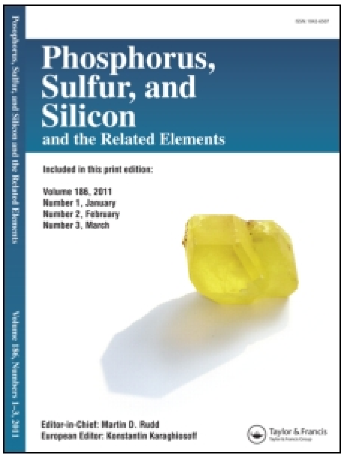

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ADDITION OF PHOSPHITES TO *N,N*-DIFERROCENYLIDENE-1,3-PHENYLENEDIMETHYLAMINE AND *N,N*-DIFERROCENYLIDENE-1,3-CYCLOHEXYLENEDIMETHYLAMINE: SYNTHESIS OF CORRESPONDING MODEL BIS-AMINOPHOSPHONATES

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The preparation of tetraalkyl 1,3-phenylene-di(methylamino)-di-ferrocenylmethyl-phosphonates (4a–c) and tetraalkyl 1,3-cyclohexylene-di(methylamino)-di-ferrocenylmethylphosphonates (5a–c) by the addition of dialkyl phosphites to N,N-diferrocenylidene-1,3-phenylenedimethylamine 1 and N,N-diferrocenylidene-1,3-cyclohexylenedimethylamine 2 is described. The diastereoselectivity, which was observed in both cases, is consistent with that observed in other cases.

Keywords Addition; azomethine bond; dialkyl phosphites; diastereoselectivity; diferrocenylmethylphosphonates

INTRODUCTION

The addition of dialkyl phosphites to azomethine bonds of various diamine-derived Schiff bases has been occasionally studied through the years. Pudovik and Pudovik[1,2] first reported the synthesis of 1,4-phenylenediamino phosphonates; this subject was later explored in detail by Failla et al.[3,4] The latter discussed the stereochemistry of the reaction demonstrating its stereodivergence. Kraicheva[5] studied the addition of dialkyl phosphites to di(anthranylmethylene)-1,3-phenylenediamine, and noted the stereodifferentiation and investigated the problem in detail. The German-Italian team (Gerhard Hägele and Paolo Finocchiaro)[3,6] studied the phosphite addition to dialkylidene-1,2-ethylenediamine[6] and dialkylidene-1,3-phenylenebis(methylamine)[3] and showed the evident diastereoselectivity. In addition, they established the configuration of the predominant diastereoisomer, indicating the formation of the *meso*-form.

Our interest in the addition of phosphorus nucleophiles to Schiff bases of selected diamines was based on two ideas: first, we are looking for new ligands, which after some modifications may serve as chiral catalysts, and, second, we have been interested for

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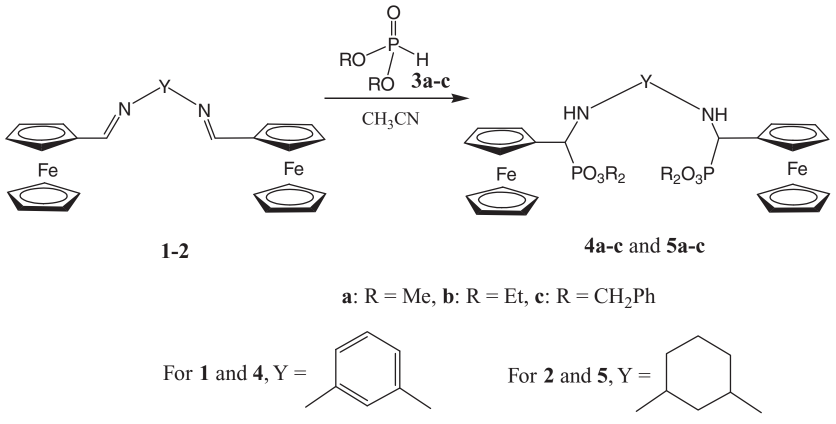
several years in the stereochemistry of the tandem addition (the bis-addition) of phosphorus nucleophiles to various bis-imines, i.e., Schiff bases of dialdehydes or diamines.[7]

Therefore, we performed the synthesis of 3-(phosphonomethylamino)methyl-benzylaminomethyl phosphonates **4a–c** and 3-(phosphonomethylamino)methyl-cyclohexylaminomethyl phosphonates **5a–c** in order to investigate the abovementioned matters.

RESULTS AND DISCUSSION

The addition of the dialkyl phosphites **3a–c** to in situ–generated Schiff bases **1** and **2** resulted in the formation of corresponding 1,3-phenylenedi(methylamino)-di-phenylmethylphosphonic derivatives **4a–c** and 1,3-cyclohexylenedi(methylamino)-di-ferrocenylmethylphosphonic derivatives **5a–c**, respectively, in moderate to fair yields (Scheme 1). Addition of dialkyl phosphites **3a–c** was carried out in boiling acetonitrile, where the reaction mixture was heated for several hours. After an easy work-up, the tetraalkyl diaminophosphonates **4a–c** and **5a–c** were isolated and purified by column chromatography. The bis(aminophosphonates) **4a–c** and **5a–c** were investigated by means of the ^{1}H and ^{31}P NMR spectroscopy and the elemental analysis. The spectroscopic and analytical data fully confirmed the postulated structures.



Scheme 1

The stereochemistry of the described addition is unambiguous. Normally, the addition of a phosphorus nucleophile to *N*,*N*-diferrocenylidene-1,3-phenylenedimethylamine **1** would lead to the formation of two diastereoisomeric forms, the racemic mixture and the *meso*-form, in equal amounts. The NMR spectroscopic study showed the formation of exclusively one diastereoisomeric form in all three studied cases, i.e., the addition of three dialkyl phosphites **3a–c**. Thus, the formation of 1,3-phenylenedi(methylamino)-di-phenylmethylphosphonic acid esters **4a–c** in only one diastereomeric form was demonstrated, and the complete diastereoselectivity of this reaction was confirmed. Based on studies by Caccamese et al.,[6] who established the product configuration in similar reactions, one can assume analogous formation of the *meso*-form.

The addition of the phosphites to *N*,*N*-diferrocenylidene-1,3-cyclohexylene-dimethylamine **2** was much more complex, which is due to the fact that the 1,3-cyclohexylene-dimethylamine used for the preparation of the Schiff base **2** was a mixture of *cis* and *trans* isomers. Considering this, the addition of the phosphite should result in the formation of 14 optical isomers, i.e., six pairs of enantiomers and two *meso*-like forms. Therefore, eight diastereoisomeric forms should have been visible on TLC plates as well as in the ^{1}H and ^{31}P NMR spectra. Surprisingly, the analysis demonstrated the formation of only three visible isomeric forms, which clearly showed the diastereoselectivity of this reaction. The addition of the Schiff base **2** (*cis*, *RR* and *SS* form) to each isomer led to the formation of exclusively one diastereoisomeric form. Further studies are necessary to explain the mechanism of this selectivity.

EXPERIMENTAL

All solvents (POCh-Poland) were routinely distilled and dried prior to use. 1,3-Cyclohexanebis(methylamine) and *m*-xylenediamine (Aldrich) were used as received. NMR spectra were recorded on a Varian Gemini 200 BB apparatus operating at 200 MHz (^{1}H) and 81 MHz (^{31}P). Elemental analyses were performed in the Centre for Molecular and Macromolecular Science of the Polish Academy of Science in Łódź, Poland.

Preparation of Tetraalkyl 1,3-Phenylenedi(methylamino)-di-ferrocenylmethyl-phosphonates (4a–c) and Tetraalkyl 1,3-Cyclohexylenedi-(methylamino)-di-ferrocenylmethylphosphonates (5a–c): General Procedure

Ferrocenecarboxaldehyde (0.53 g, 0.025 mol) was dissolved in methanol (60 mL), then diamine (0.0125 mol) was added. The reaction mixture was stirred at room temperature for 24 h, the solvent was evaporated, and the remaining residue consisting of the Schiff base (0.0125 mol) was dissolved in acetonitrile. To this solution, the dialkyl phosphite (0.025 mol) was added, and the mixture was refluxed for 3 days. Then the solvent was evaporated to give the respective bis-aminophosphonate as brown-red oil, which was purified by column chromatography on silica gel using hexane/ethyl acetate 1:5 as eluent.

Tetramethyl 1,3-Phenylenedi(methylamino)-di-ferrocenylmethylphosphonate (4a)

Yield: 5.42 g (58%). Calcd for $C_{34}H_{42}Fe_2N_2O_6P_2$: C, 54.57; H, 5.66; N, 3.74. Found: C, 54.14; H, 5.31; N, 3.54%.^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 7.50$ (m, 1H, *arom-H*); 7.38 (m, 3H, *arom-H*); 4.24 (m, 4H, CH^{fer}); 4.14 (m, 4H, CH^{fer}); 4.07 (s, 4H, CH_2N); 4.06 (s, 10H, $C_5H_5{}^{fer}$); 3.86 (d, $^2J_{PH} = 10.7$ Hz, 2H, CHP); 3.71 (d, $J = 9.0$ Hz, 6H, OCH_3), 3.66 (d, $J = 9.0$ Hz, 6H, OCH_3). ^{31}P NMR ($CDCl_3$, 81 MHz): $\delta = 24.4$.

Tetraethyl 1,3-Phenylenedi(methylamino)-di-ferrocenylmethylphosphonate (4b)

Yield: 4.72 g (47%). Calcd for $C_{38}H_{50}Fe_2N_2O_6P_2$: C, 56.74; H, 6.26; N, 3.48. Found: C, 56.49; H, 6.33; N, 3.42%. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 7.50$ (m, 1H, *arom-H*); 7.40 (m, 2H, *arom-H*); 7.27 (m, 1H, *arom-H*); 4.30–3.90 (m, 8H, $O\underline{CH_2}CH_3$); 4.25 (m, 4H, CH^{fer}); 4.13 (m, 4H, $(CH^{fer})_2$); 4.07 (s, 10H, $C_5H_5{}^{fer}$); 4.06 (s, 4H, $\overline{CH_2}N$); 3.76 (d, $^2J_{PH} =$

9.6 Hz, 2H, CHP); 2.01 (broad s, 2H, NH); 1.29 (t, $J = 6.8$ Hz, 6H, $OCH_2\underline{CH_3}$); 1.24 (t, $J = 6.8$ Hz, 6H, $OCH_2\underline{CH_3}$). ^{31}P NMR ($CDCl_3$, 81 MHz): $\delta = 22.1$.

Tetrabenzyl 1,3-Phenylenedi(methylamino)-diferrocenylmethylphosphonate (4c)

Yield: 6.45 g (49%). Calcd for $C_{58}H_{58}Fe_2N_2O_6P_2$: C, 66.17; H, 5.55; N, 2.66. Found: C, 65.99; H, 5.32; N, 2.72%. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 7.28$ (m, 24H, *arom-H*); 4.94 (m, 8H, $O\underline{CH_2}Ph$); 4.23 (m, 4H, CH^{fer}); 4.11 (m, 4H, CH^{fer}); 4.02 (s, 10H, $C_5H_5{}^{fer}$); 4.01 (s, 4H, $\underline{CH_2N}$); 3.80 (d, $^2J_{PH} = 11.8$ Hz, 2H, CH_2). ^{31}P NMR ($CDCl_3$, 81 MHz): $\delta = 23.5$.

Tetramethyl 1,3-Cyclohexylenedi(methylamino)-diferrocenylmethyl-phosphonate (5a)

Yield: 5.47 g (58%). Calcd for $C_{34}H_{48}Fe_2N_2O_6P_2$: C, 54.13; H, 6.41; N, 3.71. Found: C, 54.37; H, 6.09; N, 3.56%. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 4.31$ (m, 4H, CH^{fer}); 4.20 (m, 4H, CH^{fer}); 4.21 (s, 10H, CH^{fer}); 3.70 (d, $^2J_{PH} = 10.4$ Hz, 2H, CHP); 2.95 (m, 2H, CH_2N); 2.80 (m, 2H, CH_2N); 2.09–1.60 (m, 8H, $CH_2{}^{chex}$, CH^{chex}); 1.10–0.81 (m, 2H, $CH_2{}^{chex}$). ^{31}P NMR ($CDCl_3$, 81 MHz): $\delta = 24.53$ and 24.48 (2:3).

Tetraethyl 1,3-Cyclohexylenedi(methylamino)-diferrocenylmethylphosphonate (5b)

Yield: 5.77 g (57%). Calcd for $C_{38}H_{56}Fe_2N_2O_6P_2$: C, 56.31; H, 6.96; N, 3.46. Found: C, 55.98; H, 6.59; N, 3.37%. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 4.25$ (m, 4H, CH^{fer}); 4.15 (m, 4H, CH^{fer}); 4.14 (s, 10H, CH^{fer}); 3.98 (m, 8H, $O\underline{CH_2}CH_3$); 3.58 (d, $^2J_{PH} = 11.2$ Hz, 1H, CHP); 3.55 (d, $^2J_{PH} = 11.2$ Hz, 2H, CHP); 2.92 (m, 2H, CH_2N); 2.80 (m, 2H, CH_2N); 1.99–1.82 (m, 8H, $CH_2{}^{chex}$, CH^{chex}); 1.38–1.31 (m, 2H, $CH_2{}^{chex}$); 1.29 (t, $J = 6.9$ Hz, 6H, $OCH_2\underline{CH_3}$); 1.24 (t, $J = 6.9$ Hz, 6H, $OCH_2\underline{CH_3}$). ^{31}P NMR ($CDCl_3$, 81 MHz): $\delta = 22.45$; 22.39; 22.37; 22.31; 22.24 (30:20:15:2:1).

Tetrabenzyl 1,3-Cyclohexylenedi(methylamino)-diferrocenylmethyl-phosphonate (5c)

Yield: 8.07 g (61%). Calcd for $C_{58}H_{64}Fe_2N_2O_6P_2$: C, 65.79; H, 6.09; N, 2.65. Found: C, 65.51; H, 6.05; N, 2.93%. ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 7.27$ (m, 20H, *arom*-H); 4.94 (m, 8H, $O\underline{CH_2}Ph$); 4.34 (m, 4H, CH^{fer}); 4.26 (m, 4H, CH^{fer}); 4.17 (s, 10H, $C_5H_5{}^{fer}$); 4.14 (s, 4H, $\underline{CH_2N}$); 3.64 (d, $^2J_{PH} = 14.8$ Hz, 2H, CHP); 3.33 (m, 2H, CH^{chex}); 1.81 (m, 4H, $CH_2{}^{chex}$); 1.53 (m, 2H, $CH_2{}^{chex}$); 1.28 (m, 2H, $CH_2{}^{chex}$). ^{31}P NMR ($CDCl_3$, 81 MHz): $\delta = 22.9$.

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