Iranian Journal of Organic Chemistry Vol. 6, No. 3 (2014) 1305-1308

Quinoline catalyzed efficient synthesis of diaryl anilinocarbonyl phosphonate derivatives

Anvar Mirzaei*

Department of Chemistry, Faculty of Science, Sanandaj Branch, Islamic Azad University, Sanandaj, Iran.

Received: June 2014; Revised: June 2014; Accepted: July 2014

Abstract: The reaction of aryl isocyanates , diphenylphosphite in the presence of quinoline as efficient catalyst leads to diaryl anilinocarbonyl phosphonate derivatives in 94-96% yields.

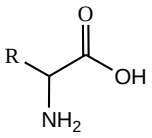
Keywords: Aryl isocyanates, Diphenylphosphite, Quinoline, α-Aminophosphonates.

Introduction

Due to obvious structural similarities of α-Aminophosphonates to α -amino acids **1** and α-aminophosphonic acids **2** (Figure **1**), they are important motifs in medicinal chemistry [1]. Many natural and unnatural aminophosphonic acids and their ester display a wide range of biological activities [2]. A considerable part of the biological activity of these compounds arises from the ability of the tetrahedral phosphonic moiety to mimic the tetrahedral intermediate of reactions involving nucleophilic substitution on the carbonyl [3]. Therefore they serve as inhibitors of enzymes such as proteases and peptide ligases. As such, aminophosphonic acids are known to act as peptide mimics [4], herbicides [5], enzyme inhibitors [6], and pharmacological [7], antibacterial [8], antiviral [9], and antitumor agents [10].

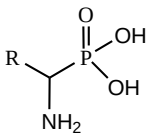
The most common route to α-aminophosphonic acids **2** is *via* chemical manipulation of the corresponding α-aminophosphonates **3** [11] (Scheme **1**). As such, α-aminophosphonates have become key targets in the synthesis of this compound class.

A number of synthetic methods for α-aminophosphonates have been developed. Of these, the nucleophilic addition of phosphites to imines, catalyzed by a base or an acid, is the most convenient. However, reactions cannot be carried out in a one-pot operation because the amine and water present during imine formation can decompose or deactivate the Lewis acid in other hand most Lewis acids are expensive [12-17].



1

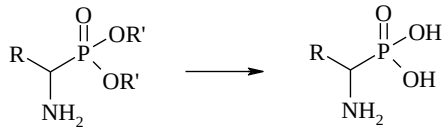
alpha-amino acid



2

alpha-aminophosphonic acid

Figure 1: Similarities between α-aminophosphonic acids and α-amino acids.



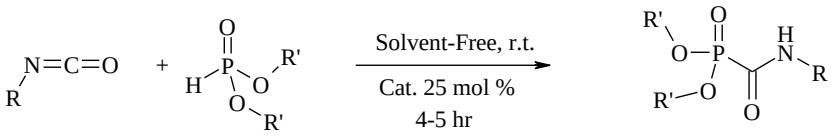
3 **2**

R'= Alkyl, Aryl

Scheme 1: α-Aminophosphonic acids from α-aminophosphonates.

*Corresponding author. Tel: (+98) 87 33288661, Fax: (+98) 87 33247713, E-mail: mirzaei.anvar@gmail.com

As part of our group current studies on the synthesis of phosphonates, and α aminophosphonates [18-20], Herein we report the results of our studies involving the reactions of Isocyanates (**1**) and Diphenylphosphite (**2**) in the presence of quinoline as efficient catalyst which constitute a synthesis of diaryl anilinocarbonyl phosphonate derivatives (**3**) (Scheme **2**).



1	R
a	Ph
b	4-Me-C_6H_4
c	4-Cl-C_6H_4
d	4-Br-C_6H_4
e	n-Bu

2	R'
a	Ph
b	Et

3	R	R'	Yield % of **3**
a	Ph	Ph	95
b	4-Me-C_6H_4	Ph	94
c	4-Cl-C_6H_4	Ph	96
d	4-Br-C_6H_4	Ph	93
e	n-Bu	Ph	0
f	Ph	Et	0

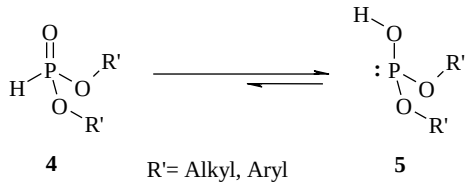
Scheme 2: Synthesis of diaryl anilinocarbonyl phosphonate derivatives.

Results and discussion

The structures of compounds **3a-3d** were deduced from their elemental analyses and their IR, ^{1}H NMR, ^{13}C and ^{31}P NMR spectral data. For example, the ^{1}H NMR spectrum of **3a** exhibited NH proton (δ 9.14, s) along with multiplets for the aromatic protons. The ^{1}H-decoupled ^{13}C NMR spectrum of **3a** showed 9 distinct resonances that confirms the proposed structure. The ^{1}H decoupled ^{31}P NMR spectrum of **3a** showed resonance at (δ 11.4 ppm). The IR spectrum of **3a** displayed NH, aromatic and P=O bands (3230, 1658, 1585, 1477 and 1225 cm^{-1}). The ^{1}H NMR and ^{13}C NMR spectra of **3b-3d** are similar to those for **3a** except for the aromatic moieties, which exhibited characteristic resonances in appropriate regions of the spectrum.

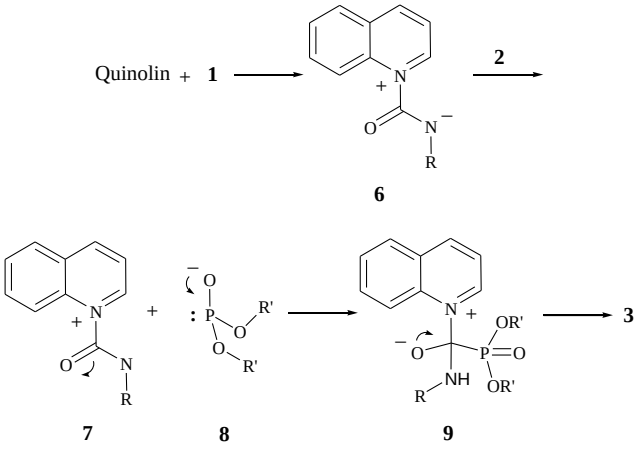
Diaryl(Alkyl) phosphites are known to exist in equilibrium between two forms, the phosphite **4** and phosphonate **5** forms with the equilibrium lying to the side of the phosphonate under neutral conditions (Scheme **3**). However, it is known that the phosphite and not the phosphonate form is the nucleophilic species [21]. It has been demonstrated that the polar solvent, presence of a base or aryl substituent can influence the balance of the equilibrium, allowing for the phosphite form to become more prevalent.

Although the mechanistic details of the reaction are not known, a plausible rationalization may be advanced to explain the product formation. Presumably, the intermediate **6** that formed from quinoline and **1**, protonated by **2** to produce **7** and **8**, reaction between this intermediates lead to **9**, then **9** could undergone elimination of quinoline to product **3** (Scheme **4**).



4 **5**

Scheme 3: Tautomeric forms of diaryl(alkyl) phosphite.



Scheme 4: Proposed mechanism for the formation of products.

Conclusion

In summary, we report a green synthesis of diaryl anilinocarbonyl phosphonate derivatives in good to excellent yields under solventless conditions. The present procedure has the advantage that, not only is

the reaction performed under solvent free conditions, but also the reactants can be mixed without any prior activation or modification. The simplicity of the present procedure makes it an interesting alternative to other approaches.

Experimental

General procedure:

All compounds were obtained from Fluka or Merck and were used without further purification. M.p.: Electrothermal-9100 apparatus. IR Spectra: Shimadzu IR-460 spectrometer. ^{1}H-, ^{13}C-, ^{31}P- NMR spectra: Bruker DRX-500 AVANCE instrument; in $CDCl_3$ at 500, 125, 200.8 MHz, respectively; δ in ppm. Elemental analyses (C, H, N) were performed with a Heraeus CHN-O-Rapid analyzer.

Typical procedure for preparation of (3):

To a stirred mixture of Isocyante **1** (2 mmol) and diaryl(alkyl) phosphite **2** (2 mmol) was added 0.064 g of quinoline (0.5 mmol) at rt. After completion of the reaction (4-5 h), the precipitate was washed with cold ether (10 mL) to afford pure title compounds.

Data:

diphenyl anilinocarbonyl phosphonate (3a):

White powder, mp 125–127 °C, 0.33 g, yield 95%. IR (KBr) (νmax/cm^{-1}): 3230 (NH), 1658, 1585, 1477, 1225, 1175, 735. Anal. Calcd for $C_{19}H_{16}NO_4P$ (353.31): C, 64.59; H, 4.56; N, 3.96. Found (%): C, 64.75; H, 4.65; N, 4.02. ^{1}HNMR: δ 7.17-7.25 (3H, m, 3 CH), 7.27-7.32 (4H, m, 4 CH), 7.34-7.38 (6H, m, 6 CH), 7.61 (2 H, ^{3}J= 5, 2 CH), 9.15 (1H, br s, NH) ppm. ^{13}C NMR: δ 120.3 (2 CH), 120.7 (4 CH, $^{3}J_{PC}$= 5Hz), 125.9 (CH), 126.0 (2 CH), 128.8 (2 CH), 129.9 (4 CH), 136.3 (C, $^{3}J_{PC}$= 8 Hz), 149.5 (2 C, $^{3}J_{PC}$= 7.5 Hz), 161.4 (C=O, $^{1}J_{PC}$= 231.3 Hz). ^{31}P NMR: 11.4.

*Diphenyl [(4-tpluidinocarbonyl] phosphonate (**3b**):*

White powder, mp 136–138 °C, 0.34 g, yield 94%. IR (KBr) (νmax/cm^{-1}): 3180 (NH), 1648, 1593, 1489, 1216, 1069, 734. Anal. Calcd for $C_{20}H_{18}NO_4P$ (367.34): C, 65.39; H, 4.94; N, 3.81. Found (%): C, 65.46; H, 4.98; N, 3.93. ^{1}HNMR: δ 2.3 (3H, s, CH_3), 7.04-7.13 (3H, m, 3 CH), 7.15-7.26 (4H, m, 4 CH), 7.30-7.37 (5H, m, 5 CH), 7.54 (2 H, ^{3}J= 6, 2 CH), 9.0 (1H, br s, NH) ppm. ^{13}C NMR: δ 20.3 (CH_3), 119.1 (2 CH), 120.4 (4 CH, $^{3}J_{PC}$= 5.8Hz), 125.6 (2 CH), 126.4 (C), 129.1 (2 CH), 129.7 (4 CH), 136.6 (C, $^{3}J_{PC}$= 6.5 Hz), 150.5 (2 C, $^{3}J_{PC}$= 8.0 Hz), 161.6 (C=O, $^{1}J_{PC}$= 237.6 Hz). ^{31}P NMR: 8.1.

*Diphenyl [(4-chloroanilino)carbonyl] phosphonate (**3c**):*

White powder, mp 145–147 °C, 0.37 g, yield 96%. IR (KBr) (νmax/cm^{-1}): 3200 (NH), 1668, 1589, 1487, 1231, 1171, 750, 733. Anal. Calcd for $C_{19}H_{15}NClO_4P$ (387.75): C, 58.85; H, 3.90; N, 3.61. Found (%): C, 59.0; H, 3.95; N, 3.72. ^{1}HNMR: δ 7.05-7.21 (6H, m, 6 CH), 7.44-7.56 (6H, m, 6 CH), 7.60 (2 H, ^{3}J= 5, 2 CH), 9.26 (1H, br s, NH) ppm. ^{13}C NMR: δ 119.9 (2 CH), 120.7 (4 CH, $^{3}J_{PC}$= 6 Hz), 125.9 (2 CH), 126.8 (C), 129.3 (2 CH), 129.5 (4 CH), 136.8 (C, $^{3}J_{PC}$= 6 Hz), 151.5 (2 C, $^{3}J_{PC}$= 9.0 Hz), 162.0 (C=O, $^{1}J_{PC}$= 234.1 Hz). ^{31}P NMR: 6.4.

*Diphenyl [(4-broanilino)carbonyl] phosphonate (**3d**):*

White powder, mp 148–150 °C, 0.40 g, yield 93%. IR (KBr) (νmax/cm^{-1}): 3205 (NH), 1674, 1600, 1499, 1240, 1177, 744, 730. Anal. Calcd for $C_{19}H_{15}NBrO_4P$ (432.20): C, 52.80; H, 3.50; N, 3.24. Found (%): C, 52.91; H, 3.64; N, 3.18. ^{1}HNMR: δ 7.00-7.17 (6H, m, 6 CH), 7.35-7.46 (6H, m, 6 CH), 7.63 (2 H, ^{3}J= 6, 2 CH), 9.14 (1H, br s, NH) ppm. ^{13}C NMR: δ 119.1 (2 CH), 121.2 (4 CH, $^{3}J_{PC}$= 5 Hz), 126.3 (2 CH), 126.7 (C), 129.6 (2 CH), 130.1 (4 CH), 134.9 (C, $^{3}J_{PC}$= 5 Hz), 151.7 (2 C, $^{3}J_{PC}$= 8.5 Hz), 162.0 (C=O, $^{1}J_{PC}$= 235.4 Hz). ^{31}P NMR: 9.2.

References

[1] Huang, J.; Chen, R. *Heteroat. Chem.*, **2000**, *11*, 480.

[2] Quin, L. in "*A Guide to Organophosphorus Chemistry*" Wiley- Interscience, New York, **2000**, pp: 351-386.

[3] Hiratake, J.; Oda, J. *Biosci., Biotechnol., Biochem.*, **1997**, *61*, 211.

[4] Kafarski, P.; Lejczak, B. *Phosphorous, Sulfur Silicon Relat. Elem.*, **1991**, *63*, 193.

[5] Xiao, L.; Li, K.; Shi, D. *Phosphorus, Sulfur Silicon Relat. Elem.*, **2008**, *183*, 3156.

[6] Allen, M.; Fuhrer, W.; Tuck, B. *J. Med. Chem.*, **1989**, *32*, 1652.

[7] Atherton, F.; Hassal, C.; Lambert, R. *J. Med. Chem.*, **1986**, *29*, 29.

[8] Pratt, R. *Science*, **1989**, *246*, 917.

[9] Huang, J.; Chen, R. *Heteroat. Chem.*, **2000**, *11*, 480.

[10] Lavielle, G.; Hautefaye, P.; Boutin, J.; Pierré, A. *J. Med. Chem.*, **1991**, *34*, 1998.

[11] Irishi, N. *Tetrahedron: Asymmetry* **2008**, *19*, 2335.

[12] Azizi, N.; Saidi, M. R. *Tetrahedron* **2003**, *59*, 5329.

[13] Xu, F.; Luo, Y. W. J.; Shen, Q.; Chen, H. *Heteroat. Chem.* **2006**, *17*, 389.

[14] Bioton, L. D.; Villemin, D.; Lohier, J. F.; Sopkova, J. *Tetrahedron* **2007**, 63, 9677.
[15] Xu, F.; Luo, Y.; Deng, M.; Shen, Q. *Eur. J. Org. Chem*. **2003**, *24*, 4728.
[16] Vanderhoydonck, B.; Stevens, C. V. *J. Org. Chem*. **2005**, *70*, 191.
[17] Atherton, F. R.; Hassal, C. H.; Lambert, R. W. *J. Med. Chem*. **1986**, *29*, 29.
[18] Yavari, I.; Mirzaei, A.; Moradi, L. *Synth. Commun.* **2010**, *40*, 2407.
[19] Yavari, I.; Mirzaei, A.; Khalili, G. *Helv. Chim. Acta* **2010**, *93*, 654.
[20] Mirzaei, A. *Iran. J. Org. Chem.* **2013**, *5*, 1085.
[21] Engl, R.; Chon, J. in "*Synthesis of Carbon-Phosphorous Bonds*" 2end Ed. CRC Press, New York, **2000**, p: 4-5.