(2-Hydroxyphenylmethylene)bis(phosphine oxides): a Facile Rearrangement into 2-(Phosphinylmethyl)phenyl Phosphinates

Alexander N. Bovin, Alla N. Yarkevich, Alexander V. Kharitonov and Eugene N. Tsvetkov*

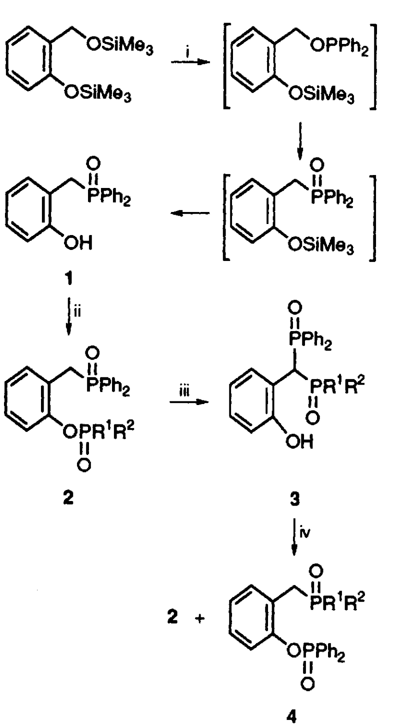
Institute of Physiologically Active Substances, Russian Academy of Sciences, Chernogolovka, 142432 Moscow region, Russia

(2-Hydroxyphenylmethylene)bis(phosphine oxides) **3** prepared from 2-(diphenylphosphinylmethyl)phenyl phosphinates **2** by oxygen-to-carbon 1,4-phosphinyl migration easily rearrange back into a mixture of 2-(phosphinylmethyl)phenyl phosphinates **2** and **4** under basic conditions or upon heating.

Since the pioneering work of Melvin,[1] methods of P–C bond formation by metallation-induced 1,3-phosphorus migration from oxygen or nitrogen to carbon in aryl phosphates (or diamidophosphates, phosphinates *etc.*)[2] and vinyl phosphates[3] have expanded greatly in the last ten years. Recently the similar 1,3-carbon-to-carbon rearrangement also was reported for diethyl 1-alkyl-1*H*-1,2,4-triazol-1-ylphosphonate.[4]

By analogy we attempted to realize 1,4-phosphorus migration (from oxygen to carbon) for derivatives of phenol **1**, initially to prepare 2-(diphenylphosphinylmethyl)phenyl phosphinates **2** for the purpose of preparing (2-hydroxyphenylmethylene)bis(phosphine oxides) **3** since these may serve as prospective end groups for podands.[5] The known[6] diphenyl(2-hydroxyphenylmethyl)phosphine oxide **1** was obtained conveniently (Scheme 1) from 1-trimethylsiloxy-2-(trimethylsiloxymethyl)benzene by reaction with chlorodiphenylphosphine followed by hydrolysis. The phosphinates **2a–2h** prepared from **1** easily rearranged into bis(phosphine oxides) **3** (Table 1) in the presence of $LiN(SiMe_3)_2$ generated *in situ* from phenyllithium and hexamethyldisilazane. The yields of **3** from phosphinates **2a–2e** were good, but in the case of more electronegative substituents R^1 and R^2 at migrating phosphorus (compounds **2f–2h**) the yields were only moderate. The reaction mixtures of **3f–3h** after work-up also contained phenol **1** (35–50%) and initial phosphinates **2f–2h** (15–20%). Attempts to prepare the bis(phosphine oxide) **3i** failed, the only products after work-up were compounds **1** (35%) and **2i** (20%).

Unexpectedly we discovered that attempting to alkylate the free OH-group (K_2CO_3, refluxing dioxane) of the phenol **3a** led to regeneration of the initial phosphinate **2a** (91%), *i.e.* the phosphinyl group has migrated back onto oxygen. It was found this rearrangement took place in solution for all of compounds **3** (Table 2) upon heating and was solvent dependent, with the rate following the sequence $MeCO_2H$ < EtOH < benzene < acetone. Addition of base (pyridine or NEt_3) to solutions of **3** further accelerated the process. Thus, the rearrangement of **3a**, **3f–3h** in refluxing butan-2-one was complete in ≤1.5 h. The same reaction of **3b–3e** required up to 30 h to afford total conversion into migration products **2** and **4**, but under basic conditions in refluxing benzene the migration for **3b–3e** was complete in a few hours (Table 2). The ratio of **2** to **4** in the product mixture depends on the substituents R^1 and R^2: when they are both alkyl the major product is phosphinate



Scheme 1 *Reagents and conditions:* i, $ClPPh_2$, 160 °C, 2 h, then EtOH–benzene at room temp., 24 h, (82%); ii, R^1R^2POCl, NEt_3, benzene, room temp. → reflux, 1 h; iii, Et_2O–THF, $LiN(SiMe_3)_2$ (2 equiv.), −50 °C → room temp., 2 h; iv, benzene, pyridine catalyst reflux, 1–2 h

Table 1 Bis(phosphine oxides) **3** prepared by rearrangement of phosphinates **2** and partial NMR chemical shift data for **3a–3h**[a]

				NMR (CD_3OD)	
Compound	R^1, R^2	Yield[b] (%)	M. p. (°C)	δ_H (CHP^1P^2) ($^2J_{HP}$/Hz)	$\delta_P\{H\}$ ($^2J_{PP}$/Hz)
3a	Ph_2	86	210–211	5.63 (t) (12)	32.40
3b	Et_2	75	199–201	5.16 (dd) (12, 16)	34.03, 58.08 (5)
3c	Pr_2	63	171–174	5.16 (dd) (14, 16)	33.88, 54.65 (5)
3d	Bu_2	75	148–149	5.14 (dd) (14, 18)	33.72, 55.23 (6)
3e	Me, Ph	75[c]	187–189	5.23 (dd) (12, 18)	32.78, 41.31 (5.9)
			173–174	5.48 (dd) (10, 20)[d]	33.10, 42.00 (3.6)
3f	CH_2Cl, Ph	25[e]	191–193	5.57 (dd) (10, 16)	32.31, 36.23 (5.5)
3g	$(CH_2Cl)_2$	10	173–174	5.56 (t) (15)	34.21, 46.51 (5.6)
3h	$(CH_2OPh)_2$	41	139–142	5.60 (t) (15)	33.00, 44.70 (6.0)
3i	CH_2Cl, OPh	0[f]	—	—	—

[a] ^1H NMR spectra recorded at 200 MHz, ^{31}P NMR spectra at 81 MHz. [b] Isolated yields. All of compounds **3a–3h** gave satisfactory analytical data. [c] Mixture of diastereoisomers (3:1). [d] In $CDCl_3$. [e] Only one of isomers was observed by ^{31}P NMR spectroscopy. [f] Not obtained.

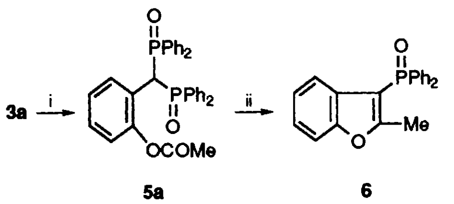
4. For **3e** the ratio of **2e** and **4e** is about 2:1, and for **3f**–**3h** isomeric phosphinates **4f**–**4h** were formed only in trace amounts. Therefore, in all cases the more electronegative phosphinyl group migrates preferentially. In this connection the by-products **2f**–**2h** of the first rearrangement (**2** → **3**) may be partly due to the result of this second rearrangement (**3** → **2**). It can be noted that the second migration, which is facilitated by bases, can be considered as a variant of the rearrangements of α-hydroxyalkylphosphonates and their analogues well described by Pudovik and co-workers.[7]

Because of the ease of rearrangement of **3a**, its acetyl derivative **5a** was prepared (in 50% yield) by heating with $(MeCO)_2O$ (100 °C, *p*-$MeC_6H_4SO_3H$ as catalyst), whilst the treatment of **3a** with $(MeCO)_2O$ in pyridine gave **5a** (Scheme 2) nearly quantitatively. An intramolecular Wittig–Horner reaction of **5a** provided diphenyl(2-methylbenzofuran-3-yl)phosphine oxide **6** in 60% yield.†

Table 2 Rearrangement of bis(phosphine oxides) **3** into mixtures of phosphinates **2** and **4**

Compound	Conditions[a] (reaction time, h)	Yield[b] (%)	
		2	**4**
3a	A(0.5), B(0.5), C(1.5), D(6)	100	—
3b	A(2),[c] B(3)	15	85
3c	A(0.5)	16	84
3d	A(1.5)	13	84
	C(20)	37	63
	D(10)[c]	10	90
3e	A(1.5), C(30)	65	35
	B(1)	50	33
3f	B(0.5)	90	9
	C(0.5)	76	15
3g	C(0.5)	100	0
3h	C(0.5)	95	<5

[a] A, In benzene with pyridine (as catalyst) reflux; B, xylol, reflux; C, butan-2-one, reflux; D, propan-2-ol, reflux. [b] Based on ^{31}P NMR spectroscopy. [c] In sealed tube, 100 °C.



Scheme 2 *Reagents and conditions:* i, $(MeCO)_2O$ (2 equiv.), pyridine, 20 °C, 3 h, (96%); ii, Cs_2CO_3 (2 equiv.), THF, reflux, 3 h (60%)

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Footnote

† Compound **6** gave satisfactory spectral and analytical data: m.p. 147–147.5 °C, ^1H NMR (200 MHz, $CDCl_3$) δ 2.56 (3H, d, J_{HP} 1.5), 6.68 (1H, d, *J* 7), 7.00 (1H, t, *J* 7), 7.21 (1H, t, *J* 7), 7.50 (7H, m), 7.75 (4H, dd, J_{HH}7, J_{HP}12); δ_P ($CDCl_3$) 21.73.

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