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# PHOSPHORYLATION OF FURFURAL BY SECONDARY PHOSPHINE OXIDES

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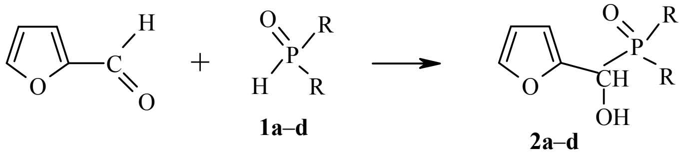
*Nucleophilic addition of secondary phosphine oxides to furfural takes place under mild conditions and gives quantitative yields of 2-(diorganylphosphorylhydroxymethyl)furans, which are polyfunctional building blocks for organic synthesis and prospective amphiphilic ligands for the design of metal complex catalysts.*

**Keywords:** diorganylphosphine oxides, 2-(diorganylphosphorylhydroxymethyl)furans, furfural, phosphorylation.

Information on the use of furfural in organophosphorus synthesis for the formation of a C–P bond is apparently limited to its reaction with phosphine [1, 2]. This reaction takes place in the presence of acids or the salts of transition metals and leads to tris(1-hydroxy-1-furylmethyl)phosphine, which is a valuable synthon and a promising ligand. Furylphosphines have been used successfully for the production of catalysts for many important organic reactions [3], and the development of new convenient approaches to the synthesis of phosphines and phosphine oxides with furan rings is therefore an urgent task.

For this purpose in the present work we studied for the first time the reaction of furfural with readily obtainable secondary phosphine oxides **1**, which can be easily prepared from elemental phosphorus [4-6].

It was found that furfural reacts with the phosphine oxides **1a-d** at room temperature or with gentle heating (50-65°C) in THF, forming 2-(diorganylphosphorylhydroxymethyl)furans **2a-d** with almost quantitative yields.



**1**, **2** **a** R = *n*-Bu; **b** R = *n*-$C_6H_{13}$; **c** R = $Ph(CH_2)_2$; **d** R = 4-$Py(CH_2)_2$

The reaction was monitored by $^{31}P$ NMR from the disappearance of the signal for the initial secondary phosphine oxides **1a-d** in the region of 30-32 ppm and from the appearance of signals in the region of 47-50 ppm, belonging to the tertiary phosphine oxides.

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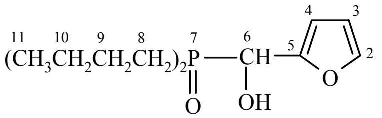
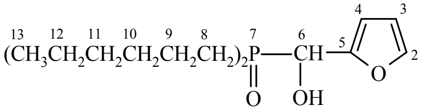
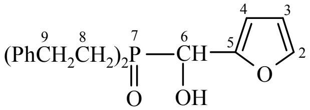
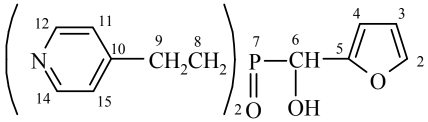
TABLE 1. The $^{1}$H, $^{13}$C, and $^{31}$P NMR Spectra of Compounds **2a-d**

| Compound | Formula | Chemical shifts (CDCl$_3$), δ, ppm. (coupling constants, *J*, Hz) | | |
|---|---|---|---|---|
| | | $^{1}$H | $^{13}$C | $^{31}$P |
| **2a** |  | 0.87 (6H, t, 11-H); 1.32 (4H, m, 10-H); 1.50 (4H, m, 9-H); 1.57-1.88 (4H, m, 8-H); 5.05 (1H, d, $^{2}J_{PH}$ = 7.8, 6-H); 6.35 (1H, t, 4-H); 6.42 (1H, t, 3-H); 6.52 (1H, br. s, 6-OH); 7.37 (1H, s, 2-H) | 12.84, 12.89 $C_{(11)}$, 22.53 $C_{(10)}$, 23.65, 23.81 $C_{(9)}$, 23.94 (d, $C_{(8)}$, $^{1}J_{PC}$ = 59.0), 24.14 (d, $C_{(8)}$, $^{1}J_{PC}$ = 61.7), 65.48 (d, $C_{(6)}$, $^{1}J_{PC}$ = 80.1), 107.93 (d, $C_{(4)}$, $^{3}J_{PC}$ = 6.1), 110.01 $C_{(3)}$, 141.62 $C_{(2)}$, 150.69 $C_{(5)}$ | 48.81 |
| **2b** |  | 0.86 (6H, t, 13-H); 1.25 (4H, m, 12-H); 1.33 (4H, m, 11-H); 1.56 (4H, m, 8-H); 1.67 (4H, m, 9-H); 1.83 (4H, m, 10-H); 5.06 (1H, d, $^{2}J_{PH}$ = 7.48, 6-H); 5.95 (1H, br. s, 6-OH); 6.35 (1H, t, 4-H); 6.42 (1H, t, 3-H); 7.24 (1H, s, 2-H) | 13.98 $C_{(13)}$, 21.22 $C_{(12)}$, 22.42 $C_{(11)}$, 24.66 (d, $C_{(8)}$, $^{1}J_{PC}$ = 62.1), 25.56 (d, $C_{(8)}$,$^{1}J_{PC}$ = 60.8), 30.85 (d, $C_{(9)}$,$^{2}J_{PC}$ = 13.7), 30.88 (d, $C_{(9)}$, $^{2}J_{PC}$ = 13.8), 31.24 (d, $C_{(10)}$, $^{3}J_{PC}$ = 5.1), 66.49 (d, $C_{(6)}$,$^{1}J_{PC}$ = 77.9), 108.68 (d, $C_{(4)}$, $^{2}J_{PC}$ = 5.6), 110.78 $C_{(3)}$, 142. 31 $C_{(2)}$, 151.08 $C_{(5)}$ | 48.92 |
| **2c** |  | 2.03 (4H, m, 8-H); 2.90 (4H, m, 9-H); 5.16 (1H, d, $^{2}J_{PH}$ = 8.0, 6-H); 6.38 (1H, t, 4-H); 6.48 (1H, t, 3-H); 6.63 (1H, br. s, 6-OH); 7.23 (10H, m, Ph); 7.40 (1H, s, 2-H) | 26.50 (d, $C_{(8)}$, $^{1}J_{PC}$ = 58.7), 27.80 (d, $C_{(8)}$, $^{1}J_{PC}$ = 59.1), 26.96 (d, $C_{(9)}$, $^{2}J_{PC}$ = 3.8), 66.67 (d, $C_{(6)}$, $^{1}J_{PC}$ = 75.4), 108.73 (d, $C_{(4)}$, $^{3}J_{PC}$ = 6.0), 110.60 $C_{(3)}$, 125.95, 126.05 C-*p*, 127.66 C-*o*, 128.18, 128.24 C-*m*, 136.67 $C_{(2)}$, 142.31 (d, C-*ipso,* $^{3}J_{PC}$ = 2.1), 149. 86 $C_{(5)}$ | 49.84 |
| **2d** |  | 2.03 (4H, m, 8-H); 2.86 (4H, m, 9-H); 5.18 (1H, d, $^{2}J_{PH}$ = 8.8, 6-H); 6.40 (1H, t, 4-H); 6.47 (1H, t, 3-H); 6.93 (1H, br. s, 6-OH); 7.11, (4H, d. d, 12-, 14-H); 7.42 (1H, s, 2-H); 8.45 (4H, t, 11-, 15-H) | 25.59 (d, $C_{(8)}$, $^{1}J_{PC}$ = 60.8), 26.13 (d, $C_{(8)}$, $^{1}J_{PC}$ = 59.1), 26.29 (d, $C_{(9)}$, $^{2}J_{PC}$ = 4.0), 65.87 (d, $C_{(6)}$, $^{1}J_{PC}$ = 81.0), 108.76 (d, $C_{(4)}$, $^{3}J_{PC}$ = 7.0), 110.69 $C_{(3)}$, 123.06, 123.14 $C_{(11)}$, $C_{(15)}$, 142.53 $C_{(2)}$, 149.05, 149.17 $C_{(12)}$, $C_{(14)}$, 149.75, 149.89 $C_{(10)}$, 150.15 $C_{(5)}$ | 47.58 |

For the case of the dibutyl- and bis(2-phenylethyl)phosphine oxides **1a**,**c** it was shown that the secondary phosphine oxides react with furfural even at 25-26°C (THF); here their degree of conversion after 24 h amounted to 80-86%. Subsequent heating of the reaction mixtures (50°C) for 2-3 h led to quantitative conversion of the phosphine oxides **1a**,**c** into the corresponding phosphorylfurans **2a**,**c**.

The reaction of furfural with dihexyl- and bis[2-(4-pyridyl)ethyl]phosphine oxides **1b**,**d** was conducted at ~50-65°C; quantitative conversion of these phosphine oxides to phosphorylfurans **2b**,**d** was observed after 20-24 h.

The most characteristic in the $^1$H and $^{13}$C NMR spectra of compounds **2a-d** are the signals of the CH group of the OCHP=O fragment: A doublet at 5.05-5.18 ppm with a geminal $^{31}$P–$^1$H spin–spin coupling constant of 7.45-8.80 Hz ($^1$H NMR) and a doublet in the region of 65.48-66.67 ppm ($^1J_{PC}$ ~75-81 Hz; $^{13}$C NMR). The anisochronism of the two chemically equivalent substituents at the phosphorus atom in the $^1$H and $^{13}$C NMR spectra is due to their diastereotopy. The same nonequivalence was observed in the $^1$H and $^{13}$C NMR spectra of 2-(diorganylphosphorylhydroxymethyl)-1-organylimidazoles [7].

In the IR spectra of **2a-d** the band for the stretching vibrations of the hydroxyl group appears in the region of 3118-3146 cm$^{-1}$, which is evidently due to the presence of an intramolecular hydrogen bond involving the phosphoryl fragment. A similar long-wave shift of the band for the stretching vibrations of the hydroxyl group was also observed for the analogous products from addition of secondary phosphine oxides to 3-(trialkylsilyl)- and 3-(trialkylgermyl)-2-propynals [8].

Thus, the reaction of furfural with secondary phosphine oxides is a convenient and effective method for the synthesis of new polyfunctional 2-(organylphosphorylhydroxymethyl)furans, which are highly reactive building blocks and prospective polydentate lipophilic ligands.

## EXPERIMENTAL

The IR spectra were obtained on a Specord IR-75 spectrometer in microlayers and in tablets with potassium bromide. The $^1$H, $^{13}$C, and $^{31}$P NMR spectra were recorded on a Bruker DPX-400 spectrometer at 400, 100, and 161 MHz respectively in deuterochloroform with HMDS as internal standard and 85% phosphoric acid as external standard.

**General Procedure.** A mixture of furfural (11 mmol) and the diorganylphosphine oxide (10 mmol) in THF (10 ml) was stirred at 50-55°C for 20-24 h while the reaction was monitored by $^{31}$P NMR spectrometry. The solvent was removed at reduced pressure, and the residue was reprecipitated from chloroform with pentane (for compounds **2a**,**b**,**d**) or recrystallized from hexane (compound **2c**). Compounds **2a-d** were obtained after evaporation of the solvent.

**2-(Dibutylphosphorylhydroxymethyl)furan (2a).** The product was a viscous nondistilling liquid. Yield 2.5 g (97%). IR spectrum (microlayer), ν, cm$^{-1}$: 1145 (P=O), 3136 bs (OH). Found %: C 60.45; H 8.97; P 11.99. $C_{13}H_{23}O_3P$. Calculated %: C 60.22; H 8.91; P 11.90.

**2-(Dihexylphosphorylhydroxymethyl)furan (2b).** The product was a viscous nondistilling liquid. Yield 3.1 g (97%). IR spectrum (microlayer), ν, cm$^{-1}$: 1146 (P=O), 3146 bs (OH). Found %: C 64.53; H 10.19; P 9.63. $C_{17}H_{31}O_3P$. Calculated %: C 64.94; H 9.84; P 9.82.

**2-[Bis(2-phenylethyl)phosphorylhydroxymethyl]furan (2c).** Yield 3.5 g (98%); mp 82-84°C (hexane). IR spectrum (potassium bromide), ν, cm$^{-1}$: 1144 (P=O), 3123 bs (OH). Found %: C 71.17; H 6.54; P 8.74. $C_{21}H_{23}O_3P$. Calculated %: C 71.14; H 6.88; P 8.90.

**2-{Bis[2-(4-pyridyl)ethyl]phosphorylhydroxymethyl}furan (2d).** The product was a viscous nondistilling liquid. Yield 3.4 g (95%). IR spectrum (microlayer), ν, cm$^{-1}$: 1156 (P=O), 3118 bs (OH). Found %: C 63.97; H 5.89; N 7.72; P 8.43. $C_{19}H_{21}N_2O_3P$. Calculated %: C 64.04; H 5.94; N 7.86; P 8.69.

The $^1$H, $^{13}$C, and $^{31}$P NMR spectra for compounds **2a-d** are given in Table 1.

## REFERENCES

1. M. Reuter and L. Orthner, Ger. Patent 1075610; *Ref. Zh. Khim.*, L83 (1961).
2. B. A. Trofimov, N. K. Gusarova, and S. N. Arbuzova, *Usp. Khim.*, **68**, 240 (1999).
3. N. G. Andersen and B. A. Keay, *Chem. Rev.*, **101**, 997 (2001).
4. B. A. Trofimov, N. K. Gusarova, and L. Brandsma, *Main Group Chem. News*, **4**, 18 (1996).
5. N. K. Gusarova, S. F. Malysheva, S. N. Arbuzova, and B. A. Trofimov, *Izv. Akad. Nauk. Ser. Khim.*, 1695 (1998).
6. N. K. Gusarova, L. Brandsma, S. N. Arbuzova, S. F. Malysheva, and B. A. Trofimov, *Zh. Org. Khim.*, **32**, 269 (1996).
7. N. K. Gusarova, S. N. Arbuzova, A. M. Reutskaya, I. I. Ivanova, L. V. Baikalova, L. M. Sinegovskaya, N. N. Chipanina, A. V. Afonin, and I. A. Zyryanova, *Khim. Geterotsikl. Soedin.*, 72 (2002).
8. N. K. Gusarova, A. M. Reutskaya, N. I. Ivanova, A. S. Medvedeva, M. M. Demina, P. S. Novopashin, A. V. Afonin, A. I. Albanov, and V. A. Trofimov, *J. Organomet. Chem.*, **659**, 172 (2002).