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Noncatalytic Regio- and Stereoselective Addition of Secondary Phosphines to Cyanoacetylenic Alcohols

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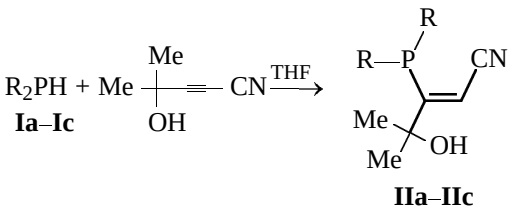
Abstract — Secondary phosphines regio- and stereoselectively add to 4-hydroxy-4-methyl-2-pentynenitrile, a typical and available representative of cyanoacetylenic alcohols, without catalyst at room temperature (THF, 3 h) to form (*Z*)-3-[dialkyl(aryl)phosphino]-4-hydroxy-4-methyl-2-pentenenitriles in 80–85% yields. These compounds relate to a new class of functionalyzed phosphines, promising ligands for the design of metal-complex catalysts.

Addition of phosphines to acetylene and its derivatives is a convenient approach to formation of a C–P bond and synthesis of unsaturated phosphines that are promising building blocks for preparing chiral phosphorus-containing ligands [1, 2]. Special place among such reactions is occupied by addition of secondary phosphines to cyanoacetylenes, permitting to prepare amphiphilic tertiary phosphines with hydrophobic substituents and polar acrylonitrile function (easily transformed to amide or carboxy groups). Such compounds are promising ligands for metal complexes that combine properties of phase-transfer and micellar catalysts. At the same time, the information on phosphorylation of cyanoacetylenes is scarce. It is known that diisopropyl- and di-*tert*-butylphosphines stereoselectively react with cyanoacetylene to form the *Z* isomers of corresponding phosphinoacrylonitriles in 28–33% yields [3]. In the case of the less sterically congested dimethylphosphine, a mixture of (*Z*)- and (*E*)-3-(dimethylphosphino)acrylonitriles (1 : 2) is formed in 50% yield [3]. The chemo-, regio-, and stereoselective addition of primary [4] and secondary [5] phosphines to phenylcyanoacetylene has been reported, leading to corresponding secondary and tertiary cyanoethenylphosphines of *Z* configuration in an almost quantitative yield. Furthermore, a short communication on the reaction of 4-hydroxy-4-methyl-2-pentynenitrile with secondary phosphines has been published [4].

In the present work with the purpose of synthesizing new functionalyzed tertiary phosphines and their derivatives, as well as gaining additional information on the regularities of phosphorylation of acetylenes with secondary phosphines, we have investigated the reactions of a typical and available [6] representative of cyanoacetylenic alcohols, 4-hydroxy-4-methyl-2-pentynenitrile with dialkyl- and bis[aryl(hetaryl)-ethyl]phosphines. The latter are nowadays easily prepared from red phosphorus and alkyl halides [7] or aryl(hetaryl)ethenes [8, 9].

Dibutyl, bis(2-phenylethyl)- and bis[2-(2-pyridyl)-ethyl]phosphines regio- and stereoselectively add to 4-hydroxy)4-methyl-2-pentynenitrile in THF at room temperature to form (*Z*)-[dialkyl(aryl)phosphino]-4-hydroxy-4-methyl-2-pentenenitriles **IIa**–**IIc** in 80–85% yields.



R = *p*-Bu (**a**), $PhCH_2CH_2$ (**b**), $2\text{-}PyCH_2CH_2$ (**c**).

The structure and configuration of compounds **IIa**–**IIc** were confirmed by their chemical transformations and NMR spectra.

The doublet ethenyl proton signals in the range 6.2–6.5 ppm ($^3J_{HP}$ 5.4 and 6.6 Hz), observed in the ^{1}H NMR spectra of phosphines **IIb** and **IIc**, should, according to published data [3, 5, 10, 11], correspond to *cis* location of hydrogen and phosphorus. However, the presence in the two-dimensional ^{1}H–^{1}H NOESY NMR spectra of these phosphines of cross peaks corresponding to interaction of protons of the ethenyl and methyl groups, that is only possible if

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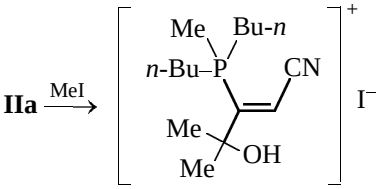
these groups are *cis* to each other, provides unambiguous evidence for *Z* configuration of compounds **IIb** and **IIc**.

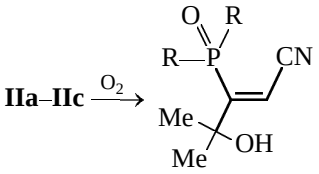
In the ^{1}H NMR spectrum of phosphine **IIa**, the doublet signal of the ethenyl proton (6.40 ppm), too, has a low $^3J_{HP}$ coupling constant (4.8 Hz), which is more characteristic of the *E* isomers of such compounds [3, 5, 10, 11]. The ^{1}H–^{1}H NOESY NMR spectrum of phosphine **IIa** does not give such an unambiguous picture as the spectra of compounds **IIb** and **IIc**, because the signal of the methyl group is overlapped by the multiplet of methylene protons of the butyl substituent. However, treatment of 3-(dibutylphosphino)-4-hydroxy-4-methyl-2-pentenenitrile (**IIa**) with methyl iodide in THF at room temperature gave phosphonium salt **III** of *Z* configuration ($^3J_{HP}$ 35.9 Hz) [10] in quantitative yield.



III

In view of this result, we assigned to 3-(dibutylphosphino)-4-hydroxy-4-methylpentenenitrile (**IIa**), like to compounds **IIb** and **IIc**, *Z* configuration.

When exposed to air, phosphines **IIb** and **IIc** are slowly (for about 2 months) oxidized to phosphine oxides **IVb** and **IVc** (isolable with 51–61%); phosphorus-containing polymers are formed under these conditions as by-products.



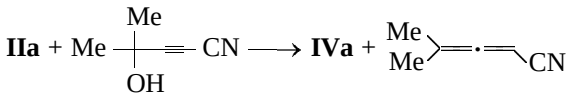
IVa–IVc

R = *n*-Bu (**a**), $PhCH_2CH_2$ (**b**), $2\text{-}PyCH_2CH_2$ (**c**).

Under analogous conditions, phosphine **IIa** gives a mixture of several organophosphorus compounds, among which 3-(butylphosphinoyl)-4-hydroxy-4-methyl-2-pentenenitrile (**IVa**). The latter product was identified by means of NMR spectroscopy (δ_P 50.8 ppm; δ 6.03 ppm, doublet). The *Z* configuration of phosphine oxides **IVa**–**IVc** was confirmed by their ^{1}H NMR spectra. The $^3J_{HP}$ coupling constants of the ethenyl proton doublets are 31.8 Hz for compound **IVa** and 32.2 Hz for compounds **IVb** and **IVc**, which is characteristic of *Z* isomers [10, 11].

Contrary to the majority of tertiary phosphines, phosphines **IIa**–**IIc** are oxidized slowly, probably because the electron density on phosphorus in them is decreased by conjugation of its lone electron pair with the double carbon–carbon bond.

Knowing that tertiary phosphines mildly reduce cyanoacetylenic alcohols to allenes [12], we made an attempt to effect an analogous redox reaction between phosphine **IIa** and 4-hydroxy-4-methyl-2-pentynenitrile. In this case, the reaction proceeds with heat evolution (the reaction mixture warmes up to 50–55°C) and gives a mixture of products, in which we identified oxide **IVa** (by ^{31}P and ^{1}H NMR spectroscopy) and the expected reduction product of the starting hydroxyacetylene, 4-methylpenta-2,3-dienenitrile [ν, cm^{-1}: 1969.4 (C=C=C); δ, ppm: 4.99 heptet (=CHCN)] (these data agree with those reported in [12]).



Hence, the reaction of cyanoacetylenic alcohols with secondary phosphines, that proceeds regio- and stereoselectively under mild conditions as *trans* addition of nucleophiles (specifically, P-nucleophiles [3, 13]) to activated acetylenes [14], opens up a convenient and effective synthetic route to new functionalyzed tertiary phosphines, promising polydentate amphiphilic ligands for the design of catalysts of new generation [15, 16], as well as highly reactive intermediates for fine organic synthesis.

EXPERIMENTAL

The ^{1}H and ^{31}P NMR spectra were recorded on a Bruker DPX-400 spectrometer (400.13 and 161.98 MHz, respectively) in $CDCl_3$ against internal HMDS and external 85% phosphoric acid. The IR spectra were obtained on a Bruker IFS-25 spectrometer in thin layer or in KBr. All experiments were carried out under argon.

(*Z*)-3-(Dibutylphosphino)-4-hydroxy-4-methyl-2-pentenenitrile (IIa). To a solution of 0.28 g of dibutylphosphine in 4 ml of THF, a solution of 0.21 g of 4-hydroxy-4-methyl-2-pentenenitrile in 4 ml of THF was added dropwise with stirring at room temperature in 10 min. The reaction mixture was stirred at room temperature for 3 h and then passed through a bed of Al_2O_3 (1 cm). The solvent was removed at reduced pressure, and the residue was distilled in a

vacuum to give 0.41 g (81%) of phosphine **IIa** as a light yellow oil. IR spectrum, ν, cm^{-1}: 2215 (C≡N), 3300 (OH). ^1H NMR spectrum, δ, ppm: 0.93 t (6H, *Me*CH_2, $^3J_{HH}$ 6.8 Hz), 1.39–1.54 m (14H, *Me*COH, CH_2), 1.85–1.94 m and 2.08–2.17 m (4H, CH_2P), 6.40 d (1H, =CH, $^3J_{HP}$ 4.8 Hz). ^{31}P NMR spectrum: δ_P –28.7 ppm. Found, %: C 65.57; H 10.56; N 5.74; P 11.85. $C_{14}H_{26}NOP$. Calculated, %: C 65.85; H 10.26; N 5.49; P 12.13.

(*Z*)-3-[Bis(2-phenylethyl)phosphino]-4-hydroxy-4-methyl-2-pentenenitrile (IIb) was prepared similarly to phosphine **IIa** from 0.36 g of phosphine **Ib** and 0.15 g of 4-hydroxy-4-methyl-2-pentenenitrile. The resulting product was dissolved in diethyl ether, insoluble substances were filtered off, the ether was removed at reduced pressure, and the residue was dried in a vacuum to give 0.42 g (80%) of phosphine **IIb** as a yellow oil. IR spectrum, ν, cm^{-1}: 2210 (C≡N), 3300 (OH). ^1H NMR spectrum δ, ppm: 1.41 s (6H, Me), 1.81–1.95 m (4H, CH_2P), 2.60-2.75 m (4H, CH_2Ph), 6.45 d (1H, =CH, $^3J_{HP}$ 5.4 Hz), 7.15–7.27 m (10H, Ph). ^{31}P NMR spectrum: δ_P –28.9 ppm. Found, %: C 74.98; H 7.55; N 3.76; P 9.05. $C_{22}H_{26}NOP$. Calculated, %: C 75.19; H 7.46; N 3.99; P 8.81.

(*Z*)-3-{Bis[2-(2-pyridyl)ethyl]phosphino}-4-hydroxy-4-methyl-2-pentenenitrile (IIc) was prepared similarly to compound **IIa** from 0.37 g of phosphine **Ic** and 0.16 g of 4-hydroxy-4-methyl-2-pentenenitrile. Yield 0.45 g (85%), yellow oil. IR spectrum, ν, cm^{-1}: 2215 (C≡N), 3276 (OH). ^1H NMR spectrum, δ, ppm: 1.43 s (6H, Me), 2.30–2.41 m and 2.58–2.69 m (4H, CH_2P), 2.91–3.01 m (4H, CH_2), 6.25 d (1H, =CH, $^3J_{HP}$ 6.6 Hz), 7.18 d.d (2H, pyridine, $^3J_{HH}$ 7.8 Hz, $^3J_{HH}$ 12.5 Hz), 7.24 d (2H, pyridine, $^3J_{HH}$ 7.8 Hz), 7.64 d.d (2H, pyridine, $^3J_{HH}$ 7.8 Hz, $^3J_{HH}$ 7.8 Hz), 8.50 d (2H, CH=N, pyridine, $^3J_{HH}$ 12.5 Hz). ^{31}P NMR spectrum: δ_P –25.1 ppm. Found, %: C 67.68; H 7.02; N 11.60; P 8.97. $C_{20}H_{24}N_3OP$. Calculated, %: C 67.97; H 6.85; N 11.89; P 8.76.

Dibutyl[(*Z*)-2-cyano-1-(1-hydroxy-1-methylethyl)vinyl]methylphosphonium iodide (III). To a solution of 0.11 g of phosphine **IIa**, a solution of 0.4 g of methyl iodide in 3 ml of THF was added. The reaction mixture was stirred at room temperature for 8 h, the solvent and and unreacted methyl iodide were removed at reduced pressure, and the residue was dried in a vacuum to give 0.17 g (100%) of phosphonium iodide **II**, yellow oil. IR spectrum, ν, cm^{-1}: 2220 (C≡N), 3270 (OH). ^1H NMR spectrum, δ, ppm: 0.99 t (6H, *Me*CH_2, $^3J_{HH}$ 6.8 Hz), 1.40–1.65 m (8H, CH_2), 1.70 s (6H, *Me*COH), 2.50 d (3H, MeP, $^2J_{HP}$ 13.8 Hz), 2.78–2.98 m (4H, CH_2P), 6.6 d (1H, =CH, $^3J_{HP}$ 35.9 Hz). ^{31}P NMR spectrum: δ_P 33.8 ppm. Found, %: C 45.63; H 7.65; I 31.60; N 3.60; P 7.58. $C_{15}H_{29}INOP$. Calculated, %: C 45.35; H 7.36; I 31.94; N 3.53; P 7.80.

(*Z*)-3-[Bis(2-phenylethyl)phosphinoyl]-4-hydroxy-4-methyl-2-pentenenitrile (IVb). Phosphine **IIb**, 0.3 g, was allowed to stand in air for 2 months. The resulting viscous product was dissolved in 3 ml of THF, and the solution was passed through a bed of Al_2O_3 (1 cm) the solvent was removed at reduced pressure, and the residue was dried in a vacuum to give 0.19 g (61%) of phosphine oxide **IVb**, white powder, mp 100–102°C (from ether). IR spectrum, ν, cm^{-1}: 2210 (C≡N), 3300 (OH), 1160 (P=O). ^1H NMR spectrum, δ, ppm: 1.55 s (6H. Me), 2.30–2.45 m and 2.52–2.65 m (4H, CH_2P), 2.85–2.98 m and 3.00–3.10 m (4H, CH_2Ph), 5.25 s (1H, OH), 6.02 d (1H, =CH, $^3J_{HP}$ 32.3 Hz), 7.18–7.31 m (10H, Ph). ^{31}P NMR spectrum: δ_P 46.9 ppm. Found, %: C 71.65; H 7.43; N 3.72; P 8.63. $C_{22}H_{26}NO_2P$. Calculated, %: C 71.92; H 7.13; N 3.81; P 8.43.

(*Z*)-3-[Bis[2-(2-pyridyl)ethyl]phosphinoyl]-4-hydroxy-4-methyl-2-pentenenitrile (IVc) was prepared similarly to phosphine oxide **IVb** from 0.3 g of phosphine **IIc**. Yield 0.16 g (51%), yellow oil. IR spectrum, ν, cm^{-1}: 2215 (C≡N), 3270 (OH), 1152 (P=O). ^1H NMR spectrum, δ, ppm: 1.53 s (6H, Me), 2.78–2.90 m and 3.03–3.31 m (8H, CH_2), 6.04 d (1H, =CH, $^3J_{HP}$ 32.2 Hz), 7.18 d.d (2H, pyridine, $^3J_{HH}$ 7.8 Hz, $^3J_{HH}$ 12.5 Hz), 7.24 d (2H, pyridine, $^3J_{HH}$ 7.8 Hz), 8.50 d (2H, CH=N, pyridine, $^3J_{HH}$ 12.6 Hz). ^{31}P NMR spectrum: δ_P 49.1 ppm. Found, %: C 64.81; H 6.80; N 11.32; P 8.61. $C_{20}H_{24}N_3O_2P$. Calculated, %: C 65.03; H 6.55; N 11.38; P 8.38.

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