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# Diastereoselective Addition of Di-(Trimethylsilyl)Phosphite to Chiral *N*-(*R*)-α-Methylbenzyl and *N*-(1-methoxycarbonyl-*iso*-pentyl) Schiff Bases of Various Aldehydes

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ABSTRACT: *The addition of bis-(trimethylsilyl) phosphite to chiral imines of several aldehydes was diastereoselective. The separation of predominant diastereoisomers of a majority of formed aminophosphonic acids has been observed. Moreover, the ferrocene-derived acid* ***5d*** *occurred in diastereoselectivity up to 100%.* © 2010 Wiley Periodicals, Inc. Heteroatom Chem 21:326–331, 2010; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20624

## *INTRODUCTION*

Addition of dialkyl and diaryl phosphites to azomethine bond of chiral Schiff bases, such as *N*-α-methylbenzylimines, has been described in several papers [1–5]. Diastereoselectivity of reported reactions varied from 2:1 to 9:1 of diastereoisomeric ratio. Obtained diastereoisomeric aminophosphonates should be separated by chromatographic methods and then undergo hydrolysis to obtain free acids, which influenced badly substituents—such conditions are suitable neither for a furan ring [6–11] nor for a ferrocene moiety [12,13]. To avoid this problem, 100% diastereoselective addition of hypophosphorous acid to chiral Schiff bases has been applied [14–18] and formed aminophosphonous acids were subsequently oxidized to give aminophosphonic systems. Unfortunately, known oxidation methods turned out to be too rigid for both furanic and ferrocene systems. Thus, Zoń [19] and Boduszek [20] presented the method for synthesis of aminophosphonic acids through addition of bis-(trimethylsilyl) phosphite to azomethine bond of Schiff bases, where silyl esters formed decomposed to free acids in mild methanolysis conditions. They did not study the stereochemistry of addition of silyl phosphite to chiral imines.

Mikołajczyk and co-workers invented an interesting method for highly stereoselective synthesis of aminophosphonic acids using the addition of dialkyl phosphite anions to chiral sulfimines [21], which achieved promising results.

## *RESULTS AND DISCUSSION*

Considering the above, we were prompted to study this problem, especially because preliminary results demonstrated interesting phenomena accompanying this process [22]. That is why we performed the addition of bis-(trimethylsilyl) phosphite

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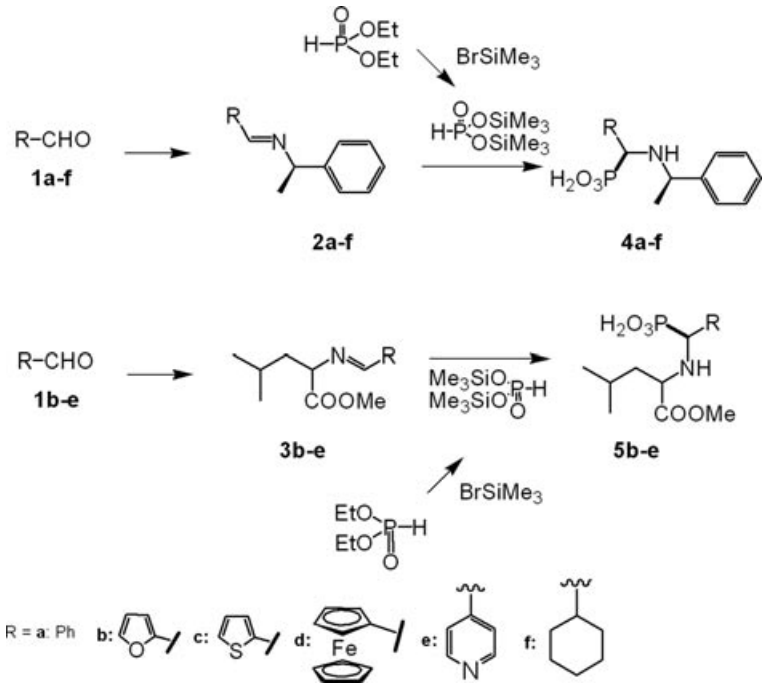



SCHEME 1

to two groups of chiral imines of various aldehydes, i.e., *N*-(*R*)-α-methylbenzylimines **2a-f** and *N*-(1-methoxycarbonyl-3-methylbutylimines) **3b-e** to investigate the stereochemistry of these reactions.

Chiral Schiff bases **2a-f** were synthesized following the classical methodology [22] by mixing (*R*)-α-methylbenzylamine with an appropriate aldehyde **1a-f** in methanol and were obtained in 95–99% yields.

Obtained imines have undergone the addition of bis-(trimethylsilyl) phosphite to their azomethine bond. Bis-(trimethylsilyl) phosphite has been prepared in situ by the reaction of diethyl phosphite with bromotrimethylsilane in dichloromethane [20]. In situ generated bis-(trimethylsilyl) phosphite underwent the reaction with chiral Schiff bases **2a-f** in dichloromethane. The conversion was monitored by means of $^{31}$P NMR, and when it was complete the reaction was quenched by methanolysis. After addition of propylene oxide, resulting acids **4a-f** were obtained in 35–70% yields (Scheme 1).

Imines **3b-e** have been synthesized by the action of triethylamine on leucine methyl ester hydrochloride and subsequent reaction of newly formed leucine methyl ester with an appropriate aldehyde **1a-f** in boiling dichloromethane for 3 days. The usual workup gave desired imines **3a-f** in 96–98% yields.

Obtained imines **3b-e** have undergone the addition of bis-(trimethylsilyl) phosphite to their azomethine bond as it took place in the case of imines **2a-f**. Bis-(trimethylsilyl) phosphite [20] generated in the same way underwent the reaction with chiral Schiff bases **3a-f** in dichloromethane. The conversion was monitored by means of $^{31}$P NMR, and when it was complete the reaction was quenched by methanolysis. After addition of propylene oxide, resulting acids **5b-e** were obtained in 20–60% yields (Scheme 1).

The diastereoselectivity of the formation of *N*-((*R*)-α-methylbenzyl)aminomethyl-phosphonic acids **4a-f** varied from de = 9% in the case of 4-pyridyl derivative **4e** up to de = 82% in the case of *N*-((*R*)-α-methylbenzyl)-amino(ferrocenyl)methyl phosphonic acid **4d** (Table 1). What is important is that the predominant diastereoisomers of aminophosphonic acids **4a, 4c, 4d**, and **4f** crystallized from the postreaction mixture alone, not contaminated by the second isomer; thus some kind of self-separation of diastereoisomers took place. In the case of 4-pyridyl derivative **4e** such a self-separation did not occur and the product was obtained as the mixture of diastereoisomers.

Compounds **4a** and **4c** crystallized as monohydrates, which was demonstrated by the elemental analysis. It was probably due to the workup; as in the case of **4c**, propylene oxide was not added to the postreaction mixture, so removal of water was not executed. As for the isolation of **4a**, water was added instead of methanol and therefore, the product could crystallize as a monohydrate.

**TABLE 1** Results of Addition of Bis-(trimethylsilyl) Phosphite to *N*-(*R*)-α-Methylbenzylimines) **2a-f**

| | | | | *A Single Isomer*[a] | | | |
|---|---|---|---|---|---|---|---|
| *No.* | *R* | *Y [%]* | *mp [°C]* | *$^{31}$P NMR* | $\alpha_D^{20}$ | *$^{31}$P NMR* | *dr (de[%])* |
| 4a | Ph | 59 | 174–177 | 15.02 | + 63.67 (c = 2.96 in 1M NaOH) | 15.84 and 15.02 | 1:5 (67) |
| 4b | 2-furyl | 66 | – | – | – | 13.69 and 12.99 | 5:4 (11) |
| 4c | 2-thienyl | 51 | 156–158 | 15.60 | + 16.93 (c = 1.75 in 1M NaOH) | 15.60 and 14.48 | 5:1 (67) |
| 4d | ferrocenyl | 32 | 200–201 | 15.64 | + 7.38 (c = 2.84 in 1M NaOH) | 15.64 and 15.25 | 9:1 (80) |
| 4e | 4-pirydyl | 58 | 215–217 | – | – | 13.74 and 13.00 | 5:6 (9) |
| 4f | cyclohexyl | 68 | 212–214 | 19.77 | + 23.02 (c = 1.04 in 1M NaOH) | 19.77 and 19.01 | 4:1 (60) |

[a]Spectral data of a self-separated diastereoisomer.

Unfortunately, the reaction with *N*-(2-furfurylidene)-(*R*)-α-methylbenzylamine **2b** was not successful, as the corresponding acid **4b** was not isolated and only the NMR investigation of the postreaction mixture demonstrated the occurrence of the reaction with a 5:4 dr.

As for the formation of *N*-(1-methoxycarbonyl-3-methylbutyl)aminomethylphosphonic acids **5b-e**, the diastereoselectivity varied from de = 14% in the case of *N*-(1-methoxycarbonyl-3-methylbutyl) amino(thienyl)-methylphosphonic acid 5c, up to de = 100% in the case of *N*-(1-methoxycarbonyl-3-methylbutyl)amino(ferrocenyl) - methylphosphonic acid 5d (Table 2). As in the previous case, the self-separation of predominant diastereoisomers of aminophosphonic acid 5b and 5c was observed. Moreover, *N*-(1-methoxycarbonyl-3-methylbutyl) amino(ferrocenyl)-methylphosphonic acid 5d occurred as the one exclusive diastereoisomer. Although its proper purity was confirmed by the NMR spectroscopy, elemental analysis of the acid 5d showed some discrepancies in C%. This is probably due to masking carbon by iron in burning analysis.

Unfortunately, the X-ray measurements could not be performed as the product 5d crystallized as powder and our attempts to grow the proper crystal failed.

Also unfortunately, the reaction with *N*-(2-benzylidene)-(1-methoxycarbonyl-3-methylbutylamine) 3a and 3f did not occur; that is why these cases are not mentioned in Table 2.

Summarizing, we have observed the separation of predominant diastereoisomers of aminophosphonic acids **4a, 4c, 4d**, and **4f**, as well as **5b**, which easily crystallized from the postreaction mixture. Moreover, the ferrocene-derived acid **5d** occurred in diastereoselectivity up to 100%.

It is very difficult to state the reason why the addition of bis-(trimethylsilyl) phosphite to both ferrocene-containing imines **2d** and **3d** turned out to be much more diastereoselective than other cases. This may be explained by the Houk model, which according to Houk is *"the same as the Felkin–Anh version of Cram's rule for nucleophilic additions"* [23]. According to this model, the hydrogen bond forms between the hydrogen of bis-(trimethylsilyl) phosphite and the nitrogen of the azomethine bond from the side opposite to the largest substituent. And in the case of ferrocenyl derivatives **2d** and **3d**, diastereoselection is reinforced due to the stabilizing interaction between the phosphorus atom orbital and the ferrocenyl substituent as it is presented in Scheme 2.

## *EXPERIMENTAL*

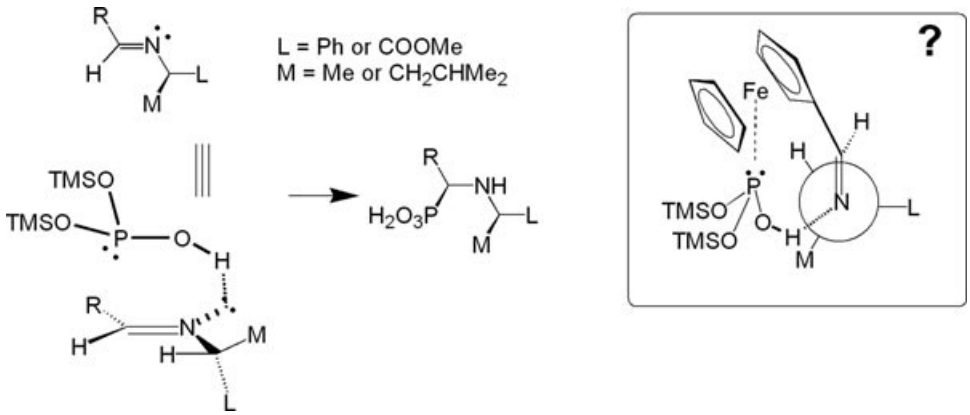
### *Aminophosphonic Acids* **4a, 4c–f**, *and* **5b–e**; *General Procedure*

Diethyl phosphite (2.5 mmol) was dissolved in dry dichloromethane and to this solution bromotrimethylsilane (6.8 mmol, 0.9 mL) was added

**TABLE 2** Results of Addition of Bis-(trimethylsilyl) Phosphite to *N*-((*S*)-1-Methoxycarbonyl-3-Methylbutylimines) **3b-e**

| | | | | *A Single Isomer*[a] | | | |
|---|---|---|---|---|---|---|---|
| *No.* | *R* | *Y [%]* | *mp [°C]* | *$^{31}$P NMR* | $\alpha_D^{20}$ | *$^{31}$P NMR* | *dr (de[%])* |
| 5b | 2-furyl | 28 | 185–186 | 13.14 | + 33.48 (c = 1.93 in 1M NaOH) | 13.14 and 12.74 | 5:1 (67) |
| 5c | 2-thienyl | 60 | 142–145 | – | – | 14.15 and 13.32 | 4:3 (14) |
| 5d | ferrocenyl | 17 | 205–206 | 16.27 | −19.89(c = 1.41 in 1M NaOH) | 16.27[b] | 100 |
| 5e | 4-pirydyl | 38 | 187–189 | – | – | 13.41 and 12.64 | 3:8 (46) |

[a]Spectral data of a self-separated diastereoisomer.
[b]The exclusive formation of the only one diastereoisomer was observed.




SCHEME 2

dropwise for 10–15 min. The mixture was stirred for 1 h at room temperature. Then, a solution of an appropiate imine (2.5 mmol) in dry dichloromethane was added and the mixture was refluxed for 4 h. Then, the solution was evaporated in vacuo and the residue was dissolved in dry methanol and stirred for 30–45 min until precipitation of a solid, which was filtered off and collected. For acids **4a** and **4f**, water was added instead of methanol and the mixture was refrigerated for 7 days until the product precipitated. In the case of **4d, 5b**, and **5e** the solid did not precipitate after methanolysis; therefore 10–20 mL of propylene oxide was added and the mixture was refrigerated for 3–7 days. Then the solid was filtered off and collected.

*N - ((R) - α - methylbenzyl) - amino(phenyl)methyl Phosphonic Acid* **4a**.

*Predominant diastereoisomer:* Calcd for $C_{15}H_{18}NO_3P.H_2O$: C, 58.25; H, 6.52; N, 4.53. Found: C, 58.66; H, 6.52; N, 4.47.

$^1$H NMR (200 MHz, $D_2O$): δ 0.94 (d, $J = 6.4$ Hz, CHC$\underline{H}_3$, 3H); 3.15 (q, $J = 6.4$ Hz, C$\underline{H}$CH$_3$, 1H); 3.12 (d, $^2J_{PH} = 17.0$ Hz, CHP, 1H); 6.81 (m, PhH, 4H); 6.99 (m, PhH, 6H).

*Minor diastereoisomer*: $^1$H NMR (200 MHz, $D_2O$): δ 0.98 (d, $J = 6.4$ Hz, CHC$\underline{H}_3$, 3H); 3.45 (q, $J = 6.4$ Hz, C$\underline{H}$CH$_3$, 1H); 3.51 (d, $^2J_{PH} = 20.0$ Hz, CHP, 1H); 6.81 – 6.99 (m, PhH, 10H).

*N - ((R) - α - methylbenzyl) - amino(thienyl)methyl Phosphonic Acid* **4c**.

*Predominant diastereoisomer:* Calcd for $C_{13}H_{16}NO_3PS{\cdot}H_2O$: C, 49.52; H, 5.75; N, 4.44. Found: C, 49.74; H, 5.79; N, 4.32.

$^1$H NMR (200 MHz, $D_2O$): δ 1.21 (d, $J = 6.6$ Hz, CHC$\underline{H}_3$, 3H); 3.75 (q, $J = 6.6$ Hz, C$\underline{H}$CH$_3$, 1H); 3.95 (d, $^2J_{PH} = 18.6$ Hz, CHP, 1H); 6.72 (m, $CH^2_{tioph}$, 1H); 6.78 (dd, $J = 3.5$ and 5.0 Hz, $CH^3_{tioph}$, 1H); 7.10 (d, $J = 5.0$ Hz, $CH^5_{tioph}$, 1H); 7.16 (m, PhH, 5H).

*Minor diastereoisomer*: $^1$H NMR (200 MHz, $D_2O$): δ 1.16 (d, $J = 6.8$ Hz, CHC$\underline{H}_3$, 3H); 3.51 (q, $J = 6.8$ Hz, C$\underline{H}$CH$_3$, 1H); 3.60 (d, $^2J_{PH} = 18.0$ Hz, CHP, 1H); 6.68 (m, $CH^2_{tioph}$, 1H); 6.86 (dd, $J = 3.5$ and 5.0 Hz, $CH^3_{tioph}$, 1H); 7.11 (d, $J = 5.0$ Hz, $CH^5_{tioph}$, 1H); 7.17 (m, PhH, 5H).

*N-((R)-α-methylbenzyl)-amino(ferrocenyl)methyl Phosphonic Acid* **4d**

*Predominant diastereoisomer:* Calcd for $C_{19}H_{22}FeNO_3P$: C, 57.16; H, 5.55; N, 3.51. Found: C, 57.08; H, 5.50; N, 3.50.

$^1$H NMR (200 MHz, $D_2O$): δ 1.35 (d, $J = 5{,}9$ Hz, $CH_3$); 3.45 (d, $^2J_{PH} = 15.0$ Hz, 1H, CHP); 3.89 (s, 5H, $C_5H^{fer}_5$); 3.96 (m, 3H, C$\underline{H}$Ph, $(CH)^{fer}_2$); 4.15 (m, 2H, $(CH)^{fer}_2$); 7.17 (d, $J = 6.8$ Hz, 1H, PhH); 7.31 (t, $J = 6.8$ Hz, 2H, PhH); 7.43 (d, $J = 6.8$ Hz, 2H, PhH).

*Minor diastereoisomer*: $^1$H NMR (200 MHz, $D_2O$): δ 1.15 (d, $J = 5{,}9$ Hz, $CH_3$); 3.14 (d, $^2J_{PH} = 14.9$ Hz, 1H, CHP); 3.89 (s, 5H, $C_5H^{fer}_5$); 3.86 (m, 3H, C$\underline{H}$Ph, $(CH)^{fer}_2$); 4.15 (m, 2H, $(CH)^{fer}_2$); 7.17 (d, $J = 6.8$ Hz, 1H, PhH); 7.31 (t, $J = 6.8$ Hz, 2H, PhH); 7.43 (d, $J = 6.8$ Hz, 2H, PhH).

*N-((R)-α-methylbenzyl)-amino(4-pyridyl)methyl Phosphonic Acid* **4e**.

*Predominant diastereoisomer:* Calcd for $C_{14}H_{17}N_2O_3P$: C, 57.53; H, 5.86; N, 9.58. Found: C, 57.32; H, 6.05; N, 9.46.

$^1$H NMR (200 MHz, $D_2O$): δ 1.20 (d, $J = 6.3$ Hz, CHC$\underline{H}_3$, 3H); 3.74 (q, $J = 6.3$ Hz, C$\underline{H}$CH$_3$, 1H); 3.56 (d, $^2J_{PH} = 19.5$ Hz, CHP, 1H); 7.01 (m, PhH, 3H); 7.18 (m, PhH, 2H); 8.00 and 8.22 (2d as the $A_2B_2$ system, $J = 5.5$ Hz, Hα and Hβ, 2 × 2H).

*Minor diastereoisomer*: $^1$H NMR (200 MHz, $D_2O$): $\delta$ 1.15 (d, $J = 6.9$ Hz, CH$\underline{CH}_3$, 3H); 3.38 (q, $J = 6.9$ Hz, $\underline{CH}CH_3$, 1H); 3.32 (d, $^2J_{PH} = 19.4$ Hz, CHP, 1H); 7.01 (m, PhH, 3H); 7.18 (m, PhH, 2H); 8.00 and 8.22 (2d as the $A_2B_2$ system, $J = 5.5$ Hz, H$\alpha$ and H$\beta$, 2 × 2H).

*N-((R)-α-methylbenzyl)-amino(cyclohexyl)methyl Phosphonic Acid* **4f**.

*Predominant diastereoisomer:* Calcd for $C_{15}H_{24}NO_3P$: C, 60.59; H, 8.14; N, 4.71. Found: C, 60.28; H, 8.01; N, 4.60.

$^1$H NMR (200 MHz, $D_2O$): $\delta$ 0.91 (m, $CH_2^{chex}$, 6H); 1.19 (d, $J = 6.6$ Hz, CH$\underline{CH}_3$, 3H); 1.38 (m, $CH_2^{chex}$ and $CH^{chex}$, 5H); 2.06 (dd, $^2J_{PH} = 15.9$ Hz and $^3J_{HH} = 2.7$ Hz, CHP, 1H); 4.10 (q, $J = 6.3$ Hz, $\underline{CH}CH_3$, 1H); 7.11–7.32 (m, PhH, 5H).

*Minor diastereoisomer*: $^1$H NMR (200 MHz, $D_2O$): $\delta$ 0.91 (m, $CH_2^{chex}$, 6H); 1.19 (d, J = 6.6 Hz, CH$\underline{CH}_3$, 3H); 1.38 (m, $CH_2^{chex}$ and $CH^{chex}$, 5H); 2.15 (dd, $^2J_{PH} = 11.5$ Hz, and $^3J_{HH} = 3.8$ Hz, CHP, 1H); 3.95 (q, $J = 6.6$ Hz, $\underline{CH}CH_3$, 1H); 7.11–7.32 (m, PhH, 5H).

*N-(1-methoxycarbonyl-3-methylbutyl)amino(2-furyl)-methylphosphonic Acid* **5b**.

*Predominant diastereoisomer:* Calcd for $C_{12}H_{20}NO_6P.H_2O$: C, 44.58; H, 6.86; N, 4.33. Found: C, 44.51; H, 7.11; N, 4.12.

$^1$H NMR (200 MHz, $D_2O$): $\delta$ 0.76 and 0.79 (2d, $J = 6.0$ Hz, CH($\underline{CH}_3$)$_2$, 6H); 1.34 (dd, $J = 6.2$ and 6.7 Hz, CH$\underline{CH}_2$, 2H); 1.40 (m, $\underline{CH}CH_2$, 1H); 2.89 (t, $J = 6.2$ Hz, $\underline{CH}$COOMe, 1H); 3.24 (s, $OCH_3$, 3H); 3.75 (d, $^2J_{PH} = 18.6$ Hz, CHP, 1H); 6.14 (t, $J = 2.6$ Hz, $CH^3_{fur}$, 1H); 6.27 (dd, $J = 2.6$ and 2.3 Hz, $CH^4_{fur}$, 1H); 7.33 (m, $CH^5_{fur}$, 1H).

*Minor diastereoisomer*: $^1$H NMR (200 MHz, $D_2O$): $\delta$ 0.95 (d, $J = 6.8$ Hz, CH($\underline{CH}_3$)$_2$, 6H); 1.15 (dd, $J = 6.2$ and 6.7 Hz, CH$\underline{CH}_2$, 2H); 1.25 (m, $\underline{CH}CH_2$, 1H); 3.16 (s, $OCH_3$, 3H); 3.27 (t, $J = 6.2$ Hz, $\underline{CH}$COOMe, 1H); 3.81 (d, $^2J_{PH} = 18.9$ Hz, CHP, 1H); 6.06 (m, $CH^3_{fur}$, 1H); 6.26 (m, $CH^4_{fur}$, 1H); 7.29 (m, $CH^5_{fur}$, 1H).

*N-(1-methoxycarbonyl-3-methylbutyl)amino(2-thienyl)-methylphosphonic Acid* **5c**.

*Predominant diastereoisomer:* Calcd for $C_{12}H_{20}NO_5PS$: C, 44.85; H, 6.27; N, 4.36. Found: C, 44.56; H, 6.11; N, 4.13.

$^1$H NMR (200 MHz, $D_2O$): $\delta$ 0.72 and 0.74 (2d, $J = 6.2$ Hz, CH($\underline{CH}_3$)$_2$, 6H); 1.34 (dd, $J = 5.6$ and 7.1 Hz, CH$\underline{CH}_2$, 2H); 1.41 (m, $\underline{CH}CH_2$, 1H); 2.93 (t, $J = 7.1$ Hz, $\underline{CH}$COOMe, 1H); 3.25 (s, $OCH_3$, 3H); 4.06 (d, $^2J_{PH} = 18.0$ Hz, CHP, 1H); 6.91 (m, $CH^3_{thioph}$, $CH^4_{thioph}$, 2H); 7.22 (m, $CH^5_{thioph}$, 1H).

*Minor diastereoisomer*: $^1$H NMR (200 MHz, $D_2O$): $\delta$ 0.70 and 0.80 (2d, $J = 5.6$ Hz, CH($\underline{CH}_3$)$_2$, 6H); 1.45 (dd, $J = 5.6$ and 6.6 Hz, CH$\underline{CH}_2$, 2H); 1.42 (m, $\underline{CH}CH_2$, 1H); 2.94 (t, $J = 6.6$ Hz, $\underline{CH}$COOMe, 1H); 3.25 (s, $OCH_3$, 3H); 3.89 (d, $^2J_{PH} = 17.3$ Hz, CHP, 1H); 6.89 (m, $CH^3_{thioph}$, $CH^4_{thioph}$, 2H); 7.20 (m, $CH^5_{thioph}$, 1H).

*N - (1 - methoxycarbonyl - 3 - methylbutyl)amino (ferrocenyl)-methylphosphonic Acid* **5d**.

*Exclusive diastereoisomer:* Calcd for $C_{18}H_{26}FeNO_5P$: C, 51.08; H, 6.19; N, 3.31. Found: C, 51.43; H, 6.45; N, 3.89.

$^1$H NMR (200 MHz, $D_2O$): $\delta$ 0.83 and 0.85 (2d, $J = 5.0$ Hz, CH($\underline{CH}_3$)$_2$, 6H); 1.45 (m, CH$\underline{CH}_2$, $\underline{CH}CH_2$, 3H); 3.21 (s, $OCH_3$, 3H); 3.26 (d, $^2J_{PH} = 12.5$ Hz, 1H, CHP); 3.93 (m, $\underline{CH}$COOMe, 1H); 4.05 (m, 3H, $(CH)^{fer}_2$); 4.18 (m, 2H, $(CH)^{fer}_2$); 4.21 (s, 5H, $C_5H^{fer}_5$).

*N-(1-methoxycarbonyl-3-methylbutyl)amino(4-pyridyl)-methylphosphonic Acid* **5e**.

*Predominant diastereoisomer:* Calcd for $C_{13}H_{21}N_2O_5P$: C, 49.37; H, 6.69; N, 8.86. Found: C, 48.89; H, 6.91; N, 8.63.

$^1$H NMR (200 MHz, $D_2O$): $\delta$ 0.67 and 0.69 (2d, $J = 4.2$ Hz, CH($\underline{CH}_3$)$_2$, 6H); 1.28 (dd, $J = 7.3$ and 6.9 Hz, CH$\underline{CH}_2$, 2H); 1.36 (m, $\underline{CH}CH_2$, 1H); 2.93 (t, $J = 7.3$ Hz, $\underline{CH}$COOMe, 1H); 3.23 (s, $OCH_3$, 3H); 3.61 (d, $^2J_{PH} = 18.7$ Hz, CHP, 1H); 7.36 and 8.29 (2d as the AA'BB' system, $J = 4.9$ Hz, H$\alpha$ and H$\beta$, 2 × 2H).

*Minor diastereoisomer*: $^1$H NMR (200 MHz, $D_2O$): $\delta$ 0.67 and 0.69 (2d, $J = 4.2$ Hz, CH($\underline{CH}_3$)$_2$, 6H); 1.28 (dd, $J = 7.3$ and 6.9 Hz, CH$\underline{CH}_2$, 2H); 1.36 (m, $\underline{CH}CH_2$, 1H); 2.93 (t, $J = 7.3$ Hz, $\underline{CH}$COOMe, 1H); 3.23 (s, $OCH_3$, 3H); 3.78 (d, $^2J_{PH} = 18.0$ Hz, CHP, 1H); 7.36 and 8.26 (2d as the AA'BB' system, $J = 4.9$ Hz, H$\alpha$ and H$\beta$, 2 × 2H).

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