Studies on Organophosphorus Compounds 91: A Novel Synthesis of 1-Hydrazinoalkylphosphonic Acids and Derivatives Thereof

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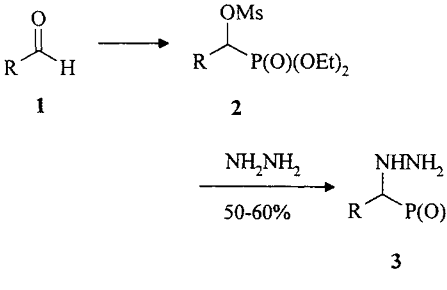
Condensation of diethyl phosphite with aldehydes followed by subsequent sulfonylation of the resulting hydroxy group formed with mesyl chloride gave the corresponding 1-sulfonyloxyalkylphosphonates, which led to the convenient synthesis of 1-hydrazinoalkylphosphonates via nucleophilic substitution by hydrazine. The products could be converted to the corresponding 1-hydrazinoalkylphosphonic acids by acid hydrolysis in high yield.

As an analog of 1-aminoalkylphosphonic acids, 1-hydrazinoalkylphosphonic acids and their derivatives are of potential biological importance. For example, several of these compounds show a good safening effect against the phytotoxic action of chloroacetanilide herbicides.[1] Several procedures for the preparation of the title compounds have been reported. Rachon et al. have described the synthesis of these compounds via base-catalyzed condensation of diethyl phosphite with aliphatic aldazines followed by subsequent acid hydrolysis.[2] This method, however, was not suitable to aryl aldazines and therefore its scope of applications was markedly limited. Maier et al. reported the synthesis of 1-hydrazinomethylphosphonic acid and its derivatives by a similar approach.[3] Based on a selective reduction with $NaBH_3CN$ or $BH_3 \cdot THF$, we described a convenient synthesis of 1-hydrazino- and 2-hydrazinophosphonic acids from the corresponding hydrazone derivatives prepared easily from diethyl oxophosphonates.[4] Herein, we wish to report a novel and general method for the synthesis of 1-hydrazinoalkylphosphonic acids via nucleophilic substitution of 1-sulfonyloxyalkylphosphonates by hydrazine.

As shown in Equation 1, base-catalyzed condensation of diethyl phosphite with aldehydes led to the formation of the corresponding 1-hydroxyalkylphosphonates,[5] which reacted with mesyl chloride to give 1-mesyloxyalkylphosphonates **2** in a one-pot procedure. With the mesyloxy substituent as a good leaving group, compounds **2** could be converted to other types of phosphonates by nucleophilic substitution, as indicated by our previous investigations.[6] Here we used hydrazine hydrate as the nucleophile. As demonstrated by our experiments, nucleophilic substitution by hydrazine in compounds **2** led to the convenient synthesis of the corresponding 1-hydrazinoalkylphosphonates **3** in good yield.



(Eqn 1)

In this substitution reaction, the reaction temperature should be kept below 55 °C, otherwise side reactions occur and the yield of product **3** is significantly reduced. With the use of anhydrous hydrazine instead of hydrazine hydrate as the nucleophile, no remarkable improvement of the yield of product was observed. The resulting diethyl 1-hydrazinoalkylphosphonates **3** were isolated and identified as their oxalates **4**. By condensation with aryl aldehydes, compounds **3** were converted to the corresponding hydrazone derivatives **5** in almost quantitative yield. However, the condensation products of compound **3** with alkyl aldehydes or ketones are unstable and gradually decompose on standing.

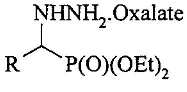
By acidic hydrolysis, compounds **3** were readily converted to the corresponding free acids **6** in high yield.

The above reactions provide a novel, convenient and general synthetic route to 1-hydrazinoalkylphosphonic acids and derivatives thereof.

Table 1. Synthesis of Product **4**

Compound	R	Yield (%)[a,b]	mp (°C)	MS (m/z)	^{31}P NMR δ	IR ν (cm^{-1})
4a	H	50	72–74	182, 152, 138	25.64	3400, 1650, 1230, 1025
4b	Me	53	102–103	196, 166	26.23	3400, 1650, 1230, 1025
4c	Et	56	71–73	210, 180, 164	26.15	3400, 1650, 1240, 1020
4d	$PhCH_2$	61	98–100	272, 242, 186	25.81	3400, 1620, 1220, 1030
4e	Ph	55	116–118	276, 248, 142	24.93	3400, 1620, 1230, 1020
4f	4-MeC_6H_4	60	80–82	272, 242, 186	23.31	3400, 1650, 1240, 1020
4g	4-$MeOC_6H_4$	52	136–138	278, 248, 168	25.25	3400, 1650, 1240, 1020
4h	4-FC_6H_4	54	84–86	276, 246, 139	22.95	3400, 1650, 1230, 1020
4i	4-ClC_6H_4	52	96–98	292/294, 155/157	22.63	3400, 1650, 1230, 1025

[a] Isolated yield based on corresponding aldehyde **1**.
[b] Satisfactory microanalyses obtained: C ± 0.38; H ± 0.22; N ± 0.28.



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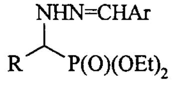

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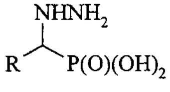

6

4,6	R	4,6	R	4,6	R
a	H	**d**	$PhCH_2$	**g**	$4\text{-}MeOC_6H_4$
b	Me	**e**	Ph	**h**	$4\text{-}FC_6H_4$
c	Et	**f**	$4\text{-}MeC_6H_4$	**i**	$4\text{-}ClC_6H_4$

5 R = Ph, $4\text{-}MeC_6H_4$, $4\text{-}MeOC_6H_4$, $4\text{-}FC_6H_4$
Ar = Ph, $4\text{-}MeC_6H_4$, $4\text{-}MeOC_6H_4$, $4\text{-}FC_6H_4$, $4\text{-}ClC_6H_4$, $2,4\text{-}Cl_2C_6H_3$, $4\text{-}NO_2C_6H_4$

Mps are uncorrected. IR spectra were recorded on an IR-440 spectrometer. ^1H NMR spectra were taken on a Varian EM-360 spectrometer. ^{31}P NMR spectra were measured on an AMX-300 NMR spectrometer with TMS as the internal standard and 85% H_3PO_4 as the external standard. EIMS spectra were obtained on a Finnigan-4201 mass spectrometer.

Diethyl α-Hydrazinobenzylphosphonate Oxalate (4e); Typical Procedure:

A mixture of benzaldehyde (10 mL, 0.1 mol), diethyl phosphite (13 mL, 0.1 mol) and Et_3N (7 mL, 0.05 mol) was heated at 75°C for 30 min. The reaction mixture was cooled down to r.t. and CH_2Cl_2 (100 mL) and Et_3N (8.4 mL, 0.06 mol) were then added. After stirring at 0°C for 10 min, the mixture was treated with mesyl chloride (8.5 mL, 0.11 mol) dropwise. After the complete addition, the mixture was allowed to warm up to r.t. and stirred for an additional 2 h. The resulting mixture was filtered and the filtrate was washed with water (3 × 20 mL), dried (Na_2SO_4) and concentrated in vacuo to leave the crude product **2e** (32 g) as a colorless oil, which was used directly in the next step without further purification.

Hydrazine hydrate (19.4 mL, 0.4 mol) was added dropwise with stirring to **2e** (32 g) in EtOH (40 mL) at 0°C with the aid of an ice-cooled bath. After the complete addition, the mixture was allowed to warmed up to 50°C and stirred for 15 h. The mixture was then concentrated in vacuo and the residue was dissolved in water (100 mL), which was extracted with Et_2O (3 × 50 mL) and then saturated with NaCl. The saturated solution was extracted with CH_2Cl_2 (4 × 50 mL). The combined CH_2Cl_2 extracts were dried (Na_2SO_4), filtered and concentrated in vacuo to leave the product **3e**; yield: 14.2 g (55%); yellowish oil; characterized as its oxalate **4e** (Table 1).

Table 2. Compounds **5** synthesized

Compound[a]	R	Ar	mp (°C)	MS (m/z)	^{31}P NMR δ	IR ν (cm^{-1})
5a	Ph	Ph	100–102	298, 260	21.53	3200, 3030, 1600, 1255, 1025
5b	Ph	$4\text{-}MeC_6H_4$	103–132	361, 322	21.73	3200, 3040, 1600, 1250, 1025
5c	Ph	$4\text{-}MeOC_6H_4$	119–121	377, 237	20.51	3200, 3030, 1600, 1250, 1025
5d	Ph	$4\text{-}FC_6H_4$	108–110	365, 244	21.10	3200, 3020, 1650, 1250, 1025
5e	Ph	$4\text{-}ClC_6H_4$	114–16	381, 264	21.32	3200, 3025, 1600, 1250, 1025
5f	Ph	$2,4\text{-}Cl_2C_6H_3$	118–20	416, 348	20.92	3200, 3030, 1650, 1250, 1025
5g	Ph	$4\text{-}NO_2C_6H_4$	148–150	392, 324	20.81	3200, 1600, 1510, 1340, 1235, 1020, 980
5h	$4\text{-}MeC_6H_4$	Ph	70–72	361, 223	21.65	3200, 3030, 1600, 1250, 1030
5i	$4\text{-}MeC_6H_4$	$4\text{-}MeC_6H_4$	64–66	375, 237	21.33	3200, 3030, 1600, 1255, 1030
5j	$4\text{-}MeC_6H_4$	$4\text{-}MeOC_6H_4$	62–64	391, 253	21.42	3200, 3030, 1600, 1250, 1025
5k	$4\text{-}MeC_6H_4$	$4\text{-}ClC_6H_4$	70–72	395, 257	21.44	3200, 3040, 1600, 1250, 1030
5l	$4\text{-}MeC_6H_4$	$2,4\text{-}Cl_2C_6H_3$	72–74	429, 291	21.62	3200, 3030, 1590, 1245, 1025
5m	$4\text{-}MeC_6H_4$	$4\text{-}FC_6H_4$	62–64	379, 241	21.40	3200, 3040, 1590, 1250, 1025
5n	$4\text{-}MeC_6H_4$	$4\text{-}NO_2C_6H_4$	84–86	406, 268	21.38	3200, 3050, 1580, 1250, 1020
5o	$4\text{-}MeOC_6H_4$	Ph	80–81	360, 322	21.55	3200, 3030, 1590, 1250, 1030
5p	$4\text{-}MeOC_6H_4$	$4\text{-}MeC_6H_4$	126	391, 254	22.69	3300, 1610, 1510, 1250, 1040, 980
5q	$4\text{-}MeOC_6H_4$	$4\text{-}MeOC_6H_4$	124–126	407, 384	22.45	3300, 1600, 1510, 1245, 1020
5r	$4\text{-}MeOC_6H_4$	$4\text{-}FC_6H_4$	94–95	395, 345	22.34	3300, 3030, 1600, 1250, 1025
5s	$4\text{-}MeOC_6H_4$	$4\text{-}ClC_6H_4$	112	411, 364	22.36	3200, 1610, 1510, 1240, 1030, 980
5t	$4\text{-}MeOC_6H_4$	$2,4\text{-}Cl_2C_6H_3$	160	446, 402	22.04	3200, 1610, 1510, 1260, 1050, 980
5u	$4\text{-}MeOC_6H_4$	$4\text{-}NO_2C_6H_4$	116–117	422, 402	21.69	3200, 1610, 1510, 1340, 1020, 970
5v	$4\text{-}FC_6H_4$	Ph	80–82	365, 227	21.92	3200, 3040, 1600, 1520, 1340, 1270, 1030, 740
5w	$4\text{-}FC_6H_4$	$4\text{-}MeC_6H_4$	73–75	379, 241	22.12	3200, 3030, 1600, 1250, 1020
5x	$4\text{-}FC_6H_4$	$4\text{-}MeOC_6H_4$	74–76	395, 257	22.08	3200, 3030, 1600, 1250, 1025
5y	$4\text{-}FC_6H_4$	$4\text{-}ClC_6H_4$	84–86	399, 261	21.42	3200, 3040, 1590, 1240, 1020
5z	$4\text{-}FC_6H_4$	$2,4\text{-}Cl_2C_6H_3$	86–88	433, 295	21.37	3200, 3050, 1600, 1250, 1025
5a′	$4\text{-}FC_6H_4$	$4\text{-}NO_2C_6H_4$	94–96	410, 272	21.13	3200, 3050, 1580, 1250, 1020, 740
5b′	$4\text{-}FC_6H_4$	$4\text{-}FC_6H_4$	80–82	383, 245	21.85	3200, 1580, 1465, 1230, 1025, 970, 740
5c′	$4\text{-}ClC_6H_4$	Ph	92–94	381, 243	21.22	3200, 3040, 1600, 1250, 1020
5d′	$4\text{-}ClC_6H_4$	$4\text{-}MeC_6H_4$	70–72	395, 257	21.25	3200, 3020, 1600, 1250, 1025
5e′	$4\text{-}ClC_6H_4$	$4\text{-}ClC_6H_4$	78–80	415, 277	21.10	3200, 3040, 1590, 1250, 1025
5f′	$4\text{-}ClC_6H_4$	$2,4\text{-}Cl_2C_6H_3$	84–86	449, 311	21.22	3200, 3030, 1600, 1250, 1020
5g′	$4\text{-}ClC_6H_4$	$4\text{-}NO_2C_6H_4$	104–106	426, 288	21.55	3200, 3050, 1580, 1245, 1020, 970
5h′	$4\text{-}ClC_6H_4$	$4\text{-}FC_6H_4$	75–77	399, 261	21.60	3200, 3040, 1590, 1245, 1025

[a] Satisfactory microanalyses obtained: C ± 0.31, H ± 0.21, N ± 0.28.

Table 3. Synthesis of Product **6**

Compound	R	Yield (%)[a,b]	Lit mp (°C)	mp (°C)	^{31}P NMR δ	IR ν (cm^{-1})
6a	H	75	72–74	74–76	15.02	3400, 1650, 1250, 1030
6b	Me	71	174–178	176–178	15.22	3600, 1610, 1130, 1010
6c	Et	70	168–171	168–170	15.44	3400, 1620, 1250, 1020
6d	$PhCH_2$	77		204–206	15.60	3600, 1610, 1120, 1025
6e	Ph	84		211–213	15.48	3400, 1605, 1250
6f	$4\text{-}MeC_6H_4$	85		198–200	15.68	3300, 1605, 1250
6g	$4\text{-}MeOC_6H_4$	71		203–205	15.82	3300, 1600, 1250
6h	$4\text{-}FC_6H_4$	82		206–208	15.41	3300, 1600, 1250
6i	$4\text{-}ClC_6H_4$	74		217–219	15.24	3300, 1590, 1250

[a] Yield of isolated product based on compound **3**.

[b] Satisfactory microanalyses obtained: C ± 0.32; H ± 0.22; N ± 0.25.

Table 4. ^1H NMR Spectra of Compounds **4**, **5** and **6**

Compound	^1H NMR ($CDCl_3$) δ, J (Hz)
4a	1.22 (t, 6 H, $J = 7$, CH_3), 3.45 (d, 2 H, $J = 16$ CH_2P), 4.15 (m, 4 H, $2 \times CH_2O$)
4b	1.18 (t, 6 H, $J = 8$, CH_3), 3.34 (m, 4 H, $2 \times CH_2O$), 4.25 (d, 1 H, $J = 18$, $CH-P$)
4c	0.94–1.74 (m, 9 H), 3.2–3.8 (m, 1 H), 3.9–4.4 (m, 4 H), 4.55 (d, 1 H, $J = 18$, $CH-P$)
4d	1.05 (t, 6 H, $2 \times CH_3$), 2.5–3.5 (m, 1 H), 3.4–4.3 (m, 6 H), 7.2 (s, 5 H, C_6H_5)
4e	1.03 (t, 6 H, $2 \times CH_3$), 2.6–3.6 (m, 1 H), 3.8 (m, 4 H, $2 \times CH_2O$), 4.28 (d, 1 H, $J = 20$, $CH-P$)
4f	1.00, 1.10 (2 t, 6 H, $J = 7$, $2 \times CH_3$), 2.17 (s, 3 H, CH_3), 3.95 (m, 4 H, $2 \times CH_2O$), 4.15 (d, 1 H, $J = 18$, $CH-P$), 7.16 (m, 4 H, C_6H_4)
4g	0.98–1.28 (m, 6 H, $J = 7$, $2 \times CH_3$), 3.74–4.16 (m, 7 H, $2 \times OCH_2 + OCH_3$), 4.32–4.56 (d, 1 H, CH), 6.88–7.36 (m, 4 H, C_6H_4)
4h	1.10, 1.20 (2 t, 3 H, $J = 7$, CH_3), 4.05 (m, 4 H, $2 \times CH_2O$), 4.25 (d, 1 H, $J = 18$, CH), 7.20 (m, 2 H, C_6H_4), 7.40 (m, 2 H, C_6H_4)
4i	1.00, 1.10 (2 t, 6 H, $J = 7$, $2 \times CH_3$), 4.00 (m, 4 H, $2 \times CH_2O$), 4.40 (d, 1 H, $J = 20$, $CH-P$), 7.30 (m, 4 H, C_6H_4)
5a	1.12, 1.46 (m, 6 H, $J = 7$, $2 \times CH_3$), 3.3–4.48 (m, 5 H, $2 \times CH_2O$, CH)
5b	1.0–1.44 (m, 6 H, $J = 7$, $2 \times CH_3$), 2.34 (s, 3 H, $Ar-CH_3$), 3.88–4.4 (m, 5 H, $2 \times CH_3O$, CH)
5c	1.12–1.36 (q, 6 H, $2 \times CH_3$), 3.8 (s, 3 H, OCH_3), 3.82–4.2 (m, 4 H, $2 \times CH_2O$), 6.84–7.74 (m, ArH)
5d	1.08–1.40 (q, 6 H, $2 \times CH_3$), 3.8–4.2 (s, 3 H, OCH_3), 7.2–7.6 (m, 9 H, C_6H_5, C_6H_4)
5e	1.04–1.42 (m, 6 H, $2 \times CH_3$), 3.64–4.42 (m, 4 H, $2 \times CH_2O$), 7.2–7.84 (m, 9 H, C_6H_5, C_6H_4)
5f	1.02, 1.48 (m, 6 H, $2 \times CH_3$), 3.64–4.42 (q, 4 H, $2 \times CH_2O$), 4.76–4.98 (d, 1 H, $J = 20$, $CH-P$), 7.2–7.88 (m, 8 H, C_6H_4, C_6H_3)
5g	1.0–1.42 (m, 6 H, $2 \times CH_3$), 3.7–4.4 (m, 4 H, $2 \times CH_2$), 4.76–5.00 (d, 1 H, $J = 20$, $CH-P$), 7.2–8.28 (m, 9 H, C_6H_5, C_6H_4)
5h	1.10, 1.25 (2 t, 6 H, $J = 7$, $2 \times CH_3$), 2.18 (s, 3 H, CH_3), 4.05 (m, 4 H, $2 \times CH_2O$), 4.85 (d, 1 H, $J = 20$, $CH-P$), 6.00 (br, 1 H, NH), 6.90–7.50 (m, 10 H, $C_6H_4 + C_6H_5CH=N$)
5i	1.15, 1.26 (2 t, 6 H, $J = 7$, $2 \times CH_3$), 2.17, 2.25 (2 s, 6 H, $2 \times CH_3$), 4.05 (m, 4 H, $2 \times CH_2O$), 4.85 (d, 1 H, $J = 21$, $CH-P$), 5.59 (br, 1 H, NH), 6.90–7.50 (m, 9 H, $2 \times C_6H_4$, $+ CH=N$)
5j	1.15, 1.26 (2 t, 2×3 H, $J = 7$, $2 \times CH_3$), 2.17 (s, 3 H, CH_3), 3.70 (s, 3 H, CH_3O), 4.10 (m, 4 H, $2 \times CH_2O$), 4.85 (d, 1 H, $J = 20$, $CH-P$), 5.9 (br, 1 H, NH), 6.90–7.40 (m, 9 H, $2 \times C_6H_4$, $CH=N$)
5k	1.15, 1.28 (2 t, 2×3 H, $J = 7$, $2 \times CH_3$), 2.20 (s, 3 H, CH_3), 4.05 (m, 4 H, $2 \times CH_2O$), 4.85 (d, 1 H, $J = 20$, $CH-P$), 6.00 (br, 1 H, NH), 6.90–7.60 (m, 9 H, $2 \times C_6H_4$, $CH=N$)
5l	1.15, 1.30 (2 t, 2×3 H, $J = 7$, $2 \times CH_3$), 2.20 (s, 3 H, CH_3), 4.05 (m, 4 H, $2 \times CH_2O$), 4.85 (d, 1 H, $J = 20$, $CH-P$), 6.05 (br, 1 H, NH), 6.90–7.80 (m, 9 H, $2 \times C_6H_4$, $CH=N$)
5m	1.15, 1.30 (2 t, 2×3 H, $J = 7$, $2 \times CH_3$), 2.22 (s, 3 H, CH_3), 4.05 (m, 4 H, $2 \times CH_2O$), 4.90 (d, 1 H, $J = 20$, $CH-P$), 6.10 (br, 1 H, NH) 6.90–7.80 (m, 8 H, C_6H_4, C_6H_3, $CH=N$)
5n	1.15, 1.30 (2 t, 2×3 H, $J = 7$, CH_3), 2.20 (s, 3 H, CH_3), 4.10 (m, 4 H, $2 \times CH_2O$), 4.90 (d, 1 H, $J = 20$, $CH-P$), 6.10 (br, 1 H, NH), 6.90, 7.90 (m, 9 H, $2 \times C_6H_4$, $CH=N$)
5o	1.12, 1.36 (q, 6 H, $2 \times CH_3$), 3.8 (s, 3 H, CH_3), 4.05 (m, 4 H, $2 \times CH_2O$), 4.85 (d, 1 H, $J = 20$, $CH+P$), 6.02 (br, 1 H, NH), 7.2–8.28 (m, 9 H, C_6H_5, C_6H_4).
5p	1.12–1.34 (m, 6 H, $2 \times CH_3$), 2.31 (s, 3 H, $Ar-CH_3$), 3.78–4.16 (m, 7 H, $2 \times CH_2O$, OCH_3), 4.81–4.88 (d, 1 H, $J = 20$, $CH-P$), 6.86–7.62 (m, 9 H, $2 \times C_6H_4$, $CH=N$)
5q	1.15, 1.26 (2 t, 2×3 H, $J = 7$, $2 \times CH_3$), 3.8 (s, 3 H, OCH_3), 3.82–4.00 (m, 4 H, $2 \times CH_2O$), 4.90 (d, 1 H, $J = 20$, $CH-P$), 6.1 (br, 1 H, NH), 6.90–7.80 (m, 7 H, $2 \times C_6H_3$, $CH=N$)
5r	1.14, 1.22 (2 t, 2×3 H, $J = 7$, $2 \times CH_3$), 3.8 (s, 3 H, OCH_3), 3.8–4.02 (m, 4 H, $2 \times CH_2O$), 4.90 (d, 1 H, $J = 20$, $CH-P$), 6.8–7.9 (m, 7 H, $2 \times CH_3$, $CH=N$)
5s	1.12–1.32 (m, 6 H, $2 \times CH_3$), 3.93–4.13 (m, 7 H, $2 \times CH_2$, OCH_3), 4.80–4.88 (d, 1 H, $J = 20$, $CH-P$), 6.87–7.79 (m, 9 H, $2 \times C_6H_4$, $CH=N$)
5t	1.13–1.40 (m, 6 H, $2 \times CH_3$), 3.83–4.16 (m, 7 H, $2 \times CH_2O$, OCH_3), 4.83–4.9 (d, 1 H, $J = 20$, $CH-P$), 6.88–8.16 (m, 8 H, C_6H_4, C_6H_3, $CH=N$)
5u	1.13–1.33 (m, 6 H, $2 \times CH_3$), 3.8–4.16 (m, 7 H, $2 \times CH_2O$, OCH_3), 4.86–4.93 (d, 1 H, $J = 20$, $CH-P$), 6.89–8.14 (m, 9 H, $2 \times C_6H_4$, $CH=N$)

Table 4. (continued)

Compound	^1H NMR ($CDCl_3$) δ, J (Hz)
5v	1.15, 1.30 (2t, 6H, $J = 7$, $2\times CH_3$), 4.05 (m, 4H, $2\times CH_2O$), 4.95 (d, 1H, $J = 20$, CH–P), 6.05 (br, 1H, NH), 7.00–7.50 (m, 10H, C_6H_5, C_6H_4, CH=N)
5w	1.10, 1.28 (2t, 6H, $J = 7$, $2\times CH_3$), 3.70 (s, 3H, CH_3O), 4.05 (m, 4H, $2\times CH_2O$), 5.00 (d, 1H, $J = 20$, CH–P), 6.00 (br, 1H, NH), 5.90–7.60 (m, 9H, $2\times C_6H_4$, CH=N)
5x	1.10, 1.25 (2t, 6H, $J = 7$, $2\times CH_3$), 3.70 (s, 3H, CH_3O), 4.05 (m, 4H, $2\times CH_2O$), 5.05 (d, 1H, $J = 20$, CH–P), 6.00 (br, 1H, NH), 6.90–7.60 (m, 9H, $2\times C_6H_4$, CH=N)
5y	1.15, 1.30 (2t, 6H, $J = 7$, $2\times CH_3$), 4.10 (m, 4H, $2\times CH_2O$), 5.00 (d, 1H, $J = 21$, CH–P), 6.10 (br, 1H, NH), 7.00–7.70 (m, 9H, $2\times C_6H_4$, CH=N)
5z	1.19, 1.33 (2t, 6H, $J = 7$, $2\times CH_3$), 4.10 (m, 4H, $2\times CH_2O$), 5.00 (d, 1H, $J = 21$, CH–P), 6.10 (br, 1H, NH), 7.00–7.74 (m, 9H, $2\times C_6H_4$, CH=N)
5a′	1.15, 1.30 (2t, 6H, $J = 7$, $2\times CH_3$), 4.10 (m, 4H, $2\times CH_2O$), 5.00 (d, 1H, $J = 20$, CH–P), 6.00 (br, 1H, NH), 7.00–7.90 (m, 8H, C_6H_4, C_6H_3, CH=N)
5b′	1.16, 1.30 (2t, 6H, $J = 7$, $2\times CH_3$), 4.10 (m, 4H, $2\times CH_2O$), 5.10 (d 1H, $J = 20$, CH–P), 6.08 (br, 1H, NH), 7.1–8.00 (m, 9H, $2\times C_6H_4$, CH=N)
5c′	1.15, 1.30 (2t, 6H, $J = 7$, $2\times CH_3$), 4.10 (m, 4H, $2\times CH_2O$), 5.20 (d, 1H, $J = 20$, CH–P), 6.10 (br, 1H, NH), 7.10–7.80 (m, 10H, C_6H_5, C_6H_4, CH=N)
5d′	1.15, 1.30 (2t, 6H, $J = 7$, $2\times CH_3$), 2.17 (s, 3H, CH_3), 4.10 (m, 4H, $2\times CH_2O$), 5.20 (d, 1H, $J = 20$, CH–P), 6.10 (br, 1H, NH)
5e′	1.15, 1.30, (2t, 6H, $J = 7$, CH_3), 4.05 (m, 4H, $2\times CH_2O$), 5.22 (d, 1H, $J = 20$, CH–P), 6.10 (br, 1H, NH), 7.10–7.70 (m, 9H, $2\times C_6H_4$, CH=N)
5f′	1.14, 1.28 (2t, 6H, $J = 7$, $2\times CH_3$), 4.10 (m, 4H, $2\times CH_2O$), 5.20 (d, 1H, $J = 20$, CH–P), 6.15 (br, 1H, NH), 7.20–7.90 (m, 9H, $2\times C_6H_4$, CH=N)
5g′	1.15, 1.30 (2t, 6H, $J = 7$, $2\times CH_3$), 4.10 (m, 4H, $2\times CH_2O$), 5.20 (d, 1H, $J = 20$, CH–P), 6.20 (br, 1H, NH), 7.20–7.80 (m, 8H, C_6H_4, C_6H_3, CH=N)
5h′	1.15, 1.30 (2t, 6H, $J = 7$, $2\times CH_3$), 4.05 (m, 4H, $2\times CH_2$), 5.22 (d, 1H, $J = 20$, CH–P), 6.10 (br, 1H, NH), 7.10, 7.70 (m, 9H, $2\times C_6H_4$, CH=N)
6a	1.1–1.8 (m, 2H), 3.3–4.1 (m, 1H)
6b	2.22 (s, 3H, CH_3), 3.1–3.8 (m, 2H, CH_2)
6c	2.22 (s, 3H, CH_3), 3.1–3.6 (m, 2H, CH_2)
6d	3.1–3.8 (m, 2H, CH_2), 4.1–4.5 (m, 1H), 7.70 (s, 5H, C_6H_5)
6e	2.22 (s, 3H, CH_3), 4.15 (d, 1H, $J = 18$, CH), 5.00 (d, 1H, $J = 20$, CH–P), 7.1–7.7 (m, 5H, C_6H_5)
6f	2.22 (s, 3H, CH_3), 4.15 (d, 1H, $J = 18$, CH), 7.20 (m, 4H, C_6H_4)
6g	2.18 (s, 3H, CH_3), 4.15 (d, 1H, $J = 18$, CH), 5.05 (d, 1H, $J = 20$, CH–P), 7.2–7.6 (m, 4H, C_6H_4)
6h	4.10 (d, 1H, $J = 18$, CH), 7.00 (m, 2H, C_6H_4), 7.20 (m, 4H, C_6H_4)
6i	2.35 (s, 3H, CH_3), 4.17 (d, 1H, $J = 18$, CH), 5.00 (d, 1H, $J = 20$, CH–P), 7.1–7.8 (m, 4H, C_6H_4)

Diethyl α-(2′-Benzylidenehydrazino)benzylphosphonate (5a); Typical Procedure:

Compound **3e** (0.26 g, 1.0 mmol) prepared similarly to **4e** was dissolved in Et_2O (20 mL) and benzaldehyde (0.1 mL, 1.0 mmol) was then added at r.t. with stirring. A white precipitate was formed immediately. The mixture was stirred for 10 min and filtered. The precipitate was washed with Et_2O and dried in a vacuum dryer to give the pure product **5a** as a white solid (Table 2).

α-Hydrazinobenzylphosphonic Acid (6e); Typical Procedure:

Compound **3e** (2.6 g, 10 mmol) prepared as above was dissolved in 6 N HCl (60 mL) and the mixture was stirred at 85 °C for 10 h. The mixture was concentrated in vacuo and the residue was dissolved in EtOH (4 mL). Propylene oxide was added dropwise until the pH of the solution was approximately 7. The resulting mixture was filtered and the precipitate was washed with EtOH. The precipitate was dried in a vacuum dryer to give the product **6e** as a white solid; yield: 1.7 g (84%); (Table 3).

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(1) Diel, P.; Maier, L. Eur. Pat. Appl. EP 143078 1985; *Chem. Abstr.* **1985**, *103*, 215544m.

(2) Rachon, J.; Wasielewski, C. *Rocz. Chem.* **1976**, *50*, 477.

(3) Diel, P.; Maier, L. *Phosphorus, Sulfur, Silicon* **1988**, *36*, 85.

(4) Yuan, C.; Chen, S.; Xie, R.; Feng, H. *Phosphorus, Sulfur, Silicon* **1995**, *106*, 115.

(5) Baraldi, P.G.; Guarneri, M.; Moroder, F.; Pollini, G.P.; Simoni, D. *Synthesis* **1982**, 653.

(6) Li, C.; Yuan, C. *Tetrahedron Lett.* **1993**, *34*, 1515.