Reactions of dibenzylphosphine oxide with α,β-unsaturated nitriles: synthesis of aminophospholene oxides

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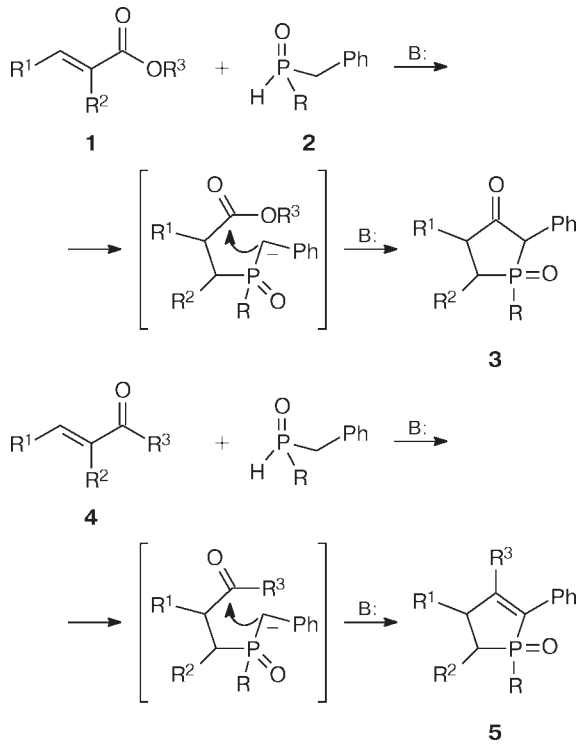
The reactions of dibenzylphosphine oxide with α,β-unsaturated nitriles in the presence of two equivalents of NaH in Bu^{t}OMe afforded substituted aminophospholene oxides in 20—83% yields. In the presence of bulky substituents at the α and γ positions of unsaturated nitriles, cyclization of the initially formed adducts proceeds with high stereoselectivity to give the single stereoisomer of aminophospholene oxide.

Key words: aminophospholene oxides, dibenzylphosphine oxide, α,β-unsaturated nitriles, heterocycles, terpenoids, nucleophilic addition, phosphorylation.

The use of readily available natural terpenoids in the synthesis of new biologically active compounds and chiral auxiliary agents calls for selective procedures for the introduction of heteroatomic functional groups, which can substantially change the polarity, solubility, and coordination ability of the starting terpene molecules. In this respect, phosphorus-containing functional groups, which often impart biological activity to the compounds, are very attractive substituents. Particular attention has been given to chiral organophosphorus compounds in which both the phosphorus[1,2] and the adjacent carbon atoms[1—3] are chiral. The use of chiral organophosphorus compounds in the enantioselective synthesis is well known. A few examples of phosphorus-containing terpenes reported in the literature provide evidence that phosphorylated terpenes show promise as auxiliary chiral agents.[4,5] Among phosphorus-containing derivatives of terpenes, phosphates of acyclic allylic alcohols (geraniol, nerol, linalool, nerolidol, *etc*.) have received the most study because they play an important role in the biosynthesis of terpenes in plants. Due to high lability of terpenes and severe conditions of phosphorylation of olefins, general procedures for the selective introduction of phosphorus substituents into terpene molecules are lacking.

The addition of phosphorus(III) halides to dienes has commonly been used for the preparation of five-membered phosphorus-containing heterocycles for years.[6—8] In 1970s, it was found[9] that the reactions of α,β-unsaturated esters (**1**) with secondary phosphine oxides (**2**) containing the benzyl group afforded the corresponding phosphorus-containing heterocycles **3**. Unsaturated ketones (**4**) behave analogously to give heterocycles **5** [10] (Scheme 1).

Scheme 1



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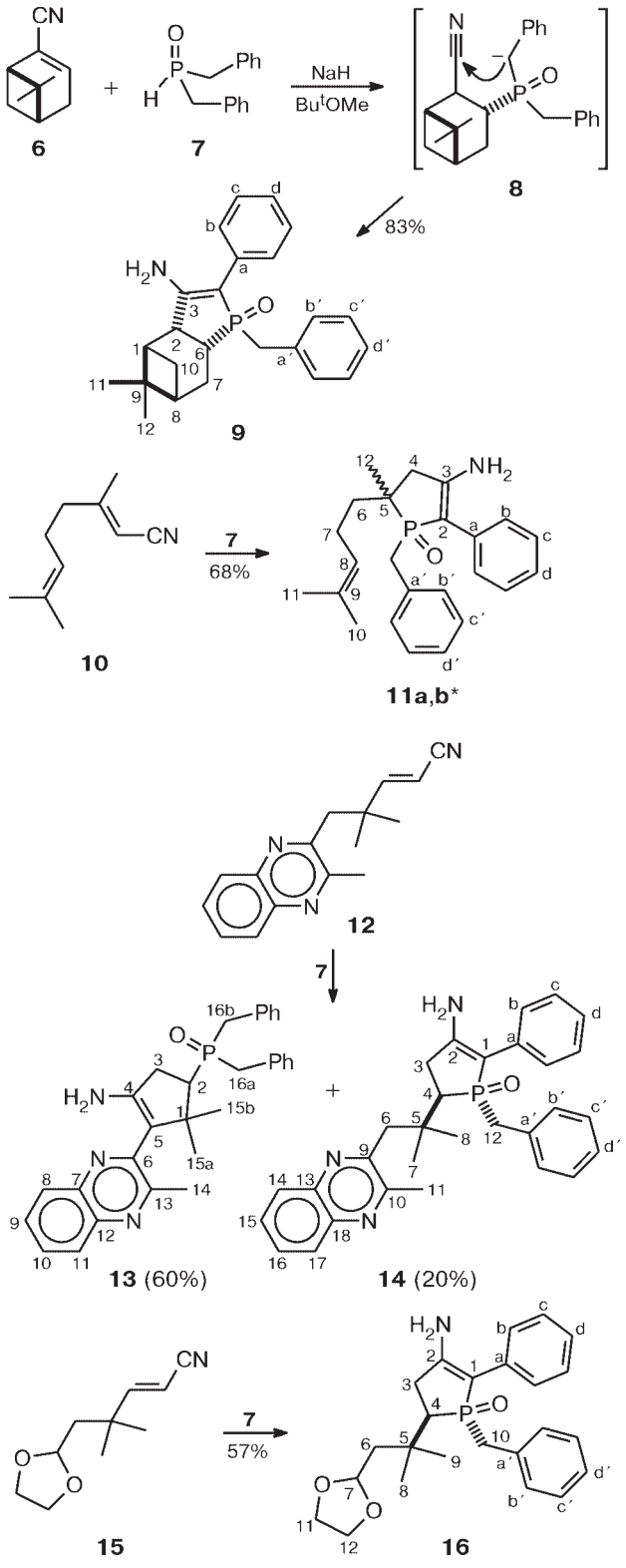
Scheme 2

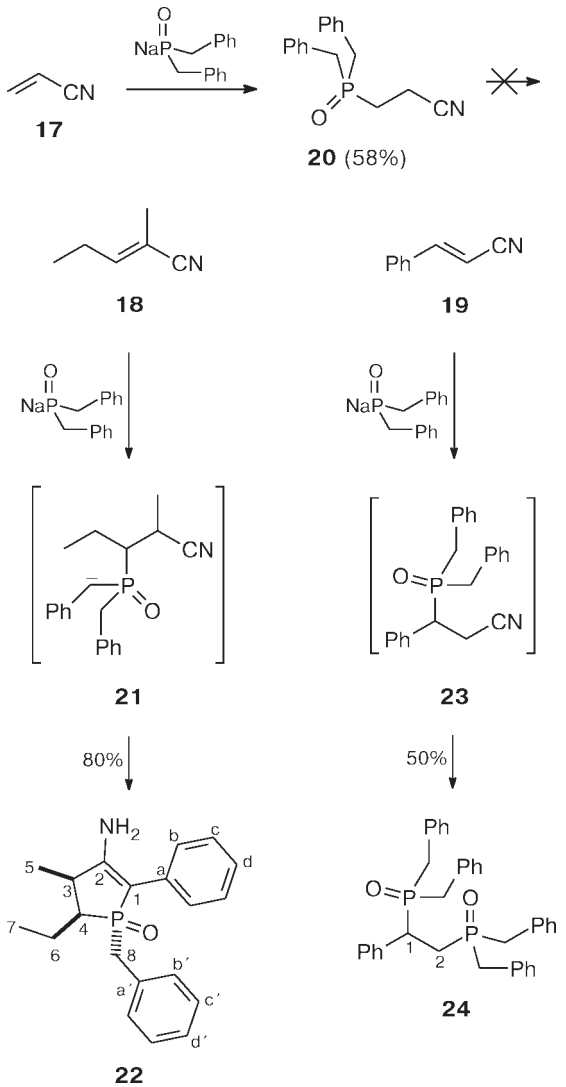


* Two epimers (3 : 2).

Note. The atomic numbering scheme is given for the interpretation of the NMR spectra.

Previously, using myrtenic acid nitrile as an example, we have demonstrated that aminophospholene oxides can be prepared by the reactions of dibenzylphosphine oxide (**7**) with α,β-unsaturated nitriles.[11] In the present study, we examined the scope of this procedure for the preparation of aminophospholene oxides and extended the range of substrates by involving both terpenic α,β-unsaturated nitriles (**10**, **12**, and **15**) (Scheme 2) containing different carbon skeletons and simplest unsaturated nitriles (**17**, **18**, and **19**) (Scheme 3). Under the action of dibenzylphosphine oxide **7**, all nitriles, except for acrylonitrile and cinnamonitrile, were transformed into the corresponding aminophospholene oxides in good yields.

Scheme 3



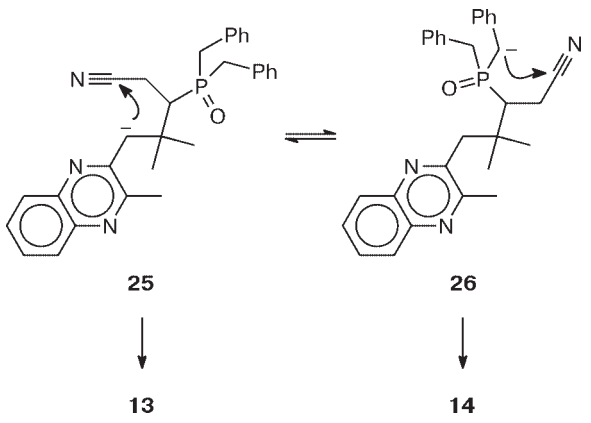
The mechanism of the addition of dibenzylphosphine oxide to unsaturated esters[12] involves the initial addition

of the phosphinite anion to the double carbon-carbon bond followed by cyclization of the resulting benzyl anion at the carboxy group (see Scheme 1). Most likely, the reactions of α,β-unsaturated nitriles proceed by the same mechanism. In the studies of the reactions of esters,[12] it was demonstrated that the use of the second equivalent of a base (for the purpose of generating dianions) in the case of sterically hindered substrates leads to an increase in the yields of phospholene oxides. Taking into account that the substrates under study are sterically crowded molecules as well, we used two equivalents of the base.

The reaction of geranyl nitrile **10** with dibenzylphosphine oxide (**7**) afforded a mixture of epimers **11a**,**b** in a ratio of 3 : 2. The major isomer was isolated by crystallization. However, we failed to establish its three-dimensional structure. Generally, the configurations of substituents in the phospholene ring are determined from the spin-spin coupling constants of the protons geminal with respect to the phosphorus atom.[13] However, compound **11** contains no these hydrogen atoms and, consequently, it is impossible to establish the mutual arrangement of the C(12) atom and the phosphoryl oxygen atom by spectroscopic methods.

The reaction of quinoxaline-containing nitrile **12** also afforded two products, which are structural isomers **13** and **14**. The nitrile, which was initially formed upon the addition of the phosphorus-containing reagent, contains two types of benzylic methylene groups (at the α position of the benzene rings and at the α position of the quinoxaline fragment). Hence, two types of carbanions can be produced. The latter can undergo subsequent cyclization to give the final products (Scheme 4). Due to a substantial difference in properties, compounds **13** and **14** were easily separated and obtained in the individual form. Aminophospholene oxide **14** was isolated as the only epimer. NMR spectroscopy did not reveal another epimer in noticeable amounts even in the crude product.

Scheme 4



The geminal spin-spin coupling constant $^2J_{P-C(4)-H(4)}$ = 8.9 Hz is indicative of the mutual *cis* arrangement of the alkyl substituent and the phosphoryl oxygen atom in the phospholene ring.[13] The fact that the yield of aminophospholene oxide **14** is lower than that of enamine **13** bearing the exocyclic phosphorus atom is attributable to lower stability of anion **26** (compared to **25**) due to stronger electron-withdrawing properties of the quinoxaline fragment compared to the unsubstituted benzene ring.

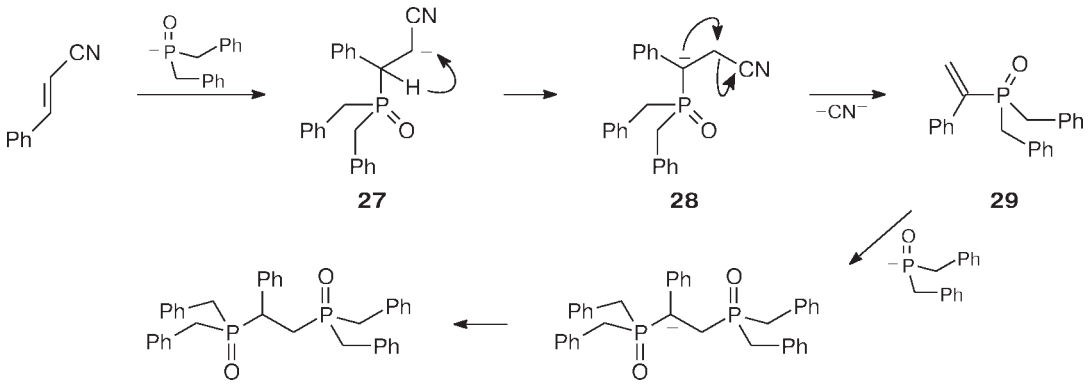
The reaction of nitrile **15** also gave rise to the single stereoisomer of aminophospholene oxide **16**. The signal for the H(4) proton in the ^{1}H NMR spectrum is involved in a complex strongly coupled spin system. Analysis of this system gave the spin-spin coupling constant $^2J_{P-C(4)-H(4)}$ = 8.8 Hz, which is indicative of the mutual *cis* arrangement of the alkyl substituent and the phosphoryl oxygen atom in the phospholene ring of compounds **16**.

As in the case of the above-described terpene derivatives, the addition of dibenzylphosphine oxide to the simplest nitriles **17**, **18**, and **19** proceeded very readily, but the resulting products are substantially different. In the reaction with acrylonitrile **17**, phosphine oxide **20** was isolated as the reaction product in good yield. Attempts to subject this product to subsequent cyclization failed, whereas the reaction with nitrile **18** afforded aminophospholene oxide **22.** The reaction of cinnamonitrile (**19**) yielded diphosphine dioxide **24**, which can formally be considered as the product of the replacement of the CN group by the dibenzylphosphinite anion in intermediate **23**. However, according to the published data, the addition of the phosphorus-containing reagent at the CN group is much more probable than the direct replacement of the CN group by the phosphorus-containing reagent.[14,15] Hence, we assumed the mechanism of formation of compound **24** (Scheme 5), which involves (*a*) the rearrangement of the initially formed anion **27** into the benzylic anion **28**, (*b*) elimination of the cyanide anion to give the substituted α-styrene **29**, and (*c*) the addition of the second equivalent of the phosphorus-containing reagent at the activated double bond.

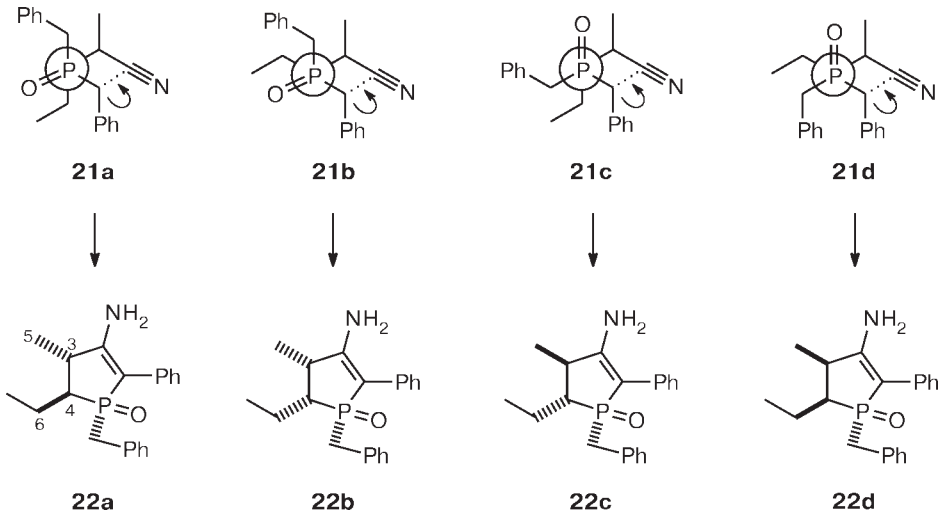
Nitrile **18** can produce four diastereomers (Scheme 6). According to the results of calculations, the heats of formation of these isomers differ only slightly (Table 1). However, the only stereoisomer of aminophospholene oxide **22** was isolated as the reaction product. The configuration of aminophospholene oxide **22** was unambiguously established based on analysis of the spin-spin coupling constants $^2J_{H-C-P}$, $^3J_{H-H}$, $^3J_{H-P}$, and $^3J_{C-P}$ in the NMR spectra of compound **22** and the results of calculations.

First, the geminal spin-spin coupling constant $^2J_{H(4)-C(4)-P}$ = 8.8 Hz (see Table 1) is indicative of the cisoid arrangement of the ethyl group and the phosphoryl oxygen atom (this arrangement of the substituents is

Scheme 5



Scheme 6



E_{ster}/kcal mol^{-1} (MM2) = –0.4 (**21a**), 0.3 (**21b**), –3.0 (**21c**), –3.6 (**21d**).

typical of compounds **13** and **15**). Hence, structures **22b** and **22c** must be rejected. Second, it is known that the spin-spin coupling constants $^3J_{H-C-C-P}$ and $^3J_{C-C-C-P}$ depend on the corresponding dihedral angles and obey the Karplus equation.[13,16] In the spectrum of compound **22**, the vicinal spin-spin coupling constant $^3J_{H(3)-C(3)-C(4)-P}$ is rather small (2.2 Hz), which is indicative of the orthogonal arrangement (or nearly orthogonal) of the H(3)—C(3) and C(4)—P bonds. To the contrary, the spin-spin coupling constant $^3J_{C(5)-C(3)-C(4)-P}$ is rather large (8.7 Hz), which points to the synclinal or anticlinal arrangement of the C(5)—C(3) and C(4)—P bonds. According to the results of semiempirical quantum-chemical calculations (PM3 method), in the case of the *cis* arrangement of the methyl group with respect to the phosphoryl oxygen atom (as in isomer **22d**), the dihedral angle between the H(3)—C(3) and C(4)—P bonds is 92° (as opposed to 140° for isomer **22a**), which is in the excellent agreement with the spin-spin coupling constant $^3J_{H(3)-C(3)-C(4)-P}$. The C(5)—C(3)—C(4)—P dihedral angle (149°) in iso-

Table 1. Enthalpies of formation (ΔH_f°) and the dihedral angles (φ) of conformers **22a—d** calculated by the PM3 method

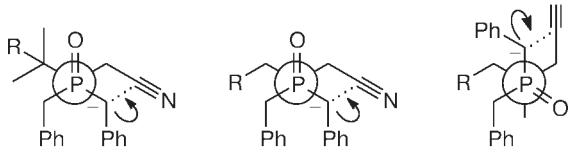
Conformer	ΔH°_f /kcal mol^{-1}	φ_1	φ_2
		deg	
22a	–4.9	–140	100
22b	–2.8	–147	93
22c	–4.3	100	–141
22d	–3.6	92	–149

Note. φ_1 and φ_2 are the H(3)—C(3)—C(4)—P and C(5)—C(3)—C(4)—P dihedral angles, respectively. The experimental spin-spin coupling constants for compound **22**: $^3J_{H(3)-C(3)-C(4)-P}$ = 2.2 Hz and $^3J_{C(5)-C(3)-C(4)-P}$ = 8.7 Hz.

mer **22d** agrees well with the observed spin-spin coupling constant $^3J_{C(5)-C(3)-C(4)-P}$, which must be equal to 0—2 Hz for isomer **22a**.

The formation of the single isomer of **22** can be explained in terms of steric hindrance of the transition state giving rise to cyclization with the formation of the phospholane ring. If this transition state is close to the conformation of primary adduct **21** involved in the reaction, the relative energies of the transition states producing particular isomers can be estimated from the relative energies of the reactive conformations. These conformations and their steric energies (E_{ster}), which were calculated by molecular mechanics (the MM2 force field), are shown in Scheme 6. Apparently, isomer **22d** obtained in the experiment was generated through conformation **21d** with the lowest steric energy.

The formation of the single stereoisomer of aminophospholene oxides from nitriles **12** and **15** can also be attributed to the fact that the reaction proceeds with the participation of the most stable conformation of the initially formed phosphine oxide **30**, which must lead to products with the cisoid arrangement of the alkyl substituent relative to the phosphoryl oxygen atom. The result of the reaction of geranyl nitrile **11** yielding a mixture of epimers also agrees with the results of conformational analysis of the primary adduct according to which conformations **31a** and **31b** have close energies ($\Delta\Delta H^\circ_f = 0.6$ kcal mol^{-1}). This is a reason for the formation of a mixture of isomers.



30 **31a** **31b**

To summarize, the reactions of dibenzylphosphine oxide with α,β-unsaturated nitriles in the presence of sodium hydride afforded substituted aminophospholene oxides, which are very difficult to synthesize by other procedures.[17,18] The presence of the bulky substituents at the α and γ positions of unsaturated nitriles leads to high stereoselectivity of cyclization of the initially formed adducts and ensures the preparation of the only stereoisomer of aminophospholene oxide.

Experimental

All solvents were distilled immediately before use. Analytical TLC was carried out on Silufol (Czech Republic) and Armsorb (Armenia) plates. The spots were visualized by spraying the plates with solutions of vanilline (1 g of vanilline + 5 mL of concentrated H_2SO_4 + 100 mL of 95% EtOH) or iron chloride (10 g of $FeCl_3 \cdot 6H_2O$ in 100 mL of 95% EtOH) followed by heating to 100—150 °C. Column chromatography was carried out with the use of KSK silica gel (Russia, 0.140—0.315 mm, air-dried, activated at 140 °C for 5 h) and aluminum oxide (Russia, TU 6-09-3916-75, activated at 250 °C for 3 h). The IR spectra were measured on a Specord M-80 instrument. The UV spectra were recorded on a Specord M-40 instrument. The melting points were determined on a Kofler stage. The high-resolution mass spectra were obtained on a Finnigan MAT 8200 instrument (EI, 100—220 °C, 70 eV). The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-400 instrument (400.13 MHz for ^{1}H and 100.61 MHz for ^{13}C) for solutions in $CDCl_3$ (40—100 mg mL^{-1}) at ~20 °C. The residual signals of the solvent (δ_H 7.24 and δ_C 76.90) were used as the internal standard. The ^{31}P NMR spectra were measured on a Bruker AC-200 instrument (81.015 MHz, 80% H_3PO_4 as the external standard, δ_P 0.0) under the same conditions. The signs of the spin-spin coupling constants were not determined. The assignment of the signals was made using the ^{13}C NMR spectra recorded with the *J* modulation (proton-noise-decoupled spectra, the opposite phases for the signals of the atoms with the odd and even numbers of the attached protons, tuning to the constant J = 135 Hz) and based on the data of the 2D spectra: (1) homonuclear ^{1}H—^{1}H correlation, (2) heteronuclear ^{13}C—^{1}H correlation at the direct spin-spin coupling constants (J = 135 Hz), and (3) heteronuclear ^{13}C—^{1}H correlation at the long-range spin-spin coupling constants (J = 10 Hz).

Synthesis of the starting α,β-unsaturated nitriles. Geranyl nitrile (10),[19] 4,4-dimethyl-5-(3-methylquinoxalin-2-yl)pent-2-enenitrile (12),[20] and cinnamonitrile (19)[21] were synthesized according to known procedures. **2-Methylpent-2-enenitrile (18)** was prepared from 2-methylpent-2-enal oxime.[22]

A sample of **5-[1,3]dioxolan-2-yl-4,4-dimethylpent-2-enenitrile (15)** was kindly provided by A. V. Rukavishnikov (N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences).

Standard procedure for the preparation of aminophospholenes. Sodium hydride (0.27 g, 60% NaH, 6.80 mmol, Fluka) was added to a solution of dibenzylphosphine oxide[23] (1.56 g, 6.80 mmol) in Bu^{t}OMe (25 mL). The reaction solution was refluxed with stirring until gas evolution ceased and NaH was dissolved. A solution of unsaturated nitrile (6.80 mmol) in Bu^{t}OMe (10 mL) was added dropwise with stirring and the reaction mixture was refluxed with stirring for 1 h. Then NaH (0.27 g, 60% NaH, 6.80 mmol) was added. The mixture was refluxed for 1 h, cooled, diluted with Bu^{t}OMe (10 mL), and washed with a saturated solution of NaCl (30 mL). The organic extract was dried over Na_2SO_4 and the solvent was evaporated *in vacuo* using a water-aspirator pump. The residue was dried *in vacuo* using an oil pump. The product was purified by column chromatography or recrystallization.

1-Benzyl-5-methyl-5-(4-methylpent-3-enyl)-1-oxo-2-phenyl-4,5-dihydro-1*H*-phosphol-3-ylamine (11). The yield was 68%, m.p. 182—185 °C (from a MeCN—$CHCl_3$ mixture, 1 : 3 v/v); MS, m/z (I_{rel} (%)): 379.20590 (M^+, 24%, calculated for $C_{24}H_{30}NOP$: 379.20649), 297 (19), 288 (100), 206 (12), 91 (15), 41 (9); IR ($CHCl_3$), ν/cm^{-1}: 3500, 3400, 3100—2900, 1625, 1600, 1490, 1380, 1150, 1120. **Major isomer.** ^{31}P NMR ($CDCl_3$), δ: 65.30; ^{1}H NMR ($CDCl_3$), δ: 1.29 (d, 3 H, H(12), J = 13.2 Hz); 1.58 (m, 1 H, H(6a)); 1.60 (s, 3 H, H(10)); 1.69 (s, 3 H, H(11)); 1.77 (m, 1 H, H(6b)); 2.02 (m, 1 H, H(7a)); 2.16 (m, 3 H, H(7b) and H(4)); 3.14 (dd, 1 H, H(13a),

J = 14.6 Hz, J = 12.5 Hz); 3.24 (dd, 1 H, H(13b), J = 16.6 Hz, J = 14.6 Hz); 4.73 (s, 2 H, NH_2); 5.07 (tm, 1 H, H(8), J = 7.2 Hz); 7.06 (m, 6 H, Ar); 7.19 (t, 2 H, H(c), J = 7.6 Hz); 7.29 (d, 2 H, H(b), J = 7.7 Hz). ^{13}C NMR ($CDCl_3$), δ: 17.53 (C(11)); 21.03 (C(12), J_{C-P} = 1.0 Hz); 23.49 (C(4), J_{C-P} = 7.6 Hz); 25.49 (C(10)); 35.34 (C(6)); 36.01 (C(13), J_{C-P} = 60.0 Hz); 39.48 (C(5), J_{C-P} = 63.2 Hz); 43.81 (C(7), J_{C-P} = 11.1 Hz); 96.29 (C(2), J_{C-P} = 110.4 Hz); 123.63 (C(8)); 125.50 and 125.92 (J_{C-P} = 2.5 Hz); 127.75 (J_{C-P} = 2.0 Hz); 127.88 (J_{C-P} = 4.7 Hz); 128.46 and 129.84 (C(b), C(c), C(d), C(b´), C(c´), C(d´), J_{C-P} = 5.1 Hz); 131.88 (C(9)); 132.98 (C(a´), J_{C-P} = 6.7 Hz); 134.51 (C(a), J_{C-P} = 7.6 Hz); 153.11 (C(3), J_{C-P} = 40.3 Hz). **Minor isomer.** ^{31}P NMR ($CDCl_3$), δ: 64.56. ^{1}H NMR ($CDCl_3$), δ: 1.27 (d, 3 H, H(12), J = 15.0 Hz); 1.51 (s, 3 H, H(10)); 1.60 (s, 3 H, H(11)); 1.65, 1.90, and 2.65 (all m, 2 H each, H(4), H(6), H(7)); 3.09 (m, 2 H, H(13)); 4.49 (s, 2 H, NH_2); 5.03 (tm, 1 H, H(8), J = 5.9 Hz); 7.01—7.28 (m, 10 H, Ph). ^{13}C NMR ($CDCl_3$), δ: 17.51 (C(11)); 21.40 (C(12), J_{C-P} = 1.0 Hz); 23.28 (C(4), J_{C-P} = 5.8 Hz); 25.45 (C(10)); 35.24 (C(6)); 36.12 (C(13), J_{C-P} = 51.6 Hz); 38.41 (C(5), J_{C-P} = 65.4 Hz); 44.55 (C(7), J_{C-P} = 9.5 Hz); 124.06 (C(8)); 125.83, 125.95 (J_{C-P} = 2.9 Hz); 127.88 (J_{C-P} = 2.2 Hz); 128.02 (J_{C-P} = 3.6 Hz); 128.69 and 129.97 (C(b), C(c), C(d), C(b´), C(c´), C(d´), J_{C-P} = 3.6 Hz); 131.53 (C(9)); 133.12 (C(a´), J_{C-P} = 6.5 Hz); 134.53 (C(a), J_{C-P} = 7.6 Hz); 153.67 (C(3), J_{C-P} = 40.3 Hz).

[4-Amino-2,2-dimethyl-3-(3-methylquinoxalin-2-yl)cyclopent-3-enyl]dibenzylphosphine oxide (13) was isolated by recrystallization of the crude product, which was prepared from nitrile **12** according to a standard procedure. The yield was 60%, m.p. 194—198 °C (from CCl_4). MS, m/z (I_{rel} (%)): 481.22888 (M^+, 13%, calculated for $C_{30}H_{32}N_3OP$: 481.22829), 390 (9), 283 (19), 282 (20), 253 (35), 252 (100), 251 (14), 250 (11), 237 (12), 236 (37), 235 (10), 232 (14), 200 (14), 199 (13), 192 (10), 91 (45). IR ($CHCl_3$), ν/cm^{-1}: 3500, 3400, 3100—2900, 1640, 1600, 1500, 1380, 1170, 1120, 770, 700. UV (EtOH) λ/nm (ε): 282 (5220), 320 (4250), 394 (1420). ^{31}P NMR ($CDCl_3$), δ: 44.48. ^{1}H NMR ($CDCl_3$), δ: 1.06 and 1.58 (both s, 3 H each, H(15a) and H(15b)); 2.33 (ddd, 1 H, H(2), J = 11.0 Hz, J = 11.0 Hz, J = 8.8 Hz); 2.46 (ddd, 1 H, H(3a), J = 15.4 Hz, J = 8.8 Hz, J = 2.0 Hz); 2.63 (s, 3 H, H(14)); 2.79 (ddd, 1 H, H(3b), J = 15.4 Hz, J = 11.4 Hz, J = 11.4 Hz); 3.00 (dd, 1 H, H(16a), J = 14.5 Hz, J = 14.3 Hz); 3.20 (dd, 1 H H(16a), J = 14.5 Hz, J = 10.9 Hz); 3.25 (dd, 1 H, H(16b), J = 14.6 Hz, J = 10.3 Hz); 3.38 (dd, 1 H, H(16b), J = 14.6 Hz, J = 14.6 Hz); 7.15—7.35 (m, 10 H, Ph); 7.66 (m, 2 H, H(8) and H(11)); 7.91 (m, 2 H, H(9) and H(10)). ^{13}C NMR ($CDCl_3$), δ: 22.66 (C(14)); 25.20 (C(15b)); 28.83 (C(15a)); 33.79 (C(3)); 34.92 (C(16b), J_{C-P} = 56.5 Hz); 36.10 (C(16a), J_{C-P} = 59.2 Hz); 46.86 (C(2), J_{C-P} = 65.2); 50.87 (C(1)); 110.28 (C(5), J_{C-P} = 10.4 Hz); 126.21 (C_o, J_{C-P} = 10.2 Hz); 127.76, 128.08, 128.16, and 128.42 (C(8), C(9), C(10), C(11)); 129.66 ($C_{m/p}$, J_{C-P} = 4.7 Hz); 130.02 ($C_{m/p}$, J_{C-P} = 4.7 Hz); 133.04 (C_{ipso}, J_{C-P} = 7.8 Hz); 133.13 (C_{ipso}, J_{C-P} = 8.2 Hz); 139.66 and 140.36 (C(7) and C(12)); 143.59 (C(4), J_{C-P} = 14.4 Hz); 153.21 (C(13)); 154.79 (C(6)).

1-Benzyl-5-[1,1-dimethyl-2-(3-methylquinoxalin-2-yl)ethyl]-1-oxo-2-phenyl-4,5-dihydro-1*H*-phosphol-3-ylamine (14) was isolated by column chromatography (Al_2O_3, 1% MeOH in $CHCl_3$) from the mother liquor after recrystallization of enamine **13**. The yield was 20%. MS, m/z (I_{rel} (%)): 481.22744 (M^+, 31% calculated for $C_{30}H_{32}N_3OP$: 481.22829), 391 (10), 390 (35), 324 (24), 323 (18), 284 (21), 283 (88), 282 (100), 253 (15), 233 (10), 232 (57), 214 (10), 200 (57), 199 (16), 192 (48), 185 (10), 170 (12), 158 (23), 91 (64), 64 (15). IR ($CHCl_3$), ν/cm^{-1}: 3500, 3400, 3100—2900, 1625, 1595, 1140, 1120. ^{31}P NMR ($CDCl_3$), δ: 62.52. ^{1}H NMR ($CDCl_3$), δ: 1.16 and 1.22 (both s, 3 H each, H(7) and H(8)); 2.31 (ddd, 1 H, H(4), J = 8.9 Hz, J = 8.9 Hz, J = 6.4 Hz); 2.51 (ddd, 1 H, H(3a), J = 19.7 Hz, J = 16.5 Hz, J = 8.7 Hz); 2.70 (m, 1 H, H(3b)); 2.75 (s, 3 H, H(11)); 2.93 (dd, 1 H, H(6a), J = 13.6 Hz, J = 5.9 Hz); 3.07 (dd, 1 H, H(12a), J = 15.0 Hz, J = 15.0 Hz); 3.18 (dd, 1 H, H(12b), J = 15.0 Hz, J = 15.0 Hz); 3.28 (d, 1 H, H(6b), J = 13.6 Hz); 5.02 (s, 2 H, NH_2); 6.29 (dt, J = 7.5 Hz, J = 1.9 Hz); 6.83 (d, J = 7.4 Hz); 7.15 (m); 7.30 (t, J = 7.6 Hz); 7.51 (d, 10 H, Ph, J = 7.5 Hz); 7.60 (m, 2 H, H(15) and H(16)); 7.80 and 7.93 (both dd, 1 H each, H(14) and H(17), J = 8.1 Hz, J = 1.8 Hz). ^{13}C NMR ($CDCl_3$), δ: 23.75 (C(11)); 25.34 (C(7) or C(8), J_{C-P} = 4.4 Hz); 25.72 (C(7) or C(8), J_{C-P} = 5.1 Hz); 32.54 (C(3), J_{C-P} = 6.5 Hz); 38.10 (C(4), J_{C-P} = 64.7 Hz); 38.30 (C(5), J_{C-P} = 1.5 Hz); 39.46 (C(12), J_{C-P} = 62.5 Hz); 43.52 (C(6), J_{C-P} = 5.1 Hz); 98.57 (C(1), J_{C-P} = 112.6 Hz); 125.76 (C(d´)); 125.78 (J_{C-P} = 3.0 Hz); 128.49 and 128.57 (J_{C-P} = 3.6 Hz); 129.22 and 129.62 (C(b); C(c), C(d), C(b´), C(c´), J_{C-P} = 5.8 Hz), 127.70, 128.17, 128.80, and 129.19 (C(14), C(15), C(16), C(17)); 133.61 (C(a´), J_{C-P} = 5.8 Hz); 134.60 (C(a), J_{C-P} = 9.5 Hz); 140.36 and 140.39 (C(13) and C(18)); 154.04 and 154.47 (C(9) and C(10)); 155.70 (C(2), J_{C-P} = 40.0 Hz).

1-Benzyl-5-(2-[1,3]dioxolan-2-yl-1,1-dimethylethyl)-1-oxo-2-phenyl-4,5-dihydro-1*H*-phosphol-3-ylamine (16) was isolated from the crude product by column chromatography (Al_2O_3, $CHCl_3$). The yield was 57%. MS, m/z (I_{rel} (%)): 411.19565 (M^+, 6%, calculated for $C_{24}H_{30}NO_3P$: 411.19632), 321 (22), 320 (100), 282 (10), 276 (48), 248 (11), 232 (15), 192 (11), 170 (24), 91 (61). IR ($CHCl_3$), ν/cm^{-1}: 3500, 3400, 3100—2900, 1625, 1595, 1145, 1120. ^{31}P NMR ($CDCl_3$), δ: 61.34. ^{1}H NMR ($CDCl_3$), δ: 1.14 and 1.22 (both s, 3 H each, H(8) and H(9)); 1.60 (dd, 1 H, H(6a), J = 5.5 Hz, J = 14.3 Hz); 1.85 (dd, 1 H, H(6b), J = 14.3 Hz, J = 4.5 Hz); 2.15 (m, 2 H, H(3a) and H(4)); 2.47 (m, 1 H, H(3b)); 3.12 (dd, 1 H, H(10a), J = 15.0 Hz, J = 15.0 Hz); 3.21 (dd, 1 H, H(10b), J = 15.0 Hz, J = 15.0 Hz); 3.69 and 3.83 (both m, 2 H each, H(11) and H(12)); 4.73 (s, 2 H, NH_2); 4.78 (t, 1 H, H(7), J = 5.0 Hz); 6.88 (d, 2 H, H(b´), J = 7.4 Hz); 7.14 (m, 4 H, Ar); 7.30 (t, 2 H, H(c), J = 7.6 Hz); 7.46 (d, 2 H, H(b), J = 7.7 Hz). ^{13}C NMR ($CDCl_3$), δ: 25.45 and 26.06 (both d, C(8) and C(9), J_{C-P} = 4.4 Hz); 32.50 (C(3), J_{C-P} = 6.2 Hz); 34.60 (C(5), J_{C-P} = 2.2 Hz); 38.92 (C(4), J_{C-P} = 65.4 Hz); 39.61 (C(10), J_{C-P} = 62.5 Hz); 44.71 (C(6), J_{C-P} = 7.3 Hz); 64.14 and 64.43 (C(11) and C(12)); 99.26 (C(1), J_{C-P} = 111.5 Hz); 102.51 (C(7)); 125.95 and 125.98 (J_{C-P} = 3.0 Hz); 127.92 (J_{C-P} = 5.1 Hz); 128.00 (J_{C-P} = 2.5 Hz); 128.95 and 129.75 (C(b), C(c), C(d), C(b´), C(c´)´, C(d´), J_{C-P} = 5.1 Hz); 134.24 (C(a´), J_{C-P} = 6.2 Hz); 134.84 (C(a), J_{C-P} = 9.5 Hz); 155.37 (C(2), J_{C-P} = 40.0 Hz).

Dibenzyl(2-cyanoethyl)phosphine oxide (20) was isolated from the crude product by column chromatography (Al_2O_3, $CHCl_3$). The yield was 58%. MS, m/z (I_{rel} (%)): 283.11215 (M^+, 20%, calculated for $C_{17}H_{18}NOP$ 283.11260), 192 (100), 91 (90). IR ($CHCl_3$), ν/cm^{-1}: 3100—2900, 2250, 1490, 1450, 1150, 1120. ^{31}P NMR ($CDCl_3$), δ: 40.47. ^{1}H NMR ($CDCl_3$), δ:

1.88 m, 2.24 m, 3.13 m, 7.25 m. ^{13}C NMR ($CDCl_3$), δ: 9.80 (J_{C-P} = 2.2 Hz); 22.52 (J_{C-P} = 64.7 Hz); 36.58 (J_{C-P} = 62.5 Hz); 118.71 (J_{C-P} = 15.2 Hz); 127.29 (J_{C-P} = 2.9 Hz); 128.93 (J_{C-P} = 2.2 Hz); 129.42 (J_{C-P} = 5.1 Hz); 130.64 (J_{C-P} = 8.0 Hz).

1-Benzyl-5-ethyl-4-methyl-1-oxo-2-phenyl-4,5-dihydro-1*H*-phosphol-3-ylamine (22). The yield was 80%, m.p. 147—150 °C (from hexane). MS, *m/z* (I_{rel} (%)): 325.15946 (M^+, 11%, calculated for $C_{20}H_{24}NOP$: 325.15954), 235 (15), 234 (100), 91 (14). IR ($CHCl_3$), ν/cm^{-1}: 3100—2900, 1625, 1595, 1145, 1120. ^{31}P NMR ($CDCl_3$,), δ: 58.62. ^{1}H NMR ($CDCl_3$), δ: 0.77 (d, 3 H, H(5), *J* = 7.0 Hz); 1.01 (t, 3 H, H(7), *J* = 7.4 Hz); 1.35 (dddd, 1 H, H(4), *J* = 8.8 Hz, *J* = 5.5 Hz, *J* = 5.5 Hz, *J* = 5.3 Hz); 1.48 (m, 1 H, H(6a)); 1.80 (m, 1 H, H(6b)); 2.37 (qdd, 1 H, H(3), *J* = 7.0 Hz, *J* = 5.3 Hz, *J* = 2.2 Hz); 3.01 (m, 2 H, H(8)); 4.68 (s, 2 H, NH_2); 6.88 (dt, 2H H(b′), *J* = 6.8 Hz, *J* = 2.0 Hz); 7.17 (m, 4 H, H(d); H(c′), H(d′)); 7.35 (t, 2 H, H(c), *J* = 8.0 Hz); 7.49 (d, 2 H, H(b), *J* = 8.0 Hz). ^{13}C NMR ($CDCl_3$), δ: 13.61 (C(7), J_{C-P} = 5.8 Hz); 18.99 (C(5), J_{C-P} = 8.7 Hz); 22.23 (C(6), J_{C-P} = 2.5 Hz); 38.42 (C(8), J_{C-P} = 62.1 Hz); 40.01 (C(4), J_{C-P} = 66.9 Hz); 43.03 (C(3), J_{C-P} = 6.2 Hz); 98.18 (C(1), J_{C-P} = 110.8 Hz); 126.02 and 126.13 (J_{C-P} = 3.3 Hz); 128.01 (J_{C-P} = 5.1 Hz); 128.06 (J_{C-P} = 2.9 Hz); 128.97 and 129.74 (C(b); C(c), C(d), C(b′), C(c′), C(d′), J_{C-P} = 5.1 Hz); 133.69 (C(a′), J_{C-P} = 5.8 Hz); 134.68 (C(a), J_{C-P} = 8.4 Hz); 159.72 (C(2), J_{C-P} = 40.0 Hz).

Dibenzyl[2-(dibenzylphosphoryl)-1-phenylethyl]phosphine oxide (24). The yield was 50%, m.p. 250—251°C (from $CHCl_3$); MS, *m/z* (I_{rel} (%)): 582.21568 (M^+, 27%, calculated for $C_{36}H_{36}O_2P_2$: 582.21904), 471 (18), 334 (22), 333 (72), 230 (15), 139 (15), 91 (100); IR ($CHCl_3$), ν/cm^{-1}: 3100—2900, 1600, 1490, 1450, 1150, 1120, 830. ^{31}P NMR ($CDCl_3$), δ: 43.75 (d, *J* = 40.5 Hz); 40.95 (d, *J* = 40.5 Hz). ^{1}H NMR ($CDCl_3$), δ: 2.50 (m, 2 H, H(2)); 2.80—3.80 (m, 9 H, H(1), C$\underline{H}_2$Ph); 7.00—7.40, 7.57 (m, 25 H, Ph). ^{13}C NMR ($CDCl_3$), δ: 27.18 (C(2), J_{C-P} = 61.7 Hz, J_{C-P} = 1.3 Hz); 33.79 (C$\underline{H}_2$Ph, J_{C-P} = 60.6 Hz); 34.17 (C$\underline{H}_2$Ph, J_{C-P} = 58.2 Hz); 35.70 (C$\underline{H}_2$Ph, J_{C-P} = 60.5 Hz); 36.33 (C$\underline{H}_2$Ph, J_{C-P} = 58.3 Hz); 39.48 (C(1), J_{C-P} = 57.9 Hz, J_{C-P} = 3.6 Hz); 125.94 ($Ph_{m/p}$, J_{C-P} = 2.3 Hz); 126.13 ($Ph_{m/p}$, J_{C-P} = 2.4 Hz); 126.17 ($Ph_{m/p}$, J_{C-P} = 2.8 Hz); 126.26 ($Ph_{m/p}$, J_{C-P} = 2.6 Hz); 127.30 ($Ph_{m/p}$, J_{C-P} = 2.2 Hz); 127.81 ($Ph_{m/p}$, J_{C-P} = 2.2 Hz); 128.03—128.11 ($Ph_{m/p}$); 128.42 ($Ph_{m/p}$, J_{C-P} = 2.0 Hz); 129.59 (Ph_o, J_{C-P} = 5.2 Hz); 129.69 (Ph_o, J_{C-P} = 5.3 Hz); 129.77 (Ph_o, J_{C-P} = 5.1 Hz); 129.82 (Ph_o, J_{C-P} = 4.7 Hz); 132.19 (Ph_{ipso}, J_{C-P} = 7.4 Hz); 132.24 (Ph_{ipso}, J_{C-P} = 7.6 Hz); 132.27 (Ph_{ipso}, J_{C-P} = 7.6 Hz); 132.40 (Ph_{ipso}, J_{C-P} = 7.5 Hz); 137.05 (Ph_{ipso}, J_{C-P} = 5.3 Hz, J_{C-P} = 1.9 Hz).

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