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Addition of Di(trimethylsilyl) Phosphite to Schiff Bases of 2,5-Diformylfuran

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Abstract: A series of 2,5-Furanyl-bis-(aminomethylphosphonic Acids) has been synthesized by the addition of di(trimethylsilyl) phosphite to azomethine bond of achiral Schiff bases derved from 2,5-diformylfuran. The stereochemical aspect of this reaction has been studied and compared with the behaviour of achiral terephthalic Schiff bases in similar reaction. Whereas, addition to achiral terephthalic Schiff bases was found to be highly stereoselective, the analogous reaction with achiral 2,5-diformylfuran Schiff bases was stereoselective exclusively in the case when the substituent is benzyl.

Keywords: 2,5-diformylfuran Schiff bases, di(trimethylsilyl) phosphite, addition, azomethine bond.

Introduction

Addition of phosphorus nucleophiles to azomethine bond of terephthalic and isophthalic Schiff bases has been rather profoundly studied for past 20 years. It has been demonstrated that this additions to achiral imines is, in a majority of cases diastereoselective and, what is of great importance, a large number of additions occurred in a 100% diastereoselectivity.
For example, the addition of hypophosphorous acid to achiral *N*-alkyl terephthalic and isophthalic imines has been reported[1,2] to be diastereoselective to 100% and lead to a *meso*-form, whereas the reaction performed on *N*-aryl imines has been noted to depend on the nature of a substituent to an aromatic ring.[2] Similar results have been reported for the addition of dialkyl phosphites to achiral *N*-alkyl and *N*-aryl terephthalic and isophthalic Schiff bases[1,3–8].

The addition of di-(trimethylsilyl)-phosphite to *N*,*N*-terephthalylidene-alkyl-(or aryl-) amines resulted in the exclusive formation of only one diastereomeric form of 1,4-phenylene-bis-(*N*-alkylaminomethyl)-phosphonic acids[9]. The investigation of products identified this diastereomeric form as the pair of enantiomers.
These 1,4-phenylene and 1,3-phenylene-bis-(*N*-alkylaminomethyl)-phosphonic derivatives have been found to have coordination abilities toward Cu(II) ions[10] or diaminophosphonate peptide receptor for lysine and arginine[11]. So, investigations of these compounds and their synthesis deal with not only their mechanism but also their applications.

It is then well visible that the problem of tere- and isophthalic derivatives has been largely explored. Contrary to this, their heteroaromatic isosteres, such as, for example derivatives of 2,5-diformylfuran have not been investigated yet; the stereochemistry of addition of phosphorus nucleophiles to 2,5-diformylfuran Schiff bases still reamin unexplored.

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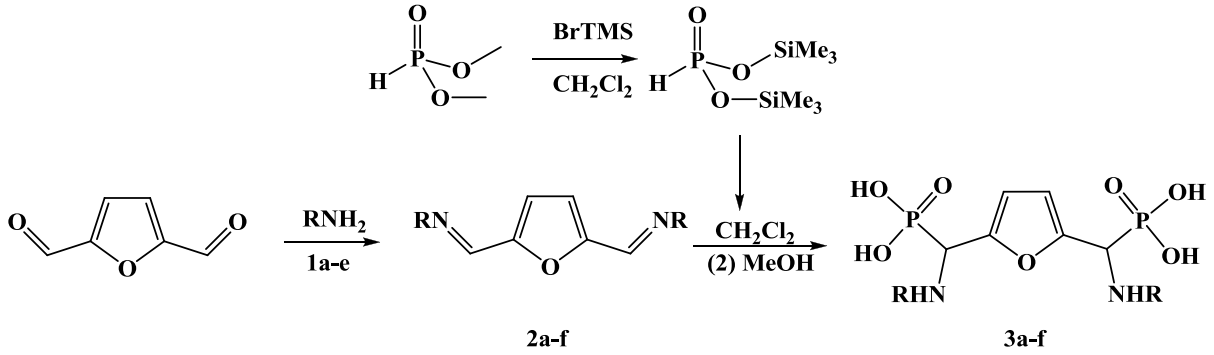
That is why, we performed the addition of di-(trimethylsilyl)-phosphite to variously *N*-substituted 2,5-diformylfuran Schiff bases adopting Boduszek's methodology[12] to our case. To our knowledge, it is the first example of the preparation of 2,5-furanyl-bis-(*N*-alkyl (or aryl) aminomethyl)-phosphonic acids *via* the addition of di(trimethylsilyl)phosphite to the azomethine bond of terephthalic Schiff bases.

Results and Discussion

We have chosen several model amines **1a–f** and prepared their imines **2a–f** with 2,5-diformylfuran. 2,5-Diformylfuran was prepared from furfural by the published procedure[13], *e.g.* lithiation in position '5' of protected furfural followed by the addition action of DMF. Imines **2a–f** were prepared following the modification of commonly known procedure by the condensation of corresponding amines **1a–e** with 2,5-diformylfuran in methanol at room temperature. Schiff bases **2a–f** were obtained in almost quantitative yields (Scheme 1).



a: R = CH_2Ph, b: R = CH_2Furh, c: R = $C(CH_3)_3$, d: R = 4-CH_3O-C_6H_4, e: R = 4-CH_3-C_6H_4, f: R = $CH(CH_3)Ph$

Scheme 1

2,5-Furanyl-bis-(*N*-alkylaminomethyl)-phosphonic acids **3a–f** were prepared using the Boduszek's method[12]. Dimethyl phosphite was reacted with bromotrimethylsilane in dry dichloromethane. In situ formed di(trimethylsilyl) phosphite then was reacted with 2,5-diformylfuran Schiff bases **2a–f** in dry dichloromethane, and in the end the reaction was stopped by methanolysis (Scheme 1). Acids **3a–f** were obtained as powder solids with moderate yields approximately 65%, which was expected, as results of terephthalic derivatives[1-9] suggested much lower conversion rate for addition to two azomethine groups. Acids **3a–f** were purified by dissolution in 10% aqueous NaOH followed by precipitation by acidification with 1 M HCl, they crystallized as hydrates and gave appropriate results of spectroscopic and elemental analysis. The exception was the *N*-*tert*-butyl derivative, which crystallized as a hydrochloride.

Table 1. Results for the addition of di(trimethylsilyl) phosphite to 2,5-diformylfuran Schiff bases

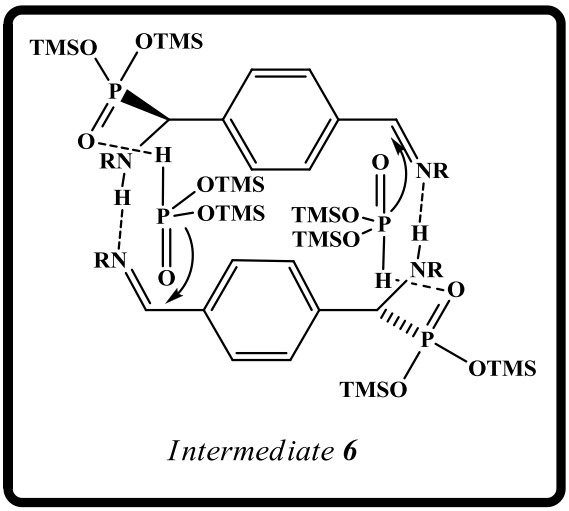
Compd no.	R	Diastereoisomeric ratio (de)	^{31}P NMR
3a	CH_2Ph	30 : 1 (94%)	14.71 and 13.37 (in NaOD/ D_2O)
3b	CH_2Fur	6 : 5 (14%)	6.23 and 6.20 (in D_2O)
3c	$C(CH_3)_3$	2 : 3 (20%)	18.38 and 18.27 (in DMSO-D_6)
3d	*p*-$CH_3OC_6H_4$	10 : 9 (5%)	15.42 and 15.18 (in NaOD/ D_2O)
3e	*p*-$CH_3C_6H_4$	5 : 4 (11%)[a]	14.51 (two overlapping) (in NaOD/ D_2O)
3f	(*R*)-$CH(CH_3)Ph$	1 : 1 : 4	15.43, 15.51 and 14.91 (in NaOD/ D_2O)

[a]Judged by the NMR experiment

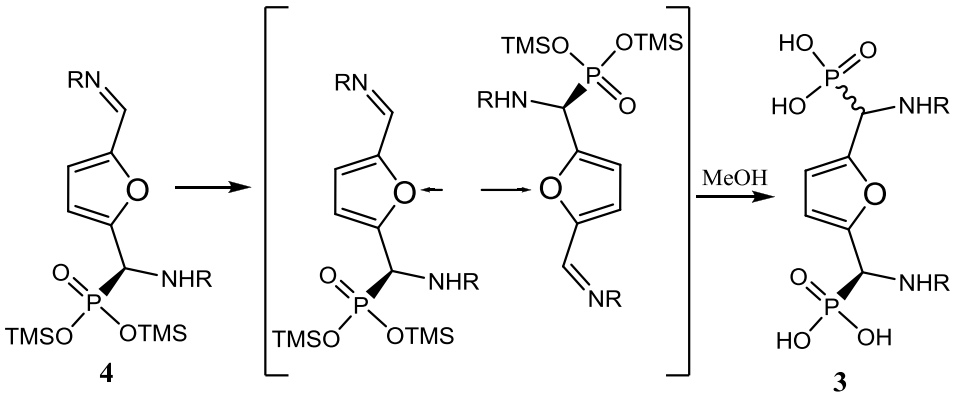
Contrary to our expectations, ^{1}H and ^{31}P NMR spectra demonstrated that 2,5-diformylfuran Schiff bases, in reactions with di(trimethylsilyl) phosphite did not demonstrate the same phenomenon as it was noticed in a case of terephthalic imines[9]. The only case, where the significant stereoselectivity has been observed was the addition of di(trimethylsilyl) phosphite to 2,5-furanyl-bis-*N*-methylenebenzylamine **2a**, as the diastereoisomeric ratio reached 30:1 (de = 94%). The rest of studied cases, although demonstrated diastereoselectivity to some extent, this extent was extremely limited. As it is visible in the table 1, the de values oscillated between 5 to 20%.

These results seem to be surprising a bit in the light of results obtained for similar additions to terephthalic Schiff bases and the question arises, why such an important difference between behaviour of terephthalic and 2,5-furanyl Schiff bases occurred. In our opinion, it may be caused by the nature of the furan ring, which gathers simultaneously properties of a heteroaromatic ring and cyclic ether. We have proposed previously the explanation of the diastereoselectivity for addition of di(trimethylsilyl) phosphite to terephthalic Schiff bases considering that Barycki *et al.*[1] suggested the two-step mechanism of this-type reaction, the addition of a nucleophile to the first azomethine bond and then to the other. In a case of terephthalic derivatives, we suggested that two imino-aminophosphonate molecules form a dimeric "*intermediate* **6**", inside which the co-ordination of di(trimethylsilyl) phosphite molecules occurs, which forces the attack from the defined side leading to the *unlike* form of 1,4-phenylene-bis-(aminomethylphosphonic acids)[9]. (*Scheme 2*) In a case of 2,5-furanyl-bis-(aminomethylphosphonic acids) **3b–e**, the formation of the dimer similar to "*intermediate* **6**" from imino-aminophosphonate derivative **4b-e** may not occur due to repulsion of ring oxygens. (*Scheme 2*).

The ^{1}H NMR spectrum of 2,5-furanyl-bis-N-(p-methylphenylaminomethylphosphonic acid **3e** demonstrated the formation of both diastereoisomeric forms in a *dr* = 10:9. Nevertheless, its ^{31}P NMR spectrum showed one signal and therefore in order to confirm the matter, the chiral salt of **3e** with (*R*)-α-methylbenzylamine was prepared in an NMR tube and the ^{31}P NMR spectrum was recorded.



Intermediate ***6***

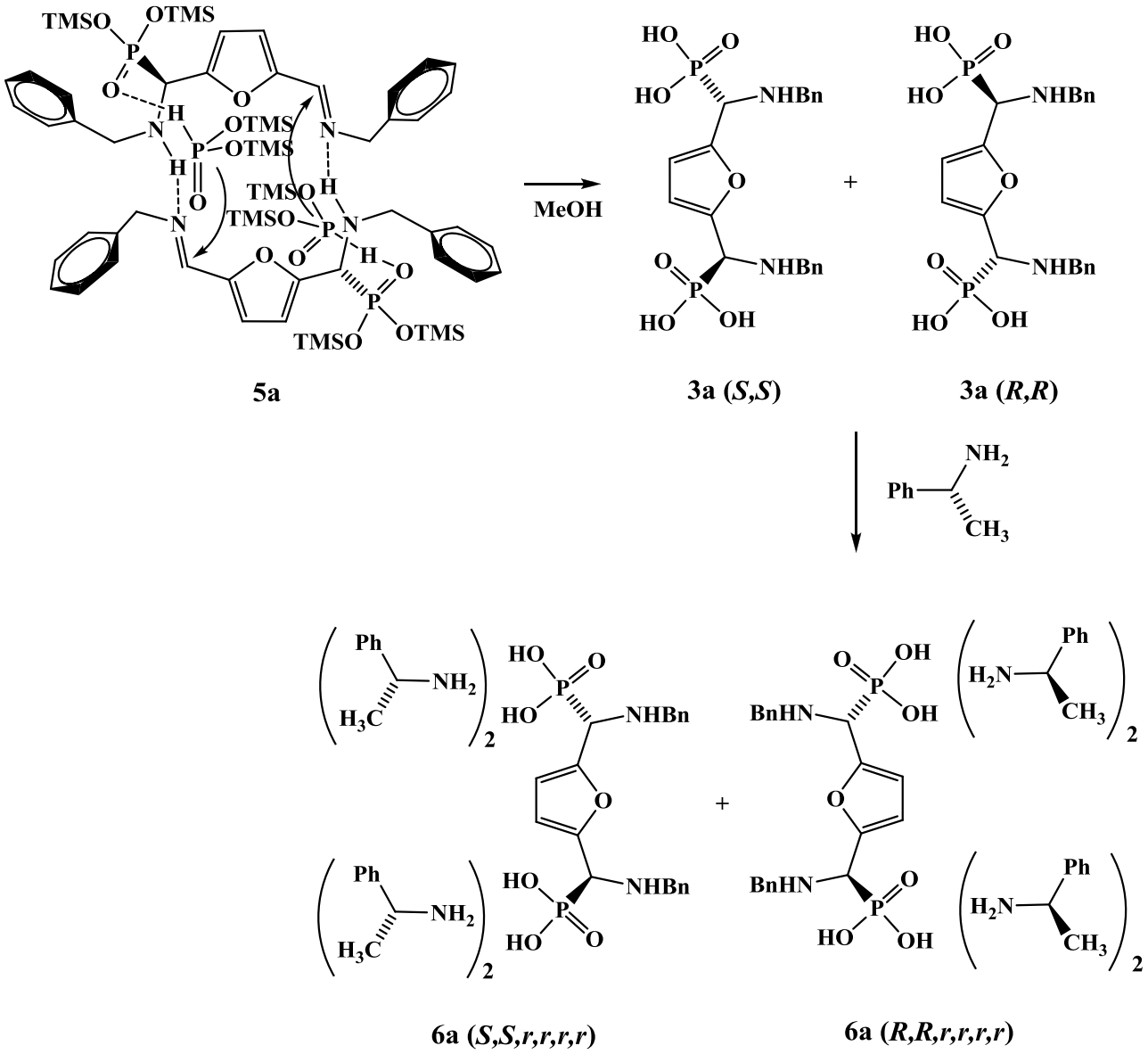


Scheme 2

We considered that the salt of both diastereomeric forms should give at least three ^{31}P NMR signals and indeed it did. The chiral salt of **3e** gave two equal signals, very closely positioned at 11.71 and 11.65 ppm (operating at 81 MHz) and the third at 11.24 ppm. First two signals represented a salt of a racemate and the third – a salt of a *unlike* form. Their ratio is like 5:5:9, so racemate to a *unlike* form is 10:9.

However, the addition of di(trimethylsilyl) phosphite to 2,5-bis-(N-benzylazomethine)-furan (**2a**) turned out to be highly diastereoselective as *dr* was 30:1 (de= 94%). The question therefore appeared why the *N*-benzyl-substituted derivative behaved in a different way. The answer might be the possibility of formation of the dimer **5a** from imino-aminophosphonate derivative **4a**, inside which the coordination of di(trimethylsilyl) phosphite molecules occurs, which attacks from the defined sides leading to two enantiomers of a di(aminophosphonic) acid **3** (*Scheme 3*).

The following experiment was performed in order to establish with a large probability, which diastereomeric form of acid **3a** occurred as a major product (*Scheme 3*). 2,5-Furanyl-bis-N-benzylaminomethylphosphonic acid (**3a**) was dissolved in acetone, and the stoichiometric amount of (*R*)-α-methylbenzylamine was added to form the ammonium salt of the phosphonic acid (**6a**). Our reasoning was as follows: if a racemate occurred as a major product, the salt of major product should give two, highest ^{31}P NMR signal and two, the highest sets of key signals in a ^{1}H NMR spectrum. Simultaneously, minor diastereomeric form being the *unlike* form, should give one, smaller ^{31}P NMR signal and one set of smaller key signals in a ^{1}H NMR spectrum. In a case, when the *unlike* form is predominant, the opposite distribution of NMR signals was expected.



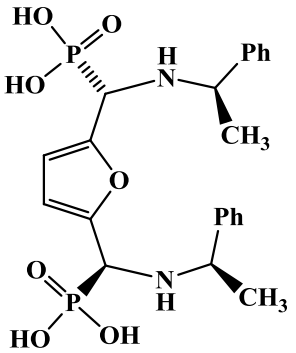
5a 3a (*S*,*S*) 3a (*R*,*R*)

Scheme 3

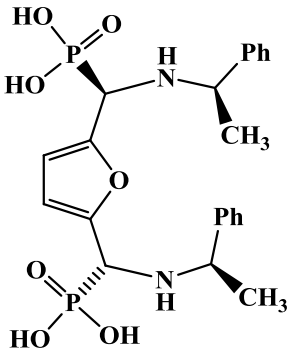
After mixing 2,5-furanyl-bis-N-benzylaminomethylphosphonic acid (**3a**) with the stoichiometric amount of (*R*)-*α*-methylbenzylamine in acetone, the formed salt **6a** precipitated. The recorded NMR spectra of the salt **6a** demonstrated visibly that the precipitate is the salt of one diastereoisomeric form and that the predominant diastereoisomeric form is the racemate, as the ^{31}P NMR spectrum showed two equal signals and ^{1}H NMR spectrum – two sets of signals. (*Scheme 3*).

Since the addition of bis(trimethylsilyl) phosphite to chiral (*R*)-*N*-*α*-methylbenzyl Schiff bases is diastereoselective[14], we performed analogous addition to the bifunctional *N*-(*R*)-*α*-methylbenzyl Schiff base **2f** derived from 2,5-diformylfuran. Using those Schiff bases, we expected to obtain exclusively the (*R*,*S*,*S*,*R*) diastereoisomer of **3f**, but in practice a mixture of all three possible diastereoisomers of 2,5-furanyl-bis-*N*-((R)-α-methylbenzylaminomethyl-

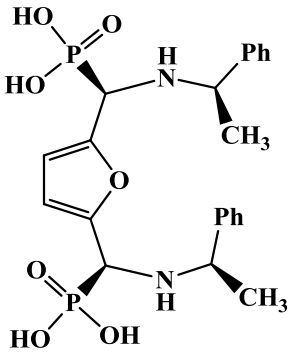
phosphonic acid) exhibited a 1:1:4 ratio for (*R,S,S,R*), (*R,R,R,R*) and (*R,S,R,R=R,S,R,R*) diastereoisomers of **3f**.



3f (*R,S,S,R*)



3f (*R,R,R,R*)



3f (*R,S,R,R=R,S,R,R*)

Scheme 4

These findings indicate to two possibilities. First of them demonstrate that the influence of the chiral substituent attached to nitrogen is competing with the phenomenon observed for the *N*-benzyl derivative **3a**, determining the stereochemistry for additions of bis(trimethylsilyl) phosphite to *N*-benzyl-2,5-diformylfuran Schiff bases. So, the discussed system is subjected to the influence of two counteracting factors controlling the stereochemistry: first is the action of the chiral centers at the nitrogen atoms; the second entails the same factor, which controls the stereochemistry of phosphite addition to achiral imines as it was described previously for terephthalic systems[6].

The second hypothesis says that the factor determining the stereochemistry in addition to the second azomethine group of imino-aminophosphonates is negative as in cases **3b-e**, therefore, in a case of 2,5-furanyl-bis-*N*-((*R*)-α-methylbenzylamino-methylphosphonic acid) **3f** the only driving force of the steroselectivity is the influence of a chiral *N*-(*R*)-α-methylbenzyl substituent. That is why diastereoselectivity is relatively low as it was proven for mono furyl derivatives in our previous study[14]. Intriguing stereochemical problems will encourage forthcoming studies.

Conclusion

In conclusion, we have found that addition of di(trimethylsilyl) phosphite to azomethine bonds of 2,5-furandicarboxaldehyde Schiff bases is not diastereoselective in most studied cases, except the addition to 2,5-bis-(*N*-benzylazomethine)-furan (**2a**), which caused the formation of the resulting 2,5-furanyl-bis-(*N*-benzylaminomethylphosphonic acid (**3a**) in 94% de. The lack of diastereoselectivity in case of additions to imines **2b-2e** is surprising considering that similar additions to terephthalic and isophthalic Schiff bases was found to be highly diastereoselective in majority of cases. Even more astonishing is the fact that additions to imines **2b-2e** are practically not diastereoselective while addition to *N*-benzyl Schiff base **2a** is stereoselective to a high degree. For this day, we are not able to give the hard proof why it happens so, but we suggest that the formation of a racemic mixture in a great majority would be cause by the formation of a hypothetical dimer **5a**. But the problem is still under study.

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Experimental

General

All solvents (POCh, Poland) were routinely distilled and dried prior to use. 2,5-Diformylfuran was prepared from furfural by the published procedure[13]. Amines, dimethyl phosphite, bromotrimethylsilane, and furfural (Aldrich) were used as received. NMR spectra were recorded on a Varian Gemini 200 BB apparatus operating at 200 MHz (^{1}H NMR) and 81 MHz (^{31}P NMR) or on a Bruker Avance III 600 MHz operating at 600 MHz (^{1}H NMR) and 243 MHz (^{31}P NMR). Elemental analyses were carried out at the Centre for Molecular and Macromolecular Science of the Polish Academy of Science in Łódź, Poland.

2,5- bis-(*N*-alkyl(–aryl)azomethine)-furans (2a-f). General procedure

2,5-Diformylfuran (0.25 g, 2 mmol) was dissolved in methanol (20 mL) and then the corresponding amine (4 mmol) was added. The mixture was stirred overnight, and the precipitated solid was then collected by filtration, dried, and recrystallized to obtain the desired Schiff bases.

2,5-bis-(*N*-benzylazomethine)-furan (2a). Yield = 57% (0.34 g); mp: 115–116°C (hexane : dichloromethane, 4:1), lit[15] 110-111°C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.25 (s, CH=N, 2H); 7,39-7.36 (m, PhH, 4H); 7.34-7.28 (m, PhH, 6H); 6.94 (s, =CH-CH=, 2H); 4.84 (s, CH_2Ph, 4H).

2,5-bis-(*N*-furfurylazomethine)-furan (2b). Yield = 78% (0.44 g); mp: 156–159°C (hexane : dichloromethane, 4:1), lit[16] 158°C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.18 (s, CH=N, 2H); 7.41 (dd, $^3J_{HH}$ = 1.8 and $^4J_{HH}$ = 0.6 Hz, H_5^{fur}, 2H); 6.94 (s, =CH-CH=, 2H); 6.37 (dd, $^3J_{HH}$ = 1.8 and 3.6 Hz, H_4^{fur}, 2H); 6.30 (dd, $^3J_{HH}$ = 3.6 and $^4J_{HH}$ = 0.6 Hz, H_5^{fur}, 2H); 4.80 (s, CH_2Fur, 4H).

2,5-bis-(*N*-tert-butylazomethine)-furan (2c). Yield = 79% (0.37 g). ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.15 (s, CH=N, 2H); 6.83 (s, =CH-CH=, 2H); 1.28 (s, $C(CH_3)_3$, 18H).
Elemental analysis: Calcd for $C_{14}H_{22}N_2O\bullet{}^1/_2CH_3OH$: C, 69.56; H, 9.66; N, 11.19. Found: C, 69.48; H, 9.75; N, 10.95.

2,5-bis-(*N*-*p*-methoxyphenylazomethine)-furan (2d). Yield = 87% (0.57 g); mp: 179–180°C (hexane : dichloromethane, 4:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.47 (s, CH=N, 2H); 7.32 (AA'XX' system, $^3J_{HH}$ = 9.0 and $^4J_{HH}$ = 3.6 and 2.4 Hz, *p*-C_6H_4, 4H); 7.14 (s, =CH-CH=, 2H); 6.97 (AA'XX' system, $^3J_{HH}$ = 9.0 and $^4J_{HH}$ = 3.6 and 2.4 Hz, *p*-C_6H_4, 4H); 3.87 (s, OCH_3, 6H).
Elemental analysis: Calcd for $C_{20}H_{18}N_2O_3\bullet{}^1/_3CH_3OH$: C, 70.78; H, 5.65; N, 8.12. Found: C, 70.81; H, 5.86; N, 7.90.

2,5-bis-(*N*-*p*-methylphenylazomethine)-furan (2e). Yield = 77% (0.48 g); mp: 175–176°C (hexane : dichloromethane, 4:1), lit[15] 170-171°C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.47 (s,

CH=N, 2H); 7.24 and 7.22 (AA'BB' system, $^3J_{HH}$ = 9.0 Hz, *p*-C_6H_4, 8H); 7.16 (s, =CH-CH=, 2H); 2.41 (s, CH_3, 6H).
Elemental analysis: Calcd for $C_{20}H_{18}N_2O\bullet{}^3/_4CH_3OH$: C, 76.35; H, 6.48; N, 8.58. Found: C, 76.15; H, 6.42; N, 8.78.

2,5-bis-(*N-(R)*-α-methylbenzylazomethine)-furan (2f). Yield = 96% (0.64 g). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.19 (s, CH=N, 2H); 7.37-7.32 (m, PhH, 8H); 7.25-7.22 (m, PhH, 2H); 6.88 (s, =CH-CH=, 2H); 4.53 (q, J = 6.6 Hz, CH(CH_3)Ph, 2H); 1.61 (d, J = 6.6 Hz, CH(CH_3)Ph, 3H).
Elemental analysis: Calcd for $C_{22}H_{22}N_2O$: C, 79.97; H, 6.71; N, 8.48. Found: C, 79.71; H, 6.88; N, 8.21.

2,5-Furanyl-bis-(aminomethylphosphonic Acids) (3a–f) General Procedure.
Dimethyl phosphite (2 mmol, 0.22 g) was dissolved in dry dichloromethane, and to this solution bromotrimethylsilane (11.2 mmol, 1.71 g) was added dropwise for 15 min. The mixture was stirred for 1 h at room temperature. Then, a solution of an appropriate Schiff base (1 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. It was stirred for 30–45 min until precipitation of a solid, which was filtered off and collected. In the case, if the solid did not precipitated, 5–10 mL of propylene oxide was added and the mixture was refrigerated for 3–7 days. Then the solid was filtered off and collected. Products were purified by dissolution in 10% aqueous NaOH followed by precipitation by acidification with 1 M HCl.

2,5-furanyl-bis-(*N*-benzylaminomethylphosphonic acid) (3a). Yield = 62% (0.29 g); mp: 211–212°C. ^{1}H NMR (200 MHz, D_2O/NaOD): δ 7.17 (m, PhH, 10H); 6.15 (s, CH^{fur}, 2H); 3.68-3.17 (m, CHP, CH_2Ph, 5H). ^{31}P NMR (81 MHz, D_2O/NaOD): δ 14.71 and 14.37 (30:1).
Elemental analysis: Calcd for $C_{20}H_{24}N_2O_7P_2\bullet 2H_2O$: C, 48.65; H, 6.22; N, 5.40. Found: C, 48.85; H, 6.35; N, 5.34.

2,5-furanyl-bis-(*N*-furfurylaminomethylphosphonic acid) (3b). Yield = 33% (0.15 g); mp: 194–196°C. ^{1}H NMR (200 MHz, D_2O): δ 7.59 (m, $H^5{}_{fur}$, 2H); 6.76 and 6.68 (2s, CH^{fur}, 2H); 6.63 (m, $H^3{}_{fur}$, 2H); 6.50 (m, $H^4{}_{fur}$, 2H); 4.60 and 4.53 (2d, $^2J_{PH}$ = 16.8 Hz, CHP, 2H); 4.40, 4.37, 4.34 and 4.29 (4d, $^2J_{HH}$ = 14.4 Hz, CH_2Fur, 4H). ^{31}P NMR (81 MHz, D_2O): δ 6.23 and 6.20 (6:5).
Elemental analysis: Calcd for $C_{16}H_{20}N_2O_9P_2\bullet H_2O\bullet CH_3OH$: C, 41.14; H, 5.28; N, 5.64. Found: C, 41.44; H, 5.11; N, 5.14.

2,5-furanyl-bis-(*N-tert*-butylaminomethylphosphonic acid) (3c). Yield = 47% (0.19 g); mp: 212–213°C. ^{1}H NMR (200 MHz, NaOD/D_2O): δ 6.12 and 6.11 (2s, =CH-CH=, 2x2H); 3.93 and 3.81 (2d, $^2J_{PH}$ = 21.2 Hz, CHP, 2x1 H); 0.95 (s, $C(CH_3)_3$, 18H). ^{31}P NMR (81 MHz, NaOD/D_2O): δ 18.38 and 18.27 (2:3).
Elemental analysis: Calcd for $C_{14}H_{28}N_2O_7P_2\bullet HCl$: C, 38.67; H, 6.72; N, 6.44. Found: C, 38.79; H, 6.58; N, 6.11.

2,5-furanyl-bis-(*N*-(*p*-methoxyphenylaminomethylphosphonic acid) (3d). Yield = 84% (0.42 g); mp: 166–167°C. ^{1}H NMR (600 MHz, DMSO-D_6): δ 6.65 (m, *p*-C_6H_4, 8H); 6.22 and

6.28 (s, CH^{fur}, 2x2H); 4.57 and 4.56 (2d, $^2J_{PH}$ = 22.2 Hz, CHP, 2H); 3.64 and 3.63 (2s, OCH_3, 6H). ^{31}P NMR (243 MHz, DMSO-D_6): δ 15.42 and 15.18 (10:9).
Elemental analysis: Calcd for $C_{20}H_{24}N_2O_9P_2 \bullet 2H_2O$: C, 44.95; H, 5.28; N, 5.24. Found: C, 44.81; H, 5.45; N, 5.02.

2,5-furanyl-bis-(*N*-(*p*-methylphenylaminomethylphosphonic acid) (3e). Yield = 68% (0.32 g); mp: 162–163°C. ^1H NMR (200 MHz, NaOD/D_2O): δ 6.86 and 6.49 (2d, J = 9.0 Hz, *p*-C_6H_4, 8H); 6.78 and 6.44 (2d, J = 8.4 Hz, *p*-C_6H_4, 8H); 5.97 (large s, CH^{fur}, 2x2H); 4.32 and 4.29 (2d, $^2J_{PH}$ = 20.0 and 20.4 Hz, CHP, 2H); 2.11 (s, CH_3, 6H). ^{31}P NMR (81 MHz, NaOD/D_2O): δ 14.51.
Elemental analysis: Calcd for $C_{20}H_{24}N_2O_7P_2 \bullet {}^3/_2H_2O$: C, 49.51; H, 6.13; N, 5.50. Found: C, 49.95; H, 5.94; N, 5.56.

2,5-furanyl-bis-*N*-((*R*)-α-methylbenzylaminomethylphosphonic acid) (3f). Yield = 39% (0.39 g); mp: 189–190°C. ^1H NMR (200 MHz, D_2O/NaOD): δ 7.31-7.07 (m, PhH, 10H); 5.98 and 5.85 (2s, CH^{fur}, 2x2H); 3.67 and 3.52 (2q, J = 6.6 Hz, $\underline{CH}(CH_3)$Ph, 2H); 3.39 and 3.25 (2d, $^2J_{PH}$ = 18.4 Hz, CHP, 2x1H); 1.19 and 1.10 (2d, J = 6.6 Hz, CH($\underline{CH_3}$)Ph, 2x3H). ^{31}P NMR (81 MHz, D_2O/NaOD): δ 15.43, 15.52 and 14.91 (1:1:4).
Elemental analysis: Calcd for $C_{22}H_{28}N_2O_7P_2 \bullet {}^5/_2H_2O$: C, 48.98; H, 6.17; N, 5.19. Found: C, 48.65; H, 6.04; N, 5.59.

2,5-furanyl-bis-(*N*-benzylaminomethylphosphonic acid) (R)-α-methylbenzylamine salt (6a).
2,5-furanyl-bis-(N-benzylaminomethylphosphonic acid) (**3a**) (0.04 g, 0.0858 mmol) was dissolved in acetone, and (*R*)-*α*-methylbenzylamine (0.04 g, 0.3432 mmol) was added during vigorous stirring. The mixture was stirred at room temperature for 24 h; the precipitated solid was filtered off, dried, and carried out NMR study.
Yield = 61% (0.05 g); mp: 203-205°C. ^1H NMR (200 MHz, D_2O): δ 7.46-7.44 (m, PhH, 10H); 6.74 and 6.60 (2s, CH^{fur}, 2x2H); 4.54 and 4.45 (2d, $^2J_{PH}$ = 17.8 Hz, CHP, 2x1H); 4.28 (q, J = 6.6 Hz, $\underline{CH}(CH_3)$Ph, 4H); 1.61 (d, J = 6.6 Hz, CH($\underline{CH_3}$)Ph, 4x3H). ^{31}P NMR (243 MHz, D_2O): δ 6.26 and 6.21 (1:1).

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