.12 and 3.31] lead to ordinary decoupled spectra. A similar phenomenon could be observed for ^{19}F NMR. These results indicate the presence of a very rapid exchange process ($t_{1/2}$ < 1 s), which could be attributed to topological stereomutation between **6-isomer-1** and **6-isomer-1'**. As for **6-isomer-2**, one of the protons ortho to P in the Martin ligands (ring a) was located upfield, and NOE intensity enhancement could be observed between this proton [δ_H (CD_3CN) 7.08] and methylene proton Ha [δ_H (CD_3CN) 4.02]. Hydrolysis of **6** lead to regeneration of **4**.

In order to elucidate the mechanism of the transformation kinetic measurements were carried out by monitoring ^{19}F NMR on **6-isomer-1** generated in situ. Table 1 shows the solvent effect with representative rates and activation parameters calculated from rates at four different temperatures. The fact that solvents of higher polarity and higher donicities lead to deceleration of rates and that the value of $\Delta S^{\neq}$ was positive implies that the rate determining step involves heterolytic cleavage of a P–O bond assisted by K^+ cation.

Table 1. Solvent Effect upon Rates of Stereomutation from **6-isomer-1-K$^+$** to **6-isomer-2-K$^+$**.

solvent	temp (K)	rate (k_{K^+}; s^{-1})	$\Delta H^{\neq}$ (kcal mol^{-1})	$\Delta S^{\neq}$ (eu)	E_T^N	ε_r	DN^N
THF	298	(1.67 ± 0.02) x 10^{-3}	25.1 ± 0.3	12.9 ± 1.1	0.207	7.58	0.52
MeCN	303	(1.54 ± 0.03) x 10^{-5}	25.5 ± 0.6	8.3 ± 2.0	0.460	35.94	0.36
DMSO	303	(5.37 ± 0.05) x 10^{-5}	26.4 ± 0.2	9.0 ± 0.6	0.444	46.45	0.77

Table 2. Counter Cation Effect upon Rates of Stereomutation from **6-isomer-1** to **6-isomer-2**.

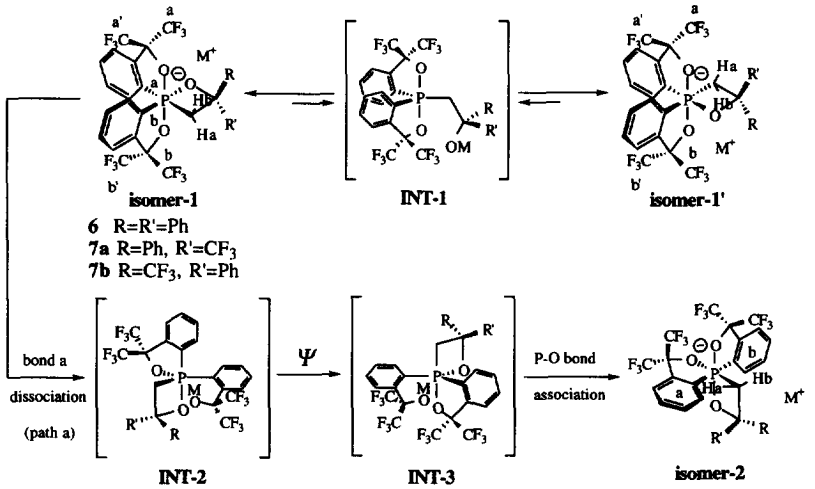
cation	solvent	temp (K)	rate k_{M^+} (s^{-1})	rate of **6-isomer-1-K$^+$** k_{K^+} (s^{-1})	relative rate k_{M^+}/k_{K^+}
Na^+	DMSO	303	(5.48 ± 0.08) x 10^{-5}	5.37 x 10^{-5}	1.02
K^++18-c-6	THF	303	(8.12 ± 0.07) x 10^{-5}	3.50 x 10^{-3} [a]	2.3 x 10^{-2}
Na^+	THF	273	(3.50 ± 0.05) x 10^{-4}	3.24 x 10^{-5} [a]	1.1 x 10
Li^+	THF	248	(2.62 ± 0.04) x 10^{-4}	2.79 x 10^{-7} [a]	9.4 x 10^2

[a] Calculated values from data of Table 1.

Therefore the counter cation effect was next examined. Although the effect was negligible in DMSO (k_{Na^+}/k_{K^+} = 1.02), it was quite significant in THF. That the rates increased in the order of $K^+ < Na^+ < Li^+$ and that crown ether substantially decreased the rate support the dissociation mechanism effected by a metal

cation. A similar solvation effect has also been observed for hexacoordinate antimony, of which a dissociation-association mechanism has been proposed.[5]

Diastereomeric phosphoranes **5a** [δ_P ($CDCl_3$) -21.5] and **5b** [δ_P ($CDCl_3$) -22.1] were prepared and separated by TLC on silica gel (hexane-CH_2Cl_2 = 3:1).[12] When pure **5a** was treated with *t*-BuOK, **7a-isomer-1** [δ_P (DMSO-d_6) -114.0] initially appeared, which converted to **7a-isomer-2** [δ_P (DMSO-d_6) -120.9]. When **5b** (**5b**:**5a** = 3:1) was treated similarly, **7b-isomer-1** [δ_P (DMSO-d_6) -113.3] emerged and changed over to **7b-isomer-2** [δ_P (DMSO-d_6) -119.5], while the initial ratio was retained throughout the sequence. Hydrolysis lead to reversion to **5a** and **5b** (**5b**:**5a** = 3:1), respectively. These results show that the transformations are stereospecific and imply that the stereomutations involve rather simple processes.



Scheme 2

Combining our present results we can rationalize the stereomutation process as shown in Scheme 2. Deprotonation of **4** instantly gives **6-isomer-1**, which is in fast equilibrium with its topomeric **6-isomer-1'** via **INT-1**. Heterolysis of one of the Martin ligand P–O bonds, a, effected by a metal cation gives **INT-2** which is more stable than the phosphorane obtained upon cleavage of bond b. A one step pseudorotation with the monodentate aryl group as the pivot, which is expected to be a low energy process, furnishes **INT-3**. Ring closure of this intermediate gives **6-isomer-2**. The fact that the transformation between **6-isomer-1** and **6-isomer-1'** is much faster than that from **6-isomer-1** to **6-isomer-2** can be attributed to the trans influence (trans carbon atom) of the dissociating P–O bond and ring strain effect of the oxaphosphetane in **6-isomer-1**. No stereomutation could be observed for **6-isomer-2** at least on the NMR timescale. Two different mechanisms have been previously proposed for the stereomutation involving hexacoordinate phosphates with six P–O bonds, a proton acid catalyzed mechanism[13] and a non-dissociative mechanism.[14] Our metal assisted dissociation mechanism which involves 12-P-6 phosphates with an oxaphosphetane ring could be considered to be similar to that of the former.

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9. Data of **4**: mp 112-114 (dec). ^{1}H NMR ($CDCl_3$) 8.06 (dd, J_{P-H}= 11.7 Hz, J = 8.3 Hz, 2H), 7.69-7.60 (m, 4H), 7.52-7.47 (m, 2H), 7.34-7.32 (m, 2H), 7.31-7.28 (m, 2H), 7.26-7.15 (m, 3H), 7.04-7.00 (m, 3H), 4.45 (s, 1H), 3.66 (dd, J_{P-H}= 14.2 Hz, J = 14.7 Hz, 1H), 3.61 (dd, J_{P-H}= 16.6 Hz, J = 14.7 Hz, 1H). ^{13}C NMR ($CDCl_3$) 146.63 (d, J_{P-C}= 12.8 Hz), 145.82 (d, J_{P-C}= 7.4 Hz), 137.00 (d, J_{P-C}= 11.0 Hz), 135.42 (d, J_{P-C}= 20.3 Hz), 133.36, 131.15 (d, J_{P-C}= 14.7 Hz), 131.00 (d, J_{P-C}= 161.8 Hz), 127.97, 127.77, 126.98, 126.95, 125.74, 125.74, 124.28 (d, J_{P-C}= 16.5Hz), 122.55 (q, J_{F-C}= 288.6 Hz), 122.10 (q, J_{F-C}= 288.6 Hz), 81.77 (sept, J_{F-C}= 31.3 Hz), 76.65 (d, J_{P-C}= 7.4 Hz), 51.50 (d, J_{P-C}= 7.4 Hz). ^{19}F NMR ($CDCl_3$) **-73.96** (q, J = 9.5 Hz, 6F), **-74.14** (q, J = 9.5 Hz, 6F). ^{31}P NMR ($CDCl_3$) **-20.5**. Anal. Calcd for $C_{32}H_{21}F_{12}O_3P$: C, 53.95; H, 2.97. Found: C, 53.74; H, 2.69.
10. The other two correspond to (1) an isomer having one Martin ligand oxygen trans to the oxaphosphetane oxygen, and the other Martin ligand oxygen trans to a Martin ligand carbon; (2) an isomer having all the oxygens trans to carbons.
11. Data of **6-isomer-1**: ^{1}H NMR (CD_3CN) **8.12-8.00** (m, 1H), **7.95-7.82** (m, 1H), 7.48-7.42 (m, 2H), 7.31-7.23 (m, 3H), 7.23-7.20 (m, 3H), 7.20-7.11 (m, 2H), 7.08-7.03 (m, 4H), 6.96-6.92 (m, 1H), 6.92-6.88 (m, 1H), **4.12** (dd, J_{P-H}= 21.1 Hz, J = 11.2 Hz, 1H), **3.31** (dd, J_{P-H}= 13.2 Hz, J = 11.2 Hz, 1H). ^{19}F NMR (CD_3CN) **-70.37** (m, 6F), **-73.06** (q, J = 11.3 Hz, 3F), **-73.40** (q, J = 10.7 Hz, 3F). ^{31}P NMR (CD_3CN) **-111.6**. Data of **6-isomer-2**: ^{1}H NMR (CD_3CN) 7.65 (dd, J_{P-H}= 12.7 Hz, J = 7.8 Hz, 1H), 7.38-7.31 (m, 4H), 7.14-7.10 (m, 2H), 7.11-7.07 (m, 1H), **7.08** (dd, J_{P-H}= 13.2 Hz, J = 7.8 Hz, 1H), 7.00-6.95 (m, 2H), 7.04-7.02 (m, 2H), 6.93-6.88 (m, 1H), 6.80-6.76 (m, 2H), 6.76-6.70 (m, 1H), 6.69-6.64 (m, 1H), **4.02** (dd, J_{P-H}= 13.2 Hz, J = 13.2 Hz, 1H), 2.66 (ddq, J_{P-H}= 13.2 Hz, J = 13.2 Hz, J_{F-H}= 2.0 Hz, 1H). ^{19}F NMR (CD_3CN) **-72.55** (q, J = 9.8 Hz, 3F), **-74.15** (q, J = 9.5 Hz, 3F), **-74.73 — -74.78** (m, 6F). ^{31}P NMR (CD_3CN) **-121.8**.
12. Data of **5a** (diastereomer of lower *Rf* value): mp 149-150 °C (dec). ^{1}H NMR ($CDCl_3$) 8.12 (dd, J = 11.7, 7.8 Hz, 2H), 7.67-7.62 (m, 4H), 7.58-7.52 (m, 2H), 7.28-7.25 (m, 2H), 7.10-7.05 (m, 1H), 7.02-6.97 (m, 2H), 5.21 (s, 1H), 3.37 (d, J = 17.6 Hz, 2H). ^{19}F NMR ($CDCl_3$) -74.25 (q, J = 9.8 Hz, 6F), -74.57 (q, J = 9.8 Hz, 6F), -82.03 (s, 3F). ^{31}P NMR ($CDCl_3$) **-21.5**. Data of **5b** (diastereomer of higher *Rf* value) : ^{1}H NMR ($CDCl_3$) 8.19 (dd, J = 11.7, 7.8 Hz, 2H), 7.73-7.68 (m, 4H), 7.68-7.60 (m, 2H), 7.48-7.45 (m, 2H), 7.36-7.28 (m, 3H), 4.51 (s, 1H), 3.44 (dd, J_{P-H}= 13.2 Hz, J = 14.2 Hz, 1H), 3.16 (dd, J_{P-H}= 17.6 Hz, J = 14.7 Hz, 1H). ^{19}F NMR ($CDCl_3$) -74.34 (s, 6F), -80.82 (s, 3F). ^{31}P NMR ($CDCl_3$) **-22.1**.
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