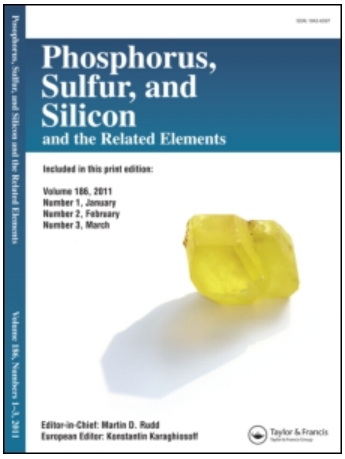

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Synthesis and NMR Spectroscopic Study of a New Anthracene Derived Schiff Base and a Bis(aminophosphonate) Obtained from It

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SYNTHESIS AND NMR SPECTROSCOPIC STUDY OF A NEW ANTHRACENE DERIVED SCHIFF BASE AND A BIS(AMINOPHOSPHONATE) OBTAINED FROM IT

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A new Schiff base N,N′*-di(9-anthrylidene)-1,3-phenylenediamine and a bis(aminophosphonate) 1,3-bis[*N*-methyl(diethoxyphosphonyl)-1-(9-anthryl)]diaminobenzene have been synthesized. The compounds have been characterized by elemental analysis, TLC, IR, and* ^{1}H, ^{13}C, *and* ^{31}P *NMR spectra. The NMR spectra reveal that the bis(aminophosphonate) is a mixture of two diastereomeric forms*—meso *or* racemic*. The two forms are indistinguishable in NMR spectra.*

Keywords: Aminophosphonic acids; anthracene derivatives; NMR spectra; Schiff bases

INTRODUCTION

Aminophosphonic acids and their derivatives are of considerable importance because of their versatile biological activity and possibility for application in agrochemistry—fungicides, herbicides, and plant growth regulators,[1–6] and in medicine—antiosteoporosis, antiarthritic, and antidiabetic drugs.[1,7–9] They are quite promising as anticancer agents.[10–14] Anthracene derived aminophosphonates might be of particular interest in this direction taking into account that the DNA-intercalating anthracene ring is the main pharmacophoric fragment of some cytostatic drugs.[15] The fluorescent properties of the anthracene moiety[16] could find application in analytical biochemistry of such compounds.[17]

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The synthetic precursors of aminophosphonates—the Schiff bases—are also of interest for pharmacology, such as antimicrobial,[18] tuberculostatic,[19] and antitumor[20,21] agents.

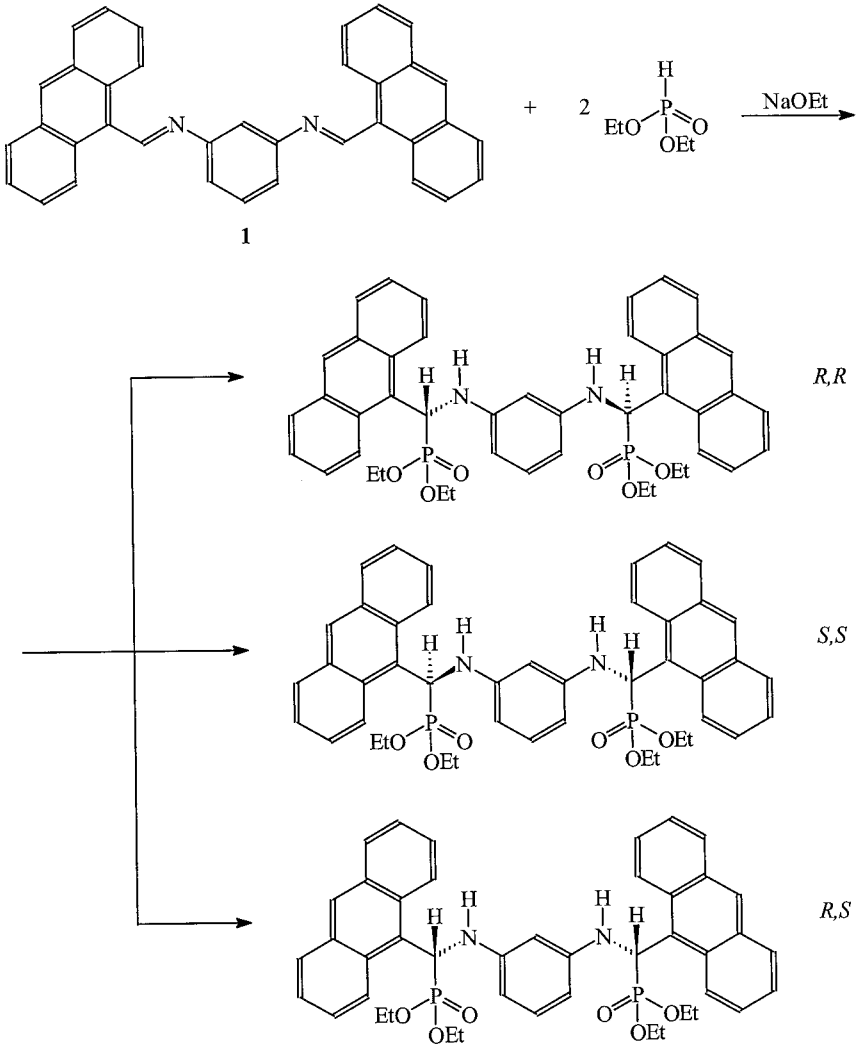
In the present work the synthesis of a new anthracene substituted bis-imine and a bis(aminophosphonate) derived from it is described, and their structure is discussed on the basis of multi-NMR specroscopic data.

RESULTS AND DISCUSSION

The new bis-imine, *N*,*N*′-di(9-anthrylidene)-1,3-phenylenediamine (**1**), was obtained from antharacene-9-carboxaldehyde and 1,3-phenylenediamine. A new bis(aminophosphonate), 1,3-bis[*N*-methyl(diethoxyphosphonyl)-1-(9-anthryl)]diaminobenzene (**2**) was synthesized through addition of diethyl phosphite to its azomethine bonds (Scheme 1). The products **1** and **2** are yellow, fluorescing crystalline solids, soluble in methanol, ethanol, chloroform, benzene, toluene. Thin layer chromatography (TLC) gave one spot for each of them. The elemental analyses are consistent with their composition. The expected absorbtion bands of the corresponding groups[22–24] are present in their IR spectra (see Experimental).

^{1}H and $^{13}C\{^{1}H\}$ spectra of the Schiff base **1** show one singlet singnal at lowest field due to the CH=N protons and carbons, respectively. For similar compounds it is known that the *trans*-configuration of the azomethine group is thermally favored,[25–27] and it should be expected that the Schiff base **1** is a *trans*-, *trans*-isomer. The protons of the anthracene residue and two protons of the phenylene ring (PhH-2 and PhH-5) in this compound give complex overlapping signals in the aromatic region of the spectra. A common signal (doublet of doublets) slightly shifted upfied appears for the protons PhH-4 and PhH-6 in **1**.

The addition of dialkyl and diaryl phosphites to bis-imines should lead to the formation of two diastereomeric forms: *meso* and *racemic*.[28] The NMR studies on the stereochemistry of the reaction have revealed in some cases the exclusive formation of only one of the forms,[28,29] while in other cases the addition products are a mixture of the two possible diastereomeric forms.[30,31] In the present case ^{1}H NMR spectra registered in DMSO-d_6 and $CDCl_3$ solutions show one set of signals for the corresponding protons in compound **2**. The signal of NH protons in the bis(aminophosphonate) appears as a triplet (in DMSO-d_6) and as a doublet of doublets (in $CDCl_3$). The signal of the methyne hydrogen of the CH(P) groups in **2** was observed as a doublet of doublets, but not as two doublets (Figure 1a). In $CDCl_3$ solution this signal transforms into one



SCHEME 1

doublet after selective irradiation of the NH protons, as well as after their D_2O exchange (Figure 1b). The methyl protons of the nonequivalent ethoxy groups give two triplets with significant chemical shift difference between them ($\Delta\delta = 0.58$ and 0.63 ppm in DMSO-d_6 and $CDCl_3$ respectively). The signals for the methylene protons of these groups of **2** appear as three multiplets in a ratio of 2:1:1. In the spectra of **2** taken

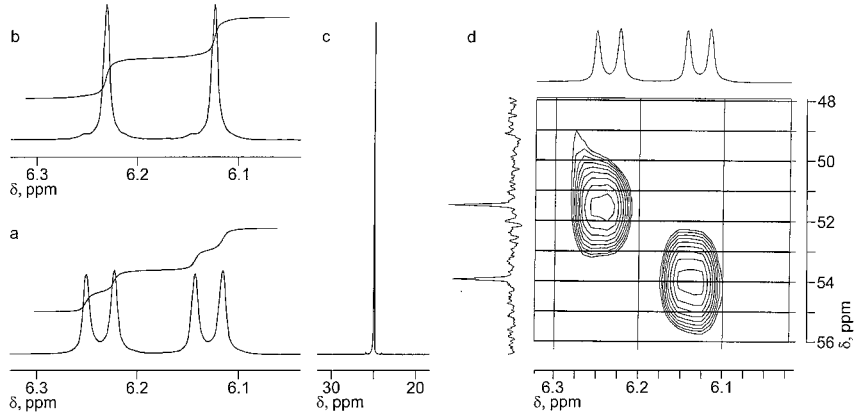


FIGURE 1 NMR spectra of CH(P) moiety of compound **2**: a), b) ^{1}H NMR spectra in $CDCl_3$ and $CDCl_3$, D_2O respectively; c) $^{31}P\{^{1}H\}$ NMR spectrum in $CDCl_3$; d) CH COSY diagram in $CDCl_3$.

in DMSO-d_6 and $CDCl_3$, the phenylene ring protons give one set of signals with expected multiplicity (see Experimental). The protons of the anthracene residue of **2** give complex poorly resolved multiplet signals.

The $^{31}P\{^{1}H\}$ NMR spectra of compound **2** measured in DMSO-d_6 and $CDCl_3$ consist of one singlet in the expected region (Figure 1c).

In addition to ^{1}H and ^{31}P NMR spectra one set of signals were registered in the ^{13}C NMR spectra of **2** taken in DMSO-d_6 and $CDCl_3$ (Table I). Thus, $^{13}C\{^{1}H\}$ NMR spectra reveal one doublet due to the asymmetric carbon atoms (Figure 1d). The coupling constants are 153 and 154 in DMSO-d_6 and $CDCl_3$ solution, respectively. One doublet appears in the spectra for the phenylene carbon atoms PhC-1, 3 which are close to the asymmetric center. CH COLOC technique was used to aid the assignment of the ^{13}C shifts of these carbons. Two doublets are well distinguished for the methyl and methylene carbon atoms, respectively, belonging to the ethoxy groups (Table I). The assignment of these signals is based on the data of 2D spectra of **2**.

TABLE I Selected ^{13}C NMR Chemical Shifts of compound **2**, δ (ppm)

	Signal assignment			
Solvent	C H_3	O C H_2	C H(P)	PhC-1,3
DMSO-d_6	15.70 (d) 16.37 (d)	62.33 (d) 62.61 (d)	50.99 (d)	147.84 (d)
$CDCl_3$	15.72 (d) 16.44 (d)	62.93 (d) 63.07 (d)	52.73 (d)	147.92 (d)

The analysis of the NMR spectra revealed that the addition of diethyl phosphite to *N,N′*-di(9-anthrylidene)-1,3-phenylenediamine leads to one of diastereomeric forms—*meso* (*R,S*) or *racemic* (*R,R* and *S,S*). These forms remained however indistinguishable under the conditions of the NMR experiments.

EXPERIMENTAL

Starting Compounds

Diethyl phosphite (Fluka, *purum*) was purified by vacuum distillation. Anthracene-9-carboxaldehyde (Fluka, *purum*) and 1,3-phenylenediamine (Fluka, *purum*) were used as received. All solvents were freshly distilled prior to use.

Apparatus and Conditions

The melting points of the products were determined on a Kofler microscope and are uncorrected.

The IR spectra were recorded on a Bruker IFS 113 spectrophotometer in KBr disks.

^{1}H (solvent DMSO-d_6) and ^{31}P (solvent DMSO-d_6 and $CDCl_3$) NMR spectra were registered on a Varian-Inova 500 MHz spectrometer at room temperature using TMS as internal reference and 85% H_3PO_4 as external reference. The remaining NMR spectra—^{1}H (solvent $CDCl_3$), $^{13}C\{^{1}H\}$, DEPT, HH COSY, CH COSY and CH COLOC (solvent DMSO-d_6 and $CDCl_3$)—were taken on a Bruker DRX-250 250 MHz spectrometer at room temperature and TMS as internal standard. D_2O exchange was applied to confirm the assignment of the signals of NH protons.

The thin layer chromatograms were performed on Kieselgel-60 F_{254} plastic sheets (Merck) at room temperature. The samples were applied as methanolic solutions and the chromatograms were developed ascendingly in the following eluting systems: a) benzene–methanol (10:1) and b) ethyl acetate–tetrahydrofuran–methanol (12:3:1). The spots were detected under UV light and in iodine vapour atmosphere.

N,N′-di(9-anthrylidene)-1,3-phenylenediamine (1)

Anthracene-9-carboxaldehyde (3.40 g, 16.50 mmol) was dissolved under heating in ethanol (200 ml) and 1,3-phenylenediamine (0.81 g, 7.50 mmol) was added. The solution was boiled for 1 h under reflux, and the yellow precipitate obtained was filtered. The crude product was recrystallized from carbon tetrachloride.

Yield: 2.65 g (73%); m.p. 230–232°C; $R_f = 0.86$ (system a). Analysis: Calcd. For $C_{36}H_{24}N_2$: C, 89.26%; H, 4.96%; N, 5.79%. Found: C, 89.23%; H, 4.93%; N, 5.65%. IR (KBr disk), $\tilde{\nu}$ (cm^{-1}): 3081, 3050, 3023 ($\nu_{C-H\,arom}$); 1625 ($\nu_{C=N}$); 1615, 1580, 1521, 1442 ($\nu_{C=C\,arom}$). ^1H NMR, δ (ppm), J_{HH} (Hz). Solvent DMSO-d_6: 9.94 (s, 2H, CH=N); 8.93–7.58 (m, 20H, anthraceneH, PhH-2, PhH-5); 7.47 (dd, $^3J = 7.61$, $^4J = 1.97$, 2H, PhH-4,6). Solvent $CDCl_3$: 9.79 (s, 2H, CH=N); 8.82–7.48 (m, 20H, anthraceneH, PhH-2, PhH-5); 7.40 (dd, $^3J = 7.56$, $^4J = 1.96$, 2H, PhH-4,6). ^{13}C NMR, δ (ppm). Solvent $CDCl_3$: 160.37 (CH=N); 153.67 (PhC-1,3); 118.94 (PhC-4,6).

1,3-Bis[*N*-methyl(diethoxyphosphonyl)-1-(9-anthryl)]diaminobenzene (2)

A saturated solution of C_2H_5ONa was added dropwise to a mixture of *N*,*N*′-di(9-anthrylidene)-1,3-phenylenediamine (2.01 g, 4.15 mmol) and diethyl phosphite (1.49 g, 10.80 mmol). The mixture was stirred for 3 h at 70–75°C. The yellow precipitate obtained was washed with water and recrystallized from ethanol.

Yield: 1.50 g (47%); m. p. 235–237°C; $R_f = 0.72$ (system a), 0.89 (system b). Analysis. Calcd. For $C_{44}H_{46}N_2O_6P_2$: C, 69.47%; H, 6.05%; N, 3.68%. Found: C, 69.63%; H, 5.99%; N, 3.86%. IR (KBr disk), $\tilde{\nu}$ (cm^{-1}): 3344 (ν_{NH}); 1606, 1535, 1523, 1477, 1447 ($\nu_{C=C\,arom}$); 1230 ($\nu_{P=O}$); 1160 (ν_{Et-OP}); 1054, 1021 (ν_{P-OEt}). ^1H NMR, δ (ppm), J_{HH} (Hz), J_{HP} (Hz). Solvent DMSO-d_6: 8.89–7.39 (m, 18H, anthraceneH); 6.24 (t, $^3J = 8.00$, 1H, PhH-5); 6.15 (s, 1H, PhH-2); 6.13 (dd, $^2J = 28.25$, $^3J = 8.25$, 2H, CHP); 6.03 (t, $^3J = 8.25$, 2H, NH); 5.59 (dd, $^3J = 8.00$, $^4J = 2.00$, 2H, PhH-4,6); 4.05 (m, $^3J = 8.04$, 4H, OCH_2); 3.63 and 3.29 (2m, 4H, OCH_2); 1.18 and 0.60 (2t, $^3J = 7.00$ and 7.00, 12H, CH_3). Solvent $CDCl_3$: 8.90–7.36 (m, 18H, anthraceneH); 6.48 (t, $^3J = 8.03$, 1H, PhH-5); 6.18 (dd, $^2J = 26.90$, $^3J = 6.93$, 2H, CHP); 5.87 (t, $^4J = 2.11$, 1H, PhH-2); 5.70 (dd, $^3J = 8.06$, $^4J = 2.15$, 2H, PhH-4,6); 4.84 (dd, $^3J = 6.99$ and 9.06, 2H, NH); 4.12 (m, 4H, OCH_2); 3.66 and 3.21 (2m, 4H, OCH_2); 1.25 and 0.62 (2t, $^3J = 7.07$ and 7.07, 12H, CH_3). ^{31}P NMR, δ (ppm). Solvent DMSO-d_6: 24.52. Solvent $CDCl_3$: 25.00. ^{13}C NMR, δ (ppm). Solvent DMSO-d_6: 129.62 (PhC-5); 102.90 (PhC-4,6); 98.32 (PhC-2). Solvent $CDCl_3$: 129.75 (PhC-5); 103.82 (PhC-4,6); 99.46 (PhC-2).

Selected part of ^{13}C NMR chemical shifts is given in Table I.

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