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First synthesis of 1,1′-ferrocene bis-aminophosphonic esters

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Abstract

The series of aminophosphonates bearing the 1,1′-bis-substituted ferrocenyl moiety was obtained by the addition of dialkyl phosphites to an azomethine bond of Schiff bases derived from 1,1′-ferrocene-bis-carboxaldehyde. This addition led to both diastereoisomeric forms demonstrating its behaviour to be contrary to the addition to terephthalic Schiff bases, which led exclusively to a *meso*-form.

Keywords: 1,1′-Ferrocenedicarboxaldehyde; Schiff bases; Aminophosphonates; Asymmetrical induction; 1,1′-bis-substituted ferrocene moiety

1. Introduction

After the first preparation of aminophosphonic acids and esters [1–3], the great development of their chemistry was observed in the aspect of the synthesis [4–6], the stereochemistry [7–9], biochemical properties [10,11] and their applications in various fields of agriculture and medicine [12–14].

Because ferrocene-derived compounds are characterized by their ability to make metal-centred redox systems to generate oxidized or reduced form of different properties they have been widely employed in various fields such as: molecular recognition as biosensors [15–19], in asymmetric catalysis [20], in polymer science as red-ox active polymers and dendrimers [21], in nonlinear optics [22], in synthesis of complex photochemical systems [23] and in pharmacology [24]. Successful attempts of the synthesis of amino acids bearing ferrocene moiety have been also performed [25–31]. Ferrocenyl amino acids found their application in food chemistry as a possible substitute for phenylalanine in the commercial sweetener aspartame [30].

Regarding all above, we wanted to combine properties of mentioned groups of compounds and recently we have reported the synthesis of aminophosphonic esters bearing ferrocenyl moiety [32,33]. In this paper, we present the first synthesis of variously N-substituted 1,1′-ferrocene-bis-aminomethane phosphonates using the addition to the azomethine bond [4]. These compounds can be converted into various bis-aminophosphonates O-substituted with polyglycols, steroids or nucleosides, which might be interesting analogues of ferrocene compounds already described in the literature [34,35].

2. Results and discussion

1,1′-Ferrocene-bis-aminophosphonates were synthesized by the addition of dialkyl phosphites to the azomethine bond of Schiff bases. As the model compounds, diethyl, dibenzyl and diphenyl phosphites were chosen.

Schiff bases of 1,1′-ferrocenedicarboxaldehyde **2a–d** were prepared following the known methodology [6,32]. They were characterised by means of elemental analyses and ^{1}H NMR spectroscopy.

The phosphite additions were carried out in toluene or in acetonitrile at a boiling temperature for 5–7 h (Scheme 1). Tetraethyl esters **3a**, **3d** and **3j** were isolated from the post-reaction mixture by the multiple washing with ether of their ethanol-aqueous acidic solution and by subsequent extraction of the alkaline aqueous mixture with dichloromethane. Resulting crude tetraethyl esters decomposed on silica gel and on neutral aluminium oxide,

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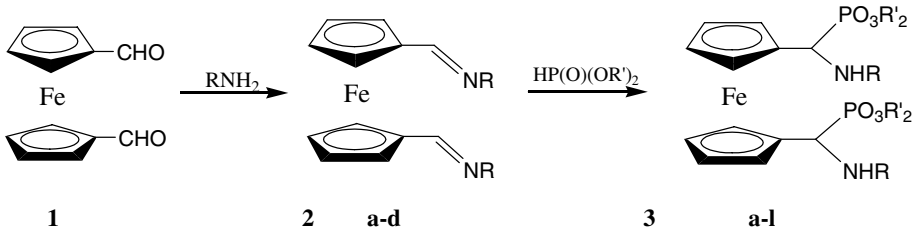


1 **2** **a-d** **3** **a-l**

2a: R = CH_2Ph; **2b**: R = CH_2Fur**;** **2c**: R = $CHPh_2$; **2d**: R = $CH(CH_3)Ph$

3a: R = CH_2Ph, R' = Et; **3b**: R = CH_2Ph, R' = CH_2Ph; **3c**: R = CH_2Ph, R' = Ph;
3d: R = CH_2Fur, R' = Et; **3e**: R = CH_2Fur, R' = CH_2Ph; **3f**: R = CH_2Fur, R' = Ph;
3g: R = $CHPh_2$, R' = Et; **3h**: R = $CHPh_2$, R' = CH_2Ph; **3i**: R = $CHPh_2$, R' = Ph;
3j: R =(*R*)-CH (CH_3)Ph, R' = Et; **3k**: R = (*R*)-CH (CH_3)Ph, R' = CH_2Ph;
3l: R = (*R*)-CH (CH_3)Ph, R' = Ph;

Fur = 

Scheme 1.

that is why they were purified by the column chromatography on cellulose powder. Tetrabenzyl esters **3b**, **3e**, **3h** and **3k** could not be treated in this way, as their hydrochlorides are not soluble in ethanol–water mixture and cellulose powder was not a suitable adsorbent to purify them. They were isolated and purified by the column chromatography on neutral aluminium oxide but partial decomposition of esters on aluminium oxide was observed, which resulted in their very moderate yields. In this way, we have obtained N-substituted diethyl and dibenzyl 1,1′-ferrocene-bis-aminomethanephosphonates **3a**–**b**, **3d**–**e**, **3h** and **3j**–**k**. The ^1H and ^{31}P NMR spectroscopy, the mass spectrometry and the elemental analysis confirmed their identity and their purity.

Tetraphenyl bis-aminophosphonates **3c**, **3f**, **3i**, **3l** decomposed in the above-described conditions. Their purification was then very troublesome and their structure was confirmed only by the NMR spectroscopy and the mass spectrometry measurements of crude products. Because the intensity of their mass peaks mostly did not exceed 5%, the high-resolution mass spectrometry (HRMS) measurements could not be performed. Their data are quoted in Section 3.

It is not the exception that aminophosphonic phenyl ester demonstrate less stability than alkyl or alkyl-aryl ones. The same case was discussed for ferrocene-derived mono-aminophosphonates [32,33] and similar situation occurred in case of (2-furyl)-*N*-tritylamino-phosphonic esters [36], which diphenyl ester could not be obtained because of its instability [37].

A very interesting matter occurred in a case of tetraethyl 1,1′-ferrocene-bis-(*N*-diphenylmethylaminomethanephosphonate) **(3g)**. The reaction of 1,1′-ferrocene-bis-(carbaldehyde-*N*-diphenylmethylimine) **(2c)** with diethyl phosphite occurred in a small degree – its conversion rate was 33%, as estimated from NMR measurements. The reaction was repeated many times, we were changing the duration, the ratio of substrates and solvent (acetonitrile and toluene) and none of them improved the conversion rate of the reaction. The isolation of the product from the post-reaction mixture was therefore impossible, so the occurring ester product was identified only by the NMR spectroscopy and mass spectrometry measurements. We have no idea why such a phenomenon occurred, especially that initial applied conditions were the same as in all other cases of the synthesis of ethyl esters **3a**, **3d**, **3j**. Nothing seems to explain such a low conversion rate of reaction in the ester **3g** synthesis.

The addition of phosphites to achiral Schiff bases of 1,1′-ferrocenedicarbaldehyde was not stereoselective at all or the stereoselectivity occurred in a very small degree. The addition of phosphites to ferrocene-bis-carbimines **2a**–**c** led to the formation of two diastereoisomeric forms (the *meso* form and the raceme mixture) of 1,1′-ferrocene-bis-methanephosphonate **3a**–**i** in a 1:1, 1:2 or 3:2 ratio, which was demonstrated by means of the ^1H and ^{31}P NMR spectroscopy. The addition of a phosphite to the chiral 1,1′-ferrocene-bis-(carbaldehyde-*N*-(R)-α-methylbenzylimine) **(2d)** led to the formation of three diastereoisomers in a 1:3:1 ratio. Unfortunately, diastereoisomers were not separated due to their fragility to silica gel and neither applied cellulose powder nor aluminium oxide were found to be efficient enough to provide a good resolution of diastereoisomers.

The addition of phosphites to terephthalic and isophthalic imines is in 100% stereoselective [38–40] leading to the formation of a *meso*-form and we suggested [39] that this stereoselective addition to completely achiral compounds originated from intermolecular interactions between two molecules of the mono-addition intermediate products and two phosphite molecules (Scheme 2(a)). In case of ferrocene derivative, it takes the most probably the conformation as in Scheme 2(b), which seems to be the most convenient one. This conformation makes the formation of the similar dimer more difficult. In addition, we suggest the probable occurrence of interactions between iron in ferrocene and oxygen from phosphonic group as presented in Scheme 2(c). These phenomena make the attack of a phosphite molecule on an azomethine bond possible from both sides.

All attempts to cleave ethyl esters **3a**, **3d**, **3g** and **3j** failed. We tried to use acidic cleavage with aqueous hydrochloric acid as well as the known [6] method with trimethylsilyl bromide. Both methods led to the variety of products, among which, we identified phosphoric acid derivatives and 1,1′-bis-(aminomethyl)ferrocene. It would suggest that the retro-addition reaction occurred. But as the rest of products remained unidentified, the retro-addition is not the exclusive reaction.

Our aim and perspective for the future is to find the way to obtain various ferrocene-derived bis-aminophosphonic acids, as they are of interest as the starting material for the synthesis of ferrocene-bearing macrocycles, *bis*-phosphonosteroids or *bis*-phosphono-nucleosides. The best method is the cleavage of title bis-esters **3a**–**l**, but as we showed, it is not a simple task. It is to remark that, in comparison to ferrocene-derived mono-aminophosphonates [32], title bis-esters **3a**–**l** behave similarly to former ones, but they are more fragile.

3. Experimental

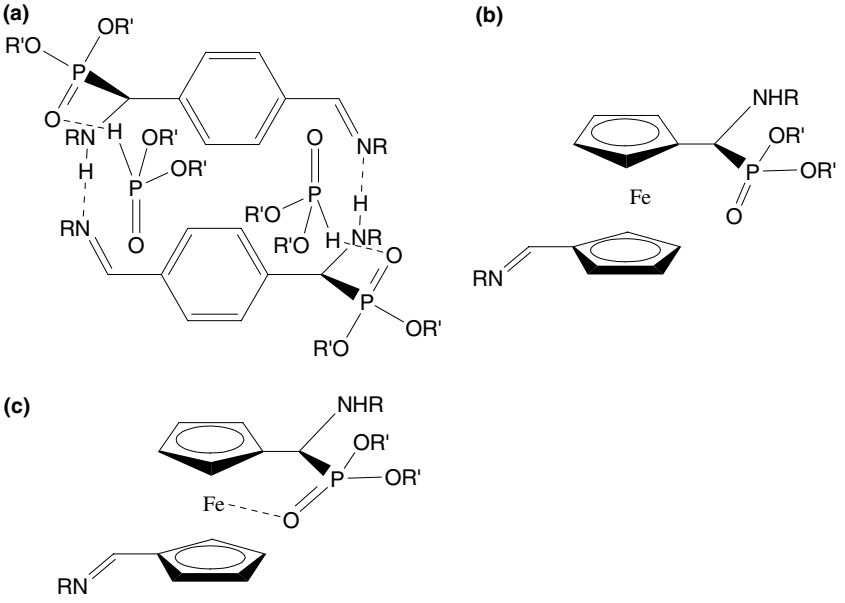
All solvents (POCh-Poland) were routinely distilled and dried prior to use [41]. Amines (Aldrich), phosphites (Aldrich) and 1,1′-ferrocenedicarboxaldehyde (Aldrich) were used as received. Cellulose powder was provided by Aldrich. All NMR spectra were recorded on a Varian Gemini 200 BB spectrometer operating at 200 MHz for ^{1}H NMR and at 81 MHz for ^{31}P NMR. Elemental analyses and mass spectra were performed in the Centre of Molecular and Macromolecular Studies (Polish Academy of Science) in Łódź.

3.1. Schiff bases of 1,1′-ferrocenedicarboxaldehyde (**2a**–**d**)

To a solution of ferrocenecarboxaldehyde (0.107 g, 0.5 mmol) in methanol (10 ml), an amine (1mmol) was added. The mixture was then stirred for 20 h at a room temperature, then the mixture was evaporated, the solid residue dissolved in benzene and precipitated with hexane to give a pure product. In a case of non-crystalline product, the residue was dissolved in benzene and filtered through a cellulose pad and then evaporated to give a pure product.

3.1.1. 1,1′-ferrocene-bis-(carbaldehyde-N-benzylimine) (**2a**)

Yield = 0.20 g (95%); (brown crystals); mp = 56–58 °C.



Scheme 2.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.11 (s, CH=N, 2H); 7.32 (m, PhH, 10 H); 4.67 (narrow m, Cp, 4H); 4.60 (s, CH_2Ph, 4H); 4.37 (narrow m, Cp, 4H).

Elemental analysis: Anal. Found: C, 74.42; H, 5.64; N, 6.53. Calc. for $C_{26}H_{24}FeN_2$: C, 74.29; H, 5.76; N, 6.66%.

3.1.2. 1,1′-ferrocene-bis-(carbaldehyde-N-furfurylimine) (**2b**)

Yield = 0.17 g (89%); (dense oily liquid).

^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.12 (s, CH=N, 2H); 7.40 (m, H_5^{fur}, 2H); 6.35 (m, H_3^{fur}, 2H); 6.27 (m, H_4^{fur}, 2H); 4.66 (narrow m, Cp, 4H); 4.59 (s, CH_2 Fur, 4H); 4.37 (narrow m, Cp, 4H).

Elemental analysis: Anal. Found: C, 66.18; H, 5.15; N, 6.91. Calc. for $C_{22}H_{20}FeN_2O_2$: C, 66.02; H, 5.04; N, 7.00%.

3.1.3. 1,1′-ferrocene-bis-(carbaldehyde-N-diphenylmethylimine) (**2c**)

Yield = 0.28 g (97%); (brown crystals); mp = 130–132 °C.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.00 (s, CH=N, 2H); 7.33 (m, PhH, 20H); 5.30 (s, $CHPh_2$, 2H); 4.61 (narrow m, Cp, 4H); 4.27 (narrow m, Cp, 4H).

Elemental analysis: Anal. Found: C, 79.89; H, 5.71; N, 5.04. Calc. for $C_{38}H_{32}FeN_2$: C, 79.72; H, 5.63; N, 4.89%.

3.1.4. 1,1′-ferrocene-bis-(carbaldehyde-N-(R)-α-methylbenzylimine) (**2d**)

Yield = 0.21 g (95%) (dense oily liquid).

^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.04 (s, CH=N, 2H); 7.32 (m, PhH, 10 H); 4.67 (narrow m, Cp, 4H); 4.56 (narrow m, Cp, 4H); 4.30 (quart, J = 6.6 Hz, *CH*Ph, 2H); 1.55 (d, J = 6.6 Hz, CH_3, 6H).

Elemental analysis: Anal. Found: C, 75.19; H, 6.41; N, 6.12. Calc. for $C_{28}H_{28}FeN_2$: C, 75.00; H, 6.29; N, 6.25%.

3.2. Dialkyl N-alkylaminoferrocenemethanephosphonates (**3a–l**)

To a solution of an imine (0.5 mmol) in toluene (10 ml), dialkyl phosphite (1 mmol) was added. The solution was refluxed for seven days. In case of ethyl derivatives **3a**, **3d** and **3j** the solvent was evaporated, the residue was dissolved in the 10% aqueous HCl–ethanol (4:1), washed with ether (3 × 20 ml), the aqueous layer extracted with dichloromethane (3 × 25 ml), the organic layers dried and evaporated to give an appropriate product. The product was purified by means of column chromatography on cellulose powder. In case of benzyl derivatives **3b**, **3e**, **3h**, **3k**, a crude product was chromatographed on aluminium oxide without previous extraction. Phenyl derivatives decomposed in above mentioned conditions.

3.2.1. Tetraethyl 1,1′-ferrocene-bis-(N-benzylaminomethanephosphonate) (**3a**)

Yield = 0.25 g (71%).

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.36 (m, PhH, 10H); 4.22–3.96 (m, CH_2CH_3, CH_2Ph, Cp, 20H); 3.69 and 3.66 (2d, $^2J_{PH}$ = 10.8 Hz, CHP, 2H); 1.94 (large s, NH, 2H); 1.27 and 1.25 (2t, J = 6.9 Hz, CH_2 CH_3, 12H). ^{31}P NMR ($CDCl_3$, 81 MHz): δ 22.22 and 22.16 (1:1).

EI-MS: m/z = 696.3 [M^+]; 420.2 [M^+−2HOP$(OEt)_2$]; 238.1 [Fc$(CHNH)_2$]; 91.1 [$^+CH_2$Ph]; 65.0 [Cp].

Elemental analysis: Anal. Found: C, 58.25; H, 6.60; N, 3.99. Calc. for $C_{34}H_{46}FeN_2O_6P_2$: C, 58.63; H, 6.66; N, 4.02%.

3.2.2. Tetrabenzyl 1,1′-ferrocene-bis-(N-benzylaminomethanephosphonate) (**3b**)

Yield = 0.23 g (48%).

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.29 (m, PhH, 30H); 4.91 (m, OCH_2Ph, 8H); 4.18–3.88 (m, Cp, CH_2Ph, 12H); 3.73 and 3.69 (2d, $^2J_{PH}$ = 8.8 Hz, CHP, 2H); 1.92 (large s, NH, 2H). ^{31}P NMR ($CDCl_3$, 81 MHz): δ 23.48 and 23.38 (1:1).

EI-MS: m/z = 945.1 [M^+]; 682.4 [M^+−HOP(O $CH_2Ph)_2$]; 420.8 [M^+−2 HOP$(OCH_2Ph)_2$]; 238.3 [Fc$(CHNH)_2$]; 107.1 [$^+OCH_2$Ph]; 91.1 [$^+CH_2$Ph]; 65.0 [Cp].

Elemental analysis: Anal. Found: C, 68.78; H, 5.72; N, 2.74. Calc. for $C_{54}H_{54}FeN_2O_6P_2$: C, 68.65; H, 5.76; N, 2.96%.

3.2.3. Tetraphenyl 1,1′-ferrocene-bis-(N-benzylaminomethanephosphonate) (**3c**)

Conversion rate = 75% *estimated by NMR*.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.23–6.80 (m, PhH, 30H); 4.49–4.09 (m, Cp, CH_2Ph, 12H); 3.71 and 3.67 (2d, $^2J_{PH}$ = 8.8 Hz, CHP, 2H); 1.99 (large s, NH, 2H). ^{31}P NMR ($CDCl_3$, 81 MHz): δ 14.91 and 14.59 (1:2).

FAB-MS: m/z = 945.1 [M^+]; 421.4 [M^+−2 HOP $(OPh)_2$]; 238.0 [Fc$(CHNH)_2$]; 93.1 [$^+$OPh]; 91.1 [$^+CH_2$Ph]; 65.0 [Cp].

3.2.4. Tetraethyl 1,1′-ferrocene-bis-(N-furfurylaminomethanephosphonate) (**3d**)

Yield = 0.23 g (66%).

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.36 (m, H_{fur}^5, 2H); 6.26 (m, H_3^{fur}, 4H); 4.26–3.93 (m, CH_2CH_3,CH_2Ph, Cp, 20H); 3.89 and 3.73 (2d, $^2J_{PH}$ = 9.8 Hz, CHP, 2H); 1.75 (large s, NH, 2H); 1.26 and 1.25 (2t, J = 6.9 Hz, CH_2CH_3, 12H).^{31}P NMR ($CDCl_3$, 81 MHz): δ 22.61 and 22.50 (1:1).

EI-MS: m/z = 676.1 [M^+]; 538.1 [M^+−HOP$(OEt)_2$]; 400.1 [M^+−2HOP$(OEt)_2$]; 238.2 [Fc$(CHNH)_2$]; 81.0 [$^+CH_2$Fur]; 65.0 [Cp].

Elemental analysis: Anal. Found: C, 52.94; H, 5.91; N, 4.49. Calc. for $C_{30}H_{42}FeN_2O_8P_2$: C, 53.27; H, 6.26; N, 4.14%.

*3.2.5. Tetrabenzyl 1,1′-ferrocene-bis-(N-furfurylaminomethanephosphonate) (**3e**)*

Yield = 0.22 g (47%).

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.29 (m, PhH, H^5_{fur}, 22H); 6.26 (m, H^{fur}_3, 2H); 6.15 (m, H^{fur}_4, 2H); 4.89 (m, OCH_2Ph, 8H); 4.14–4.04 (m, Cp, CH_2Fur, 12H); 3.73 and 3.69 (2d, $^2J_{PH}$ = 8.8 Hz, CHP, 2H); 2.05 (large s, NH, 2H). ^{31}P NMR ($CDCl_3$, 81 MHz): δ 23.12 and 22.85 (3:2).

EI-MS: m/z = 924.3 [M^+]; 662.2 [M^+−HOP$(OCH_2Ph)_2$]; 400.1 [M^+−2 HOP$(OCH_2Ph)_2$]; 238.0 [Fc$(CHNH)_2$]; 107.1 [$^+OCH_2Ph$]; 91.1 [$^+CH_2Ph$]; 81.1 [$^+CH_2Fur$]; 65.0 [Cp].

Elemental analysis: Anal. Found: C, 65.12; H, 5.67; N, 3.21. Calc. for $C_{50}H_{50}FeN_2O_8P_2$: C, 64.94; H, 5.45; N, 3.03%.

*3.2.6. Tetraphenyl 1,1′-ferrocene-bis-(N-furfurylaminomethanephosphonate) (**3f**)*

Conversion rate = 70% *estimated by NMR*.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.26 (m, PhH, H^5_{fur}, 22H); 6.31 (m, H^{fur}_3, H^{fur}_4, 4H); 4.40–4.10 (m, Cp, CH_2Fur, 12H); 3.73 and 3.69 (2d, $^2J_{PH}$ = 8.8 Hz, CHP, 2H); 2.05 (large s, NH, 2H). ^{31}P NMR ($CDCl_3$, 81 MHz): δ 14.81 and 14.63 (1:1).

FAB-MS: m/z = 868.3 [M^+]; 634.2 [M^+−HOP$(OPh)_2$]; 400.1 [M^+−2 HOP$(OPh)_2$]; 238.0 [Fc$(CHNH)_2$]; 93.1 [^+OPh]; 81.1 [$^+CH_2Fur$]; 65.0 [Cp].

*3.2.7. Tetraethyl 1,1′-ferrocene-bis-(N-diphenylmethylaminomethanephosphonate) (**3g**)*

Conversion rate = 33% *estimated by NMR*.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.32 (m, PhH, 20H); 5.59 and 5.52 (2s, *CH*Ph_2, 2H); 4.37–3.90 (m, CH_2CH_3, Cp, 16H); 3.77 and 3.76 (2d, $^2J_{PH}$ = 15.0 Hz, CHP, 2H); 2.05 (large s, NH, 2H); 1.26 and 1.25 (2t, J = 6.6 Hz, CH_2CH_3, 12H). ^{31}P NMR ($CDCl_3$, 81 MHz): δ 23.02 and 22.83 (1:1).

EI-MS: m/z = 849.1 [M^+]; 711.1 [M^+−HOP$(OEt)_2$]; 573.2 [M^+−2HOP$(OCH_2Ph)_2$]; 238.0 [Fc$(CHNH)_2$]; 167.1 [$^+CHPh_2$]; 65.0 [Cp].

*3.2.8. Tetrabenzyl 1,1′-ferrocene-bis-(N-diphenylmethylaminomethanephosphonate) (**3h**)*

Yield = 0.26 g (47%).

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.27 (m, PhH, 40H); 5.57 and 5.49 (2s, *CH*Ph_2, 2H); 4.89 (m, OCH_2Ph, 8H); 4.30–4.06 (m, Cp, 8H); 3.77 and 3.76 (2d, $^2J_{PH}$ = 13.6 Hz, CHP, 2H); 2.05 (large s, NH, 2H). ^{31}P NMR ($CDCl_3$, 81 MHz): δ 23.70 and 23.47 (3:2).

EI-MS: m/z = 1097.1 [M^+]; 572.2 [M^+−2HOP$(OCH_2Ph)_2$]; 238.0 [Fc$(CHNH)_2$]; 171.0 [$^+$P(O)(OH)(OCH_2Ph)]; 167.1 [$^+CHPh_2$]; 107.1 [$^+OCH_2Ph$]; 65.0 [Cp].

Elemental analysis: Anal. Found: C, 72.29; H, 5.95; N, 2.50. Calc. for $C_{66}H_{62}FeN_2O_6P_2$: C, 72.26; H, 5.70; N, 2.55%.

*3.2.9. Tetraphenyl 1,1′-ferrocene-bis-(N-diphenylmethylaminomethanephosphonate) (**3i**)*

Conversion rate = 78% *estimated by NMR*.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.32 (m, PhH, 40H); 5.61 and 5.54 (2s, *CH*Ph_2, 2H); 4.46–4.05 (m, Cp, 8H); 3.73 and 3.69 (2d, $^2J_{PH}$ = 8.8 Hz, CHP, 2H); 2.05 (large s, NH, 2H). ^{31}P NMR ($CDCl_3$, 81 MHz): δ 15.10 and 14.94 (2:1).

FAB-MS: m/z = 1040.6 [M^+]; 807.4 [M^+−HOP$(OPh)_2$]; 573.4 [M^+−2HOP$(OPh)_2$]; 238.9 [Fc$(CHNH)_2$]; 233.8 [$^+$P(O)(OH)(OCH_2Ph)]; 167.1 [$^+CHPh_2$]; 93.1 [^+OPh]; 65.0 [Cp].

*3.2.10. Tetraethyl 1,1′-ferrocene-bis-(N-N-(R)-α-methylbenzylaminomethanephosphonate) (**3j**)*

Yield = 0.21 g (59%).

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.38 (m, PhH, 10H); 4.41–3.78 (m, CH_2CH_3, *CH*Ph, Cp, 18H); 3.64, 3.34 and 3.51 (3d, $^2J_{PH}$ = 10.4 Hz, CHP, 2H); 1.90 (large s, NH, 2H); 1.47 (d, J = 6.6 Hz, $CHCH_3$, 6H); 1.26 and 1.24 (2t, J = 7.0 Hz, CH_2CH_3, 12H). ^{31}P NMR ($CDCl_3$, 81 MHz): δ 23.53, 22.40 and 23.14 (1:3:1).

EI-MS: m/z = 724.1 [M^+]; 586.2 [M^+−HOP$(OEt)_2$]; 448.2 [M^+−2HOP$(OEt)_2$]; 238.1 [Fc$(CHNH)_2$]; 105.0 [$^+CH(CH_3)Ph$]; 65.0 [Cp].

Elemental analysis: Anal. Found: C, 60.01; H, 6.88; N, 3.91. Calc. for $C_{36}H_{50}FeN_2O_6P_2$: C, 59.67; H, 6.96; N, 3.87%.

*3.2.11. Tetrabenzyl 1,1′-ferrocene-bis-(N-N-(R)-α-methylbenzylaminomethanephosphonate) (**3k**)*

Yield = 0.22 g (45%).

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.29 (m, PhH, 30H); 4.88 (m, OCH_2Ph, 8H); 4.34, 4.16 and 4.05 (3quart, J = 6.8 Hz, 2H); 3.87 and 3.75 (2m, Cp, 8H); 3.80, 3.69 and 3.53 (3d, $^2J_{PH}$ = 8.8 Hz, CHP, 2H); 2.03 (large s, NH, 2H). ^{31}P NMR ($CDCl_3$, 81 MHz): δ 24.15, 23.95 and 23.70 (1:3:1).

EI-MS: m/z = 973.1 [M^+]; 882.3 [M^+−CH_2Ph]; 448.2 [M^+−2HOP$(OCH_2Ph)_2$]; 238.0 [Fc$(CHNH)_2$]; 171.0 [$^+$P(O)(OH)(OCH_2Ph)]; 107.1 [$^+OCH_2Ph$]; 105.1 [$^+CH(CH_3)Ph$]; 65.0 [Cp].

Elemental analysis: Anal. Found: C, 69.35; H, 5.99; N, 2.65. Calc. for $C_{56}H_{58}FeN_2O_6P_2$: C, 69.14; H, 6.01; N, 2.88%.

*3.2.12. Tetraphenyl 1,1′-ferrocene-bis-(N-N-(R)-α-methylbenzylaminomethanephosphonate) (**3l**)*

Conversion rate = 74% *estimated by NMR*.

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.25 (m, PhH, 30H); 4.36–3.94 (m, Cp, *CH*CH_3, 10H); 3.73 and 3.69 (2d, $^2J_{PH}$ = 8.8 Hz, CHP, 2H); 2.05 (large s, NH, 2H). ^{31}P

NMR ($CDCl_3$, 81 MHz): δ 15.44, 15.37 and 15.27 (1:3:1).

FAB-MS: $m/z = 917.3$ [M^+]; 683.3 [$M^+ - HOP(OPh)_2$]; 449.2 [$M^+ - 2HOP(OPh)_2$]; 238.0 [$Fc(CHNH)_2$]; 105.1 [$^+CH(CH_3)Ph$]; 93.1 [^+OPh]; 65.0 [Cp].

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