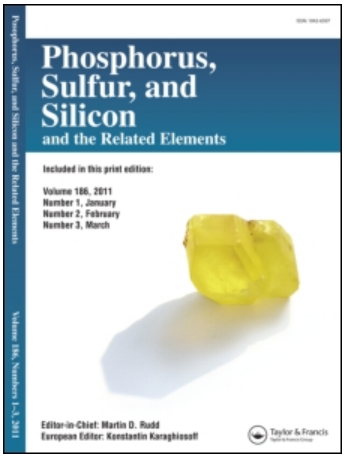

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

PREPARATION OF BENZYL *N*-BENZYLOXYCARBONYLAMINOPHOSPHONATES AND -AMINOPHOSPHONITES-THE SCOPE AND LIMITATIONS OF *O*-BENZYL-*N, N'*-DICYCLOHEXYLOISOUREA METHOD

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To cite this Article Mucha, Artur , Kafarski, Pawel , Plenat, Francoise and Cristau, Henri-Jean(1995) 'PREPARATION OF BENZYL *N*-BENZYLOXYCARBONYLAMINOPHOSPHONATES AND -AMINOPHOSPHONITES-THE SCOPE AND LIMITATIONS OF *O*-BENZYL-*N, N'*-DICYCLOHEXYLOISOUREA METHOD', Phosphorus, Sulfur, and Silicon and the Related Elements, 105: 1, 187 — 193
To link to this Article: DOI: 10.1080/10426509508042062
URL: http://dx.doi.org/10.1080/10426509508042062

Phosphorus, Sulfur, and Silicon, 1995, Vol. 105, pp. 187–193
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PREPARATION OF BENZYL *N*-BENZYLOXYCARBONYLAMINOPHOSPHONATES AND -AMINOPHOSPHONITES—THE SCOPE AND LIMITATIONS OF *O*-BENZYL-*N*,*N*′-DICYCLOHEXYLOISOUREA METHOD

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(Received April 27, 1995)

Protection of the amino group of aminophosphonic and aminophosphonous acids with benzyl chloroformate followed by esterification of the *N*-protected derivatives with *O*-benzyl-*N*,*N*′-dicyclohexylisoureas is described. The esterification of aminobenzylphosphonic and aminobenzylphosphonous acids was studied in some details in order to discuss the scope and limitation of this procedure. The differences in the reactions of aminoalkylphosphonic and aminoalkylphosphonous acids are pointed out.

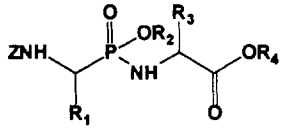
Key words: Aminobenzylphosphonic and -phosphonous acid, *N*-benzyloxycarbonyl derivatives, esterification, *O*-benzyl-*N*,*N*′-dicyclohexyloisourea, benzyl *N*-benzyloxycarbonylaminobenzylphosphonate and -phosphonite.

INTRODUCTION

Replacement of an amide bond in peptides by a phosphonamidate moiety results in phosphono peptides (**1**). These compounds, containing a tetrahedral phosphorus atom, are excellent mimics of the tetrahedral transition state of amide bond hydrolysis and may serve as powerful enzyme inhibitors[1–9] or haptens for construction of catalytic antibodies with protease-like specificity.[10–13]

The method commonly used for the synthesis of phosphono peptides relies on the conversion of *N*-protected aminophosphonate or -phosphonite monoesters to the corresponding phosphonochloridates which are then coupled with the appropriate amino ester or peptide fragment.[1–15] Preparation of the phosphorus substrates used in this synthesis usually consists of three general steps: (1) protection of the amino group of aminoalkylphosphonic acid followed by (2) esterification of the phosphonic acid moiety and (3) the selective removal of one of the phosphonate ester groups.[16–19] In this paper we report the studies considering the scope and limitations of the literature procedure for the preparation of dibenzyl esters of *N*-

protected aminoalkylphosphonic acids, as well as its usefulness for the preparation of esters of *N*-protected aminoalkylphosphonous acids. Reactions leading to monobenzyl *N*-benzyloxycarbonylaminobenzylphosphonate (**2**) and its phosphonous acid counterpart (**3**) were studied in some detail.



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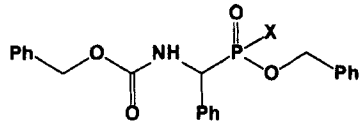
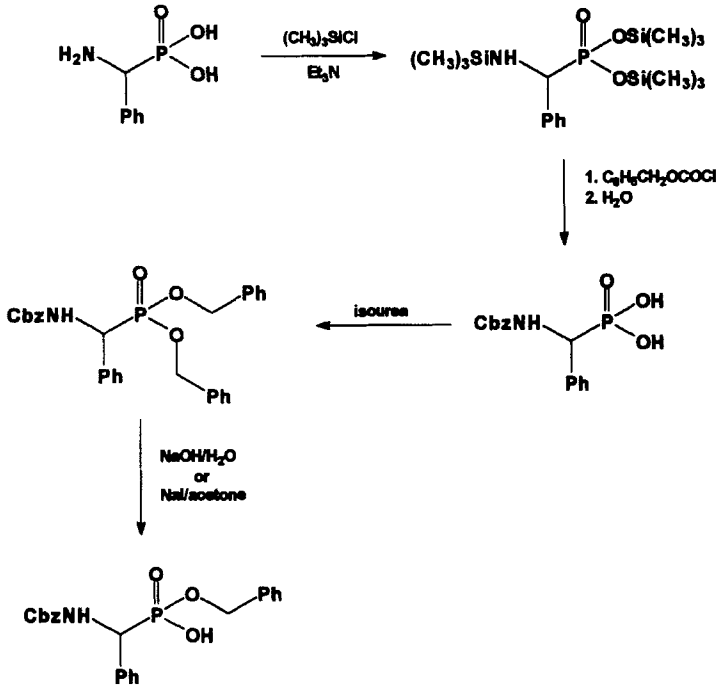


2: X = OH **3**: X = H

RESULTS AND DISCUSSION

Monobenzyl N-benzyloxycarbonylaminobenzylphosphonate

The applied synthetic strategy (Scheme 1) is standard and consists of three consecutive steps: (1) acylation of aminophosphonic acid with benzyl chloroformate[20–23]; (2) esterification of the resulting *N*-benzyloxycarbonyl derivatives using literature procedure and (3) the selective removal of one of the phosphonate ester groups.[24] Although the acylation of aminophosphonic acids seems to be a trivial

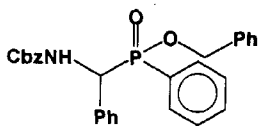


SCHEME 1

reaction, the literature data on the preparation of *N*-acylated acids are contradictory.[16] In most cases the yields of the reaction in aqueous media are moderate or even low. This is probably due to the formation of a mixed anhydride between aminophosphonic acid and the acylating agent. This anhydride readily undergoes hydrolytic cleavage. Thus, despite of literature claims,[20,21] the acylation of aminobenzylphosphonic and α-aminoethylphosphonic acid in an alkaline aqueous solution gave poor yields (13% and 5%, respectively) of the desired products. High yields of acylation were achieved by the modification of earlier procedures in which the total silylation of the aminoalkylphosphonic acid preceded the acylation.[22,23] The silylation suppressed the formation of the anhydride but not the reaction of the acylating agent with the amino group. Benzyl esters were chosen since their deprotection can be accomplished by hydrogenation under neutral, non-racemizing conditions.[7,8] Even more interesting seemed to be *p*-methoxybenzyl esters which were reported to be cleavable under estremely mild conditions.[25]

Esterification of *N*-benzyloxycarbonylaminobenzylphosphonic acid with *O*-benzyl-*N*,*N*′-dicyclohexyloisourea[26] proceeded smoothly yielding the dibenzyl ester in practically quantitative yields. Surprisingly, however and for unknown reasons the use of *O*-(*p*-methoxybenzyl)-*N*,*N*′-dicyclohexyloisourea, even in the presence of DMF (the recommended additive), failed to give the desired diester. The unreacted substrates were recovered from the reaction mixtures in high yields.

Since the esterification of *N*-benzyloxycarbonylaminobenzyl(phenyl)phosphinic acid as a rule gave also moderate or low yields of its *p*-methoxybenzyl ester in comparison to the benzyl one (**4**), we speculated that the steric hindrance introduced by the phenyl group may play a vital role here. If so, the introduction of the second ester group to *N*-protected aminobenzylphosphonic acid should be slower than the introduction of the first group and should enable to obtain compound (**2**) directly from this acid in one step. This, however, was not the case and the application of equimolar quantities of *N*-benzyloxycarbonylaminobenzylphosphonic acid and *O*-benzyl-*N*,*N*′-dicyclohexyloisourea resulted in the mixture of dibenzyl ester (33% of yield) and monobenzyl ester (24% of yield). Monobenzyl *N*-benzyloxycarbonylaminobenzylphosphonate was easily obtained from the dibenzyl ester either by alkaline hydrolysis or treating it with sodium iodide in acetone.[24]



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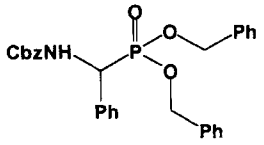
Benzyl N-benzyloxycarbonylaminobenzylphosphonite

Contrary to the acylation of phosphonic acids, protection the aminobenzylphosphonous acid with benzyl chloroformate proceeded gently in an alkaline aqueous solution as reported in the literature.[27]

The esterification of *N*-benzyloxycarbonylaminobenzylphosphonous acids with *O*-benzyl-*N*,*N*′-dicyclohexyloisourea resulted in the monobenzyl *N*-benzyloxycar-

bonylaminobenzylphosphonite in good yield as well. Unfortunately, the isolated ester appeared to be not pure and contained up to 10% of two by-products (δ 22.8 and 43.7 ppm in ^{31}P NMR). Purification of the product by means of column chromatography enabled us to separate these products and identify them as dibenzyl *N*-benzyloxycarbonylaminobenzylphosphonate (**5**) and benzyl ester of symmetrical phosphinic acid (**6**). The structure of the later one was additionally confirmed by removal of all the protecting groups which yielded bis(aminobenzyl)phosphinic acid described previously by Maier[28a] and Tyka *et al.*[28b] The more detailed study of the esterification reaction did not allow us to explain whether the creation of the contaminants accompanied the esterification step or they were formed during amidoalkylation (preparation of the substrate) and were concentrated during further steps of synthesis.



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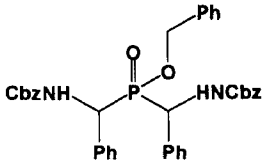

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EXPERIMENTAL

Materials and Methods

Unless otherwise stated, materials were obtained from commercial suppliers and used without purification. Triethylamine was distilled and stored over potassium hydroxide. *O*-Benzyl- and *O*-(*p*-methoxybenzyl)-*N*,*N*′-dicyclohexyloisourea were obtained according to the literature[26] and were used without further purification.

Melting points were taken on Mettler FP5 or on Boetius apparatus and were not corrected. IR spectra were recorded in KBr pellets on a Perkin Elmer 377 spectrometer. ^{1}H NMR spectra were recorded on Tesla 60 MHz or Bruker (250 MHz or 300 MHz) spectrometers. Measurements were made in $CDCl_3$, C_6D_6 and DMSO-d_6 solutions. Chemical shifts are reported in relation to tetramethylsilane used as internal standard. ^{13}C NMR spectra were recorded on Bruker 250 (250 MHz) spectrometer. ^{31}P-NMR spectra were obtained with use of broad-band ^{1}H decoupling on Bruker (250 MHz or 300 MHz) spectrometers; chemical shifts are reported as ppm relative to 85% H_3PO_4 (sealed capillary). Microanalyses were performed either by Service de Microanalyse du C.N.R.S., Ecole Nationale Superieure de Chimie, Montpellier or by Instrumental Analysis Unit of the Institute of Organic Chemistry, Biochemistry and Biotechnology, Technical University of Wrocław.

Preparation of the starting amino acids

Aminobenzylphosphonous acid.[29] Aminobenzylphosphonous acid was prepared by amidoalkylation of anhydrous hypophosphorus acid with phenylmethylidenebisacetamide in acetic acid followed by hydrolysis. The crude product was recrystallized from water. Yield: 70%; m.p.: 240–242°C (lit. m.p.: 242–243°C).

Aminoalkylphosphonic acids. Aminoalkylphosphonic acids were prepared according to the recently recommended modification[30] of the standard Oleksyszyn procedure.[31] The crude products were recrystallized from a water-ethanol mixture.

N-Benzyloxycarbonyl derivatives

N-Benzyloxycarbonylaminobenzylphosphonous acid. 4 M of an aqueous solution of sodium hydroxide was added to a mixture of aminobenzylphosphonous acid (17.1 g, 0.1 mol) in water (250 ml) in order to adjust pH to 9–10. After cooling the solution to 0°C benzyl chloroformate (17.1 g, 0.1 mol) was

added dropwise during 1 hr with stirring. The pH was maintained at 9–10 for 6 hours (0°C) by periodical addition of 4 N NaOH. Then the stirring was continued for the next 12 hrs at room temperature. The mixture was washed with ether (200 ml). The aqueous layer was poured into a mixture of water (60 ml), concentrated hydrochloric acid (40 ml) and ice (200 g). The separated solid was filtered, washed with water and dried. The crude acid was recrystallized from ethyl acetate.

Yield: 68%; m.p.: 145–147°C; IR (KBr, cm^{-1}): 3310 (NH), 2400 (PH), 1715 (C=O), 1535 (δNH), 1240 (P=O), 1140, 1020, 970 (P—O, C—O); ^1H NMR (DMSO-d_6; 300 MHz): δ 4.86 (dd, J = 9.7 Hz, J_{PH} = 18.6 Hz, 1H, NC**H**P), 5.06 (s, 2H, OCOC**H**$_2$), 6.85 (d, J = 545.5 Hz, P**H**), 7.25–7.47 (m, 10H, 2 × C$_6$**H**$_5$), 8.32 (bd, J = 9.7 Hz, 1H, N**H**); ^{31}P NMR (DMSO-d_6): δ 26.1 ppm. Anal. calc. for $C_{15}H_{16}NO_4P$: C, 59.02; H, 5.28; N, 4.59; found: C, 59.17; H, 5.44; N, 4.48%.

N-Benzyloxycarbonylaminoalkylphosphonic acids. An aminoalkylphosphonic acid (0.05 mol) was suspended in chloroform (200 ml), trimethylchlorosilane (16.3 g, 0.15 mol) was added and the mixture was stirred for 1 hr at room temperature. Triethylamine (15.2 g, 0.15 mol) in chloroform (50 ml) was added dropwise and the solution was refluxed overnight. After cooling to 0°C, benzyl chloroformate (10.2 g, 0.06 mol) was added dropwise. The solution was stirred for 1 hr at 5°C and triethylamine (10.1 g, 0.10 mol) in chloroform (50 ml) was added. The mixture was kept overnight at room temperature, then volatile products were removed under reduced pressure. The resulting oil was dissolved in a 1 M aqueous solution of sodium hydroxide (150 ml) and stirred for 2 hrs at room temperature. The alkaline solution was washed with ethyl ether (2 × 100 ml) and then acidified to pH 1. An oily product was extracted with ethyl acetate (3 × 100 ml) and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the obtained crude acid was recrystallized from an ethyl acetate-hexane mixture.

N-Benzyloxycarbonylaminobenzylphosphonic acid. Yield: 79%; m.p.: 159°C; IR (KBr, cm^{-1}): 3700–2000, 3265 (NH), 1680 (C=O), 1535 (δNH), 1185, 1140, 985 (P=O, P—O, C—O); ^1H NMR (DMSO-d_6; 60 MHz): δ 4.80 (dd, J = 9.5 Hz, J_{PH} = 14.0 Hz, 1H, NC**H**P), 5.06 (s, 2H, OCOC**H**$_2$), 7.38 (s, 10H, 2 × C$_6$**H**$_5$), 7.92 (bd, J = 9.5 Hz, 1H, N**H**); ^{31}P NMR (DMSO-d_6): δ 16.8 ppm. Anal. calc. for $C_{15}H_{16}NO_5P$: C, 56.08; H, 5.02; N, 4.36; found: C, 56.19; H, 4.85; N, 4.29%.

N-Benzyloxycarbonyl-α-aminoethylphosphonic acid. Yield: 46%; m.p.: 110°C; IR (KBr, cm^{-1}): 3700–2000, 3270 (NH), 1685 (C=O), 1545 (δNH), 1205 (P=O), 1110, 1095 (P—O, C—O); ^1H NMR (D_2O/NaOD, 60 MHz): δ 1.28 (dd, J = 7.0 Hz, J_{PH} = 14.0 Hz, 3H C**H**$_3$), 3.72 (dq, J = 7.0 Hz, J_{PH} = 16.0 Hz, 1H, NC**H**P), 5.17 (s, 2H, OCOC**H**$_2$), 7.61 (s, 5H, C$_6$**H**$_5$); ^{31}P NMR (DMSO-d_6): δ 21.6 ppm. Anal. calc. for $C_{10}H_{14}NO_5P$: C, 46.34; H, 5.44; N, 5.40; found: C, 46.61; H, 5.14; N, 5.45%.

N-Benzyloxycarbonylaminobenzyl(phenyl)phosphinic acid. It was prepared according to the literature method.[32] Benzyl carbamate (7.6 g, 0.05 mol) and pivalic acid (10.2 g, 0.1 mol) were dissolved in toluene (200 ml) and 50 ml of toluene was distilled off in order to remove water from the reaction mixture. After cooling to room temperature, powdered 4A molecular sieves (5.0 g) and benzaldehyde (5.3 g, 0.05 mol) were added and then phenyldichlorophosphine (9.0 g, 0.05 mol) dropwise with stirring. The mixture was stirred overnight at room temperature and the product precipitated from the solution. The solid material was filtered and washed with toluene, then dissolved in hot chloroform and filtered again in order to remove molecular sieves. After evaporation of the solvent the crude product was recrystallized from methanol.

Yield: 52%; m.p.: 217°C; IR (KBr, cm^{-1}): 3700–2000, 3305 (NH), 1715 (C=O), 1530 (δNH), 1235 (P=O), 1155, 1135 (P—O, C—O); ^1H NMR (DMSO-d_6, 60 MHz): δ 4.97 (s, 3H, OCOC**H**$_2$ and PO**H**), 5.13 (dd, J = 9.5 Hz, J_{PH} = 15.0 Hz, 1H, NC**H**P), 7.0–8.5 (m, 15H, 3 × C$_6$**H**$_5$), 8.2 (bd, J = 9.5 Hz, 1H, N**H**); ^{31}P NMR (DMSO-d_6): δ 29.9 ppm. Anal. calc. for $C_{21}H_{20}NO_4P$: C, 66.14; H, 5.28; N, 3.67; found: C, 65.87; H, 5.15; N, 3.59%.

Preparation of the benzyl esters

In order to obtain benzyl esters of the *N*-protected amino acids a modification of the recently published method was applied.[24] *N*-benzyloxycarbonylaminobenzylphosphonous, *N*-benzyloxycarbonylaminobenzylphenylphosphinic or *N*-benzyloxycarbonylaminobenzylphosphonic acid (5 mmol) and isourea (5 mmol for the phosphonous and phosphinic and 10 mmol for the phosphonic acid) were dissolved in benzene (100 ml) and refluxed overnight. The mixture was then cooled to room temperature and formed *N,N'*-dicyclohexylurea filtered. The benzene layer was washed with an aqueous solution of sodium bicarbonate (50 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered and the solvent was removed under reduced pressure yielding the crude product. The ester was recrystallized from ethyl acetate or an ethyl acetate-hexane mixture.

Benzyl N-benzyloxycarbonylaminobenzylphosphonite (**3**). To remove by-products the ester was additionally recrystallized from acetone. Yield: 71%; m.p.: 135°C; IR (KBr, cm^{-1}): 3250 (NH), 3020 (CH_{ar}), 2960 (CH_{al}), 2360 (PH), 1715 (C=O), 1535 (δNH), 1490, 1450 (C=C_{ar}), 1250 (P=O), 1140,

1020 (P—O, C—O); ^{1}H NMR ($CDCl_3$; 250 MHz): δ 4.87 (doubled AB system, J_{PA} = 8.0 Hz, J_{PB} = 9.8 Hz, J_{AB} = 11.7 Hz, 2H, $POCH_AH_B$), 5.10 and 5.11 (s each, 2H, $OCOCH_2$), 5.01–5.15 (m, 1H, NCHP), 5.88 (m, 1H, NH), 7.06 and 7.20 (d each, J_1 = 572.5 Hz, J_2 = 570.4 Hz, 1H together, PH), 7.16–7.37 (m, 15H, 3 × C_6H_5); ^{31}P NMR ($CDCl_3$): δ 30.0 and 33.9 ppm (1:1 ratio). Anal. calc. for $C_{22}H_{22}NO_4P$: C, 66.83; H, 5.61; N, 3.54; found: C, 66.80; H, 5.55; N, 3.39%.

Benzyl N-benzyloxycarbonylaminobenzyl(phenyl)phosphinate (**4**). Yield: 94% as a mixture of two pairs of enantiomers in 6:4 ratio; m.p.: 197°C; IR (KBr, cm^{-1}): 3215 (NH), 1715 (C=O), 1545 (δNH), 1245 (P=O), 1025 (P—O, C—O); ^{1}H NMR (C_6D_6, 250 MHz): δ 4.58 and 4.59 (d each, J_{PH} = 7.2 Hz, 1H each, $POCH_2$), 4.70 and 4.97 (AB system, J_{AB} = 13.1 Hz, 2H, $OCOCH_2$), 5.92 (dd, J = 10.3 Hz, J_{PH} = 14.5 Hz, 1H, NCHP), 6.75–8.45 (m, 21H, 4 × C_6H_5, NH); ^{31}P NMR ($CDCl_3$): δ 37.0 (minor isomer, 0.4P), 38.4 (major isomers, 0.6P) ppm. Anal. calc. for $C_{28}H_{26}NO_4P$: C, 71.33; H, 5.56; N, 2.97; found: C, 70.97; H, 5.57; N, 2.97%.

(p-Methoxy)benzyl N-benzyloxycarbonylaminobenzyl(phenyl)phosphinate. Yield 15% as a mixture of two pairs of enantiomers in 8:2 ratio; m.p.: 142°C; IR (KBr, cm^{-1}): 3210 (NH), 1710 (C=O), 1540 (δNH), 1250 (P=O), 1030 (P—O, C—O); ^{1}H NMR ($CDCl_3$, 60 MHz): δ 3.75 (s, 3H, OCH_3), 4.68 (d, J_{PH} = 7.0 Hz, 2H, $POCH_2$), 4.93 (bs, 2H, $OCOCH_2$), 5.33 (dd, J = 10.0 Hz, J_{PH} = 15.0 Hz, 1H, NCHP), 5.9–6.4 (m, 1H, NH), 6.9 (AA'BB' system, J_{AB} = 9.0 Hz, 4H, C_6H_4) 6.5–8.6 (m, 15H, 3 × C_6H_5); ^{31}P NMR ($CDCl_3$): δ 37.5 (minor isomer, 0.2P), 38.6 (major isomers, 0.8P) ppm. Anal. calc. for $C_{29}H_{28}NO_5P$: C, 69.45; H, 5.63; N, 2.79; found: C, 69.17; H, 5.86; N, 2.93%.

Dibenzyl N-benzyloxycarbonylaminobenzylphosphonate (**5**). Yield: 96%; m.p.: 134–135°C; IR (KBr, cm^{-1}): 3230 (NH), 1710 (C=O), 1550 (δNH), 1255 (P=O), 1055, 1020 (P—O, C—O); ^{1}H NMR (C_6D_6; 250 MHz): δ 4.46 and 4.75 (doubled AB system, J_{PA} = 7.3 Hz, J_{PB} = 9.0 Hz, J_{AB} = 11.8 Hz, 2H, $POCH_AH_B$), 4.95 and 5.06 (AB system, J = 12.6 Hz, 2H, $OCOCH_2$), 4.90–5.10 (m, 2H, $POCH_2$), 5.82 (dd, J = 10.1 Hz, J_{PH} = 22.3 Hz, 1H, NCHP), 6.70–7.70 (m, 21H, 3 × C_6H_5, NH); ^{31}P NMR ($CDCl_3$): δ 22.8 ppm. Anal. calc. for $C_{29}H_{28}NO_5P$: C, 69.45; H, 5.63; N, 2.79; found: C, 69.32; H, 5.64; N, 2.89%.

Monobenzyl N-benzyloxycarbonylaminobenzylphosphonate (**2**). Benzyl *N*-benzyloxycarbonylaminobenzylphosphonate was easily obtained from the dibenzyl ester by alkaline hydrolysis. Dibenzyl *N*-benzyloxycarbonylaminobenzylphosphonate (1.0 g, 2 mmol) dissolved in a 1 M aqueous solution of sodium hydroxide (5 ml) was refluxed with methanol (25 ml). Methanol was then removed under reduced pressure, the residue was diluted with water (35 ml) and the crude product was precipitated by acidification to pH 1. The obtained ester was recyrstallized from an ethyl acetate-hexane mixture.

Yield: 86%; m.p.: 159°C; IR (KBr): 3300 (NH), 1710 (C=O), 1535 (δNH), 1240 (P=O), 1050 (P—O, C—O); ^{1}H NMR (DMSO-d_6; 250 MHz): δ 4.88 and 4.92 (doubled AB system, J_{PA} = 7.5 Hz, J_{PB} = 8.5 Hz, J_{AB} = 12.0 Hz, 2H, $POCH_AH_B$), 5.02 and 5.10 (AB system, J = 12.2 Hz, 2H, $OCOCH_2$), 5.19 (dd, J = 9.8 Hz, J_{PH} = 22.2 Hz, 1H, NCHP), 6.67 (dd, J_{PH} = 5.0 Hz, J = 9.8 Hz, 1H, NH), 7.03 (bs, 1H, POH), 7.15–7.55 (m, 15H, 3 × C_6H_5); ^{31}P NMR (DMSO-d_6): δ 22.1 ppm. Anal. calc. for $C_{22}H_{22}NO_5P$: C, 64.23; H, 5.39; N, 3.40; found: C, 63.95; H, 5.26; N, 3.26%.

Treating the dibenzyl ester with sodium iodide in acetone yielded sodium benzyl *N*-benzyloxycarbonylaminobenzylphosphonate (96%), but its conversion to the acid was difficult to achieve due to the low solubility in water.

Benzyl bis(aminobenzyl)phosphinate (**6**)

Benzyl bis(aminobenzyl)phosphinate (**6**) was obtained and purified from crude benzyl *N*-benzyloxycarbonylaminobenzylphosphonite by column chromatography (silica gel Merck 60, ethyl acetate/hexane, 1:1 vol.). M.p.: 195°C; FAB MS: m/z = 636 (MH^+); IR (KBr): 3340 (NH), 3060, 3030 (CH_{ar}), 2940, 2890 (CH_{al}), 1690 (C=O), 1525 (δNH), 1490, 1450 (C=C_{ar}), 1245 (P=O), 1040, 1030, 1010 (P—O, C—O); ^{1}H NMR ($CDCl_3$, 250 MHz): δ 4.02 (dd, J_{PH} = 6.9 Hz, J = 11.3 Hz, 1H, $POCH_2$), 4.53 (dd, J_{PH} = 7.1 Hz, J = 11.3 Hz, 1H, $POCH_2$), 4.97 and 5.07 (s each, 4H together, 2 × $OCOCH_2$), 5.26 (dd, J = 10.0 Hz, J_{PH} = 12.5 Hz, 1H, NCHP), 5.44 (dd, J = 10.5 Hz, J_{PH} = 12.5 Hz, 1H, NCHP), 6.19–6.22 and 6.27–6.32 (m each, 2H, 2 × NH), 7.14–7.38 (m, 25H, 5 × C_6H_5); ^{13}C NMR ($CDCl_3$): δ 52.38 and 53.58 (d each, J_P = 97.4 Hz, J_P = 95.4 Hz, 2 × NCHP), 67.22 and 67.50 (s each, 2 × $OCOCH_2$), 67.79 (d, J_P = 7.3 Hz, $POCH_2$), 127.61–128.67 (m, aromatic carbon atoms), 133.74 and 134.41 (s each, 2 × $NCHC_{1ar}$), 135.31 (d, J_P = 5.8 Hz, $POCH_2C_{1ar}$), 135.81 and 135.87 (s each, 2 × $OCOCH_2C_{1ar}$), 155.22 and 155.42 (d each, J_P = 11.4 Hz, J_P = 9.0 Hz, 2 × C=O); ^{31}P NMR ($CDCl_3$): δ 43.9 ppm. Anal. calc. for $C_{37}H_{35}N_2O_6P$: C, 70.02; H, 5.56; N, 4.41; O, 15.13; found: C, 70.52; H, 5.94; N, 4.47; O, 15.03%.

ACKNOWLEDGEMENTS

This work was partially supported by Komitet Badań Naukowych, P. K. thanks Centre Nationale de la Recherché Scienifique for a post-doctoral position.

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