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Mendeleev Commun., 2006, **16(1)**, 48–50

Mendeleev Communications

Formation of 2,7-dioxa-5,10-diaza-3,8-diphospha-1,6(1,4)-dibenzenacyclodecaphane derivatives in the reactions of *para*-(*N*-benzylidene)aminophenol with monochlorophosphites

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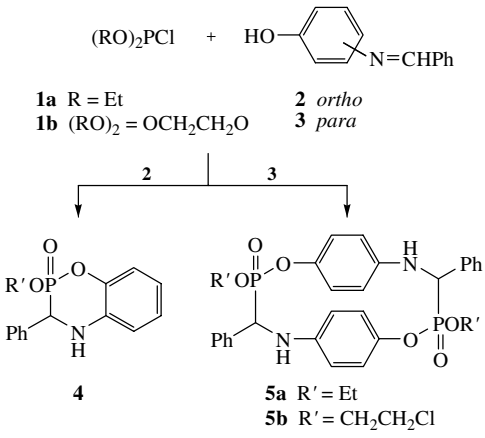
DOI: 10.1070/MC2006v016n01ABEH002221

Iminophosphites, which are formed in the reactions of *para*-(*N*-benzylidene)aminophenol with diethyl and ethylene chlorophosphites by the formation of two new intermolecular P–C bonds with the participation of HCl evolved in the course of the reaction, are condensed to form 16-membered P-macrocycles, 2,7-dioxa-5,10-diaza-3,8-diphospha-1,6(1,4)-dibenzenacyclodecaphane derivatives.

It was found previously that the reactions of monochlorophosphites with bifunctional compounds containing hydroxyl and imino groups resulted in the formation of five-,[1] six-,[2–4] and seven-membered[1] phosphacyclanes. In these reactions, an intramolecular attack of a phosphorus atom on the electrophilic carbon atom of the imino group occurred in intermediate iminophosphites with the participation of hydrogen chloride evolving in the course of reaction. This attack resulted in ring formation by a new P–C bond. If the intramolecular formation of a new P–C bond is impossible in such reactions, in particular, for steric reasons the intermolecular formation of this bond by the intermolecular attack of a phosphorus atom on the imino group under certain conditions could result in the formation of P-macrocyclic structures. Here, we report the first results of these transformations exemplified by the reaction of *para*-(*N*-benzylidene)-aminophenol with monochlorophosphites.

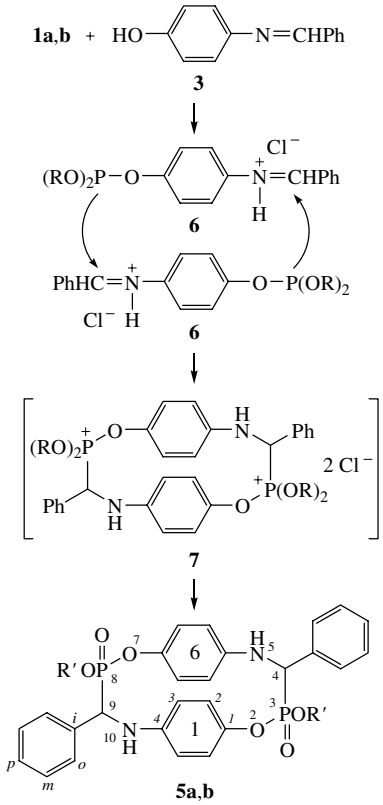
Previously,[5] it was found that the reactions of *ortho*-(*N*-benzylidene)aminophenol **2** with monochlorophosphites **1a**,**b** in chloroform resulted in the formation of 1,4,2-oxazaphosphorinanes **4** (Scheme 1). The reaction of equimolar amounts of *para*-(*N*-benzylidene)aminophenol **3** with phosphites **1a**,**b** under analogous conditions (room temperature; chloroform as a solvent) occurred in another manner† and resulted in the formation of 16-membered P-macrocyclic rings: 2,7-dioxa-5,10-diaza-3,8-diphospha-1,6(1,4)-dibenzenacyclodecaphane derivatives **5a**,**b**. The reaction products were purified by column chromatography and isolated as light brown and light yellow oils (**5a** and **5b**), which were stable in air; upon keeping in a vacuum or upon treatment with dry diethyl ether, these oils were converted into powders of analogous colours.

The structure and composition of macrocyclic compounds **5a**,**b** were determined by ^{1}H, ^{13}C and ^{31}P NMR spectroscopy,



Scheme 1

mass spectrometry, IR spectroscopy, and elemental analysis. The molecular weights of the reaction products determined by mass spectrometry (MALDI) were consistent with the molecular weights calculated from the empirical formulae of cyclodecaphanes **5a**,**b** (578 for **5a** and 646 for **5b**). The electron-ionization mass spectra contained peaks due to fragment ions containing two phosphorus atoms. The ^{1}H NMR spectra contained doublets from two HCP protons ($^2J_{HP}$ 23–24 Hz) at 4–5 ppm. Thus, the spectrum of the crude reaction mixture of compound **5a** exhibited four doublets in an analogous region. With consideration for the presence of four pairwise equal chiral centres as macrocycle constituents, these doublets were likely due to four of the six possible diastereomers (four *d*,*l* and two non-equivalent *meso* forms) of this structure. According to ^{1}H NMR data, we failed to completely separate and isolate at least one of the stereoisomers as an individual compound using column chromatography in the chosen sorbent–eluent system.



Scheme 2

Scheme 2 shows the most likely reaction path of the formation of macrocycles **5a**,**b**. Immonium salts **6** are formed at the first step of reaction from monochlorophosphites **1a**,**b** and imine **3** in the absence of an external scavenger of HCl, which is formed in this reaction. Note that, unlike their analogue prepared from *ortho*-(*N*-benzylidene)aminophenol,[5] salts **6** are sufficiently stable, and their signals in the ^{31}P NMR spectra of crude reaction mixtures were retained for three days under reaction conditions. Salts **6** underwent cyclocondensation to macrocyclic quasi-phosphonic intermediates **7** analogously to a similar dimerisation process by the mechanism of an intermolecular nucleophilic attack of phosphorus atoms on the electrophilic carbon atoms of immonium groups under mild conditions. Next, intermediates **7** were converted into final macrocycles **5a**,**b** by the Arbuzov reaction.

Thus, using the reaction of *para*-(*N*-benzylidene)aminophenol with monochlorophosphites as an example, we found that an intermolecular interaction with the formation of P-macrocycles occurred when the intramolecular cyclisation of intermediate iminophosphites was impossible. Along with *para*- and *meta*-aminophenol derivatives, other organic compounds (imino alcohols, imino acids, *etc*.) can be used as parent bifunctional compounds, which simultaneously contain hydroxyl and imino groups and meet the requirements of the intermolecular formation of P–C bonds, in these reactions. This procedure can be considered as a new strategy for designing various types of P-macrocyclic structures.

† *3,8-Diethoxy-4,9-diphenyl-2,7-dioxa-5,10-diaza-3,8-diphospha-1,6(1,4)-dibenzenacyclodecaphane-3,8-dione* **5a**. Diethyl chlorophosphite (0.8 g, 5.1 mmol) in 10 ml of $CHCl_3$ was added to a suspension of 1 g (5.1 mmol) of compound **3** in 50 ml of dry $CHCl_3$ in an atmosphere of dry argon at room temperature with stirring for 2 h. Next, the reaction mixture was additionally stirred for 5 h and kept in an atmosphere of argon for 5 days. The reaction mixture was filtered through a Schott filter, and the solvent was removed from the filtrate in a vacuum. The residue was chromatographed on silica gel in the chloroform–ethyl acetate system (2:1). The composition of eluted fractions was monitored by TLC on Silufol UV 254 plates visualised with iodine vapour. The total yield of compound **5a** was 1.7 g (58%).

3,8-Di(β-chloro)ethoxy-4,9-diphenyl-2,7-dioxa-5,10-diaza-3,8-diphospha-1,6(1,4)-dibenzenacyclodecaphane-3,8-dione **5b** was prepared analogously to compound **5a**. Toluene–acetonitrile (1:1) was used as an eluent for chromatography. Yield, 52%.

5a: ^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.99 and 1.16 (2td, $^3J_{HH}$ 7.1 Hz, $^4J_{POCCH}$ 1.5–2.0 Hz), 1.08, 1.10, 1.24, 1.25 (4t, 6H, Me, $^3J_{HH}$ 7.1 Hz for all signals), 3.69, 3.90, 4.06 (3m, 4H, CH_2O), 4.64, 4.66, 4.72, 4.74 (4d, 2H, PCH, $^2J_{HP}$ 23.0–24.0 Hz), 6.40, 6.42, 6.45, 6.47, 6.56, 6.58, 6.59, 6.83 (8br. d, 8H, C_6H_4, $^3J_{HCCH}$ 8.7–8.8 Hz), 7.38, 7.23–7.28 (2m, 10H, Ph). ^{13}C-{^{1}H} NMR (150.9 MHz, $CDCl_3$ + 3% CD_3OD) δ: 149.39, 149.43, 149.50 (3d, C^1, $^2J_{POC}$ 6.3, 5.3 and 6.1 Hz), 114.53, 116.12 (2d, C^2, $^3J_{POCC}$ 4.8 and 3.7 Hz), 115.60, 115.50 (2br. s, C^3), 143.46, 143.59, 143.73 (3br. s, C^4), 135.66, 135.56, 135.81 (3br. s, C^i), 127.81, 127.98 (2d, C^o, $^3J_{PCCC}$ 4.8 and 5.3 Hz), 128.55, 128.45 (2br. s, C^m), 121.22 (br. s, C^p), 56.51, 56.49, 57.05, 57.08 (4d, PC^4, $^1J_{PC}$ 151.1, 151.0, 151.8 and 151.6 Hz), 63.26 (br. d, CH_2, $^2J_{POC}$ 7.0 Hz), 16.30, 16.06 (2br. d, Me, $^3J_{POCC}$ 5.7 and 5.1 Hz). ^{31}P {^{1}H} NMR (36.5 MHz, $CDCl_3$) δ_P: 19.2, 19.5, 19.6, 20.1, 22.6, 22.9. IR (thin layer, ν/cm^{-1}): 980, 1028 (P–O–C), 1226 (P=O), 3306 (NH). MS (MALDI), *m*/*z*: 579 [MH]$^+$. MS (EI, 70 eV), *m*/*z* (%): 427 (6.9) [M – OEt – NC_6H_4O]$^+$, 335 (11.0) [M – OEt – NC_6H_4O – PhMe]$^+$, 290 (99.0) [EtOP(O)$OC_6H_4NHCH_2Ph]_+$, 198 (100) [$OC_6H_4NHCH_2Ph$]$^+$. Found (%): C, 61.97; H, 5.21; N, 4.69; P, 10.99. Calc. for $C_{30}H_{32}N_2O_6P_2$ (%): C, 62.28; H, 5.54; N, 4.84; P, 10.73.

5b: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.45–3.86 (2m, 4H, CH_2Cl), 4.11–4.50 (2m, 4H, CH_2O), 4.76–4.97 (m, 2H, PCH, $^2J_{HP}$ 24.3 Hz), 6.35–8.10 (m, 18H, Ph + C_6H_4). ^{31}P {^{1}H} NMR (36.5 MHz, $CDCl_3$) δ_P: 19.6, 20.0, 20.2, 20.5, 23.2, 23.5. IR (thin layer, ν/cm^{-1}): 1030, 1081 (P–O–C), 1202 (P=O), 3305 (NH). MS (MALDI), *m*/*z*: 647 [MH]$^+$. MS (EI, 70 eV), *m*/*z* (%): 323 (92.0) [$Cl(CH_2)_2OP(O)OC_6H_4NHCHPh]^+$, 260 (19.5) [$P(O)_2OC_6H_4NHCHPh]^+$, 196 (100) [$OC_6H_4NHCHPh]^+$. Found (%): C, 55.41; H, 4.27; Cl, 11.22; N, 3.92; P, 10.06. Calc. for $C_{30}H_{30}Cl_2N_2O_6P_2$ (%): C, 55.73; H, 4.64; Cl, 10.84; N, 4.33; P, 9.60.

The matrix-assisted laser-desorption ionization (MALDI) mass spectra were measured on a DYNAMO MALDI TOF mass spectrometer from Finnigan (USA). A pulse UV laser with a wavelength of 337 nm was used for laser desorption. Dihydroxybenzoic acid (DHB) served as a matrix. The sample was prepared by supporting a mixture of a matrix solution in ethanol (1 wt%) and an analyte solution in methanol (0.1 wt%) onto a substrate and dried at 40 °C. The electron-ionization (EI) mass spectra were measured on a TRACE MS Finnigan MAT instrument at an electron energy of 70 eV.

This work was supported by the Academy of Sciences of Tatarstan (grant no. 07-7.2-235/2005).

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Received: 28th July 2005; Com. 05/2555