Heteroatom Chemistry
Volume 21, Number 4, 2010

# Diastereoselective Synthesis of Chloro- and Fluoro-Aniline Containing Phosphonate Esters in a Three-Component Condensation

Malek Taher Maghsoodlou,[1] Nourallah Hazeri,[1] Sayyed Mostafa Habibi-Khorassani,[1] Ghasem Marandi,[2] Lotfali Saghatforoush,[2] Danial Saravani,[1] Niloufar Akbarzadeh Torbati,[1] Faramarz Rostami-Charati,[3] Khatereh Khandan-Barani,[1] Brian W. Skelton,[4] and Mohamed Makha[4]

[1]*Department of Chemistry, The University of Sistan & Baluchestan, P.O. Box 98135-674, Zahedan, Iran*

[2]*Department of Chemistry, Faculty of Science, Payame Noor University of Khoy, Khoy, Iran*

[3]*Gonbad Institutes of Higher Education, P.O. Box 163, Gonbad, Iran*

[4]*Chemistry School of Biomedical, Biomolecular and Chemical Science, M313, University of Western Australia, Perth, WA 6009, Australia*

*Received 4 December 2009; revised 17 March 2010*

ABSTRACT: *New phosphonate ester derivatives were obtained by in situ stereo-specific reaction between triphenyl phosphite and dialkyl acetylenedicarboxylates in the presence of a series of halogenated anilines. Spectroscopic data and X-ray crystallography analysis are in agreement with the gauche arrangement for the two vicinal protons in the structures.* © 2010 Wiley Periodicals, Inc. Heteroatom Chem 21:222–227, 2010; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20600

## *INTRODUCTION*

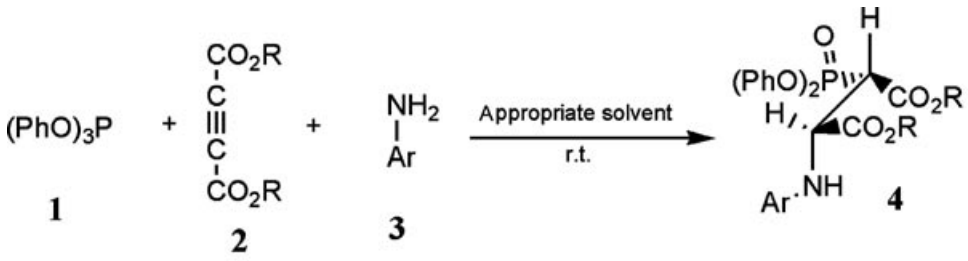
Phosphorus compounds are of great interesting compounds because of their pharmaceutical and biological activities that include antiinflammatory, cardiotonic, inotropic, antihypertensive, antimicrobial, and antibacterial properties [1–15]. We among others have reported extensive investigations of the reaction between trivalent phosphorus nucleophiles and $\alpha$-$\beta$ unsaturated carbonyl compounds in the presence of a proton source, such as CH-, NH-, OH-, or SH-compounds [16–30].

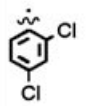
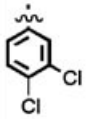
In continuation of our previous studies on the reaction between trivalent phosphorus nucleophiles and dialkyl acetylenedicarboxylates in the presence of NH-compounds [22–24,31], we successfully obtained the phosphonate ester adducts with a great control over the stereochemistry established from solution NMR studies and confirmed by single X-ray crystallography.

## *RESULTS AND DISCUSSION*

In the current work, an efficient stereoselective synthesis of phosphonate diesters is reported from the reaction between triphenyl phosphite **1** and dialkyl

*Correspondence to:* Malek Taher Maghsoodlou; e-mail: mt_maghsoodlou@yahoo.com.
Contract grant sponsor: Research Council of the University of Sistan & Baluchestan.




| 4 | R | Ar | Solvent | %Yield |
|---|---|---|---|---|
| a | Me |  | Dichloromethane | 95 |
| b | Et |  | Dichloromethane | 93 |
| c | Me |  | Dichloromethane | 90 |
| d | Me |  | Acetonitrile | 95 |
| e | Me |  | Diethyl ether | 91 |

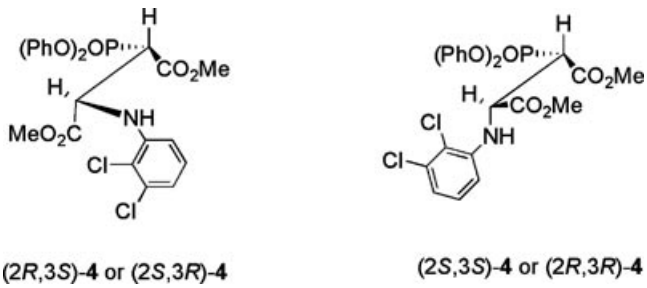
SCHEME 1

acetylenedicarboxylate **2** in the presence of NH-aromatic amines **3** (Scheme 1). These reactions proceeded smoothly at ambient temperature and are completed within 24 h in high yield. TLC and $^1$H NMR spectra of the crude products clearly indicated formation of phosphonate esters **4** (see Scheme 1).

The essential structures of the products **4a–e** were deduced from elemental analysis, IR, $^1$H, $^{13}$C, $^{31}$P NMR, and mass spectra. The mass spectra of these compounds displayed molecular ion peaks at appropriate $m/z$ values, and any initial fragmentation involves the loss of the ester and phenoxy moieties. No product other than **4a–e** could be detected by NMR spectroscopy.

The $^1$H NMR spectra of **4a** showed two singlets at $\delta$ = 3.73, 3.93 ppm for methoxy protons and a doublet of doublet at $\delta$ = 4.22 ppm ($^3J_{HH}$ = 3.8, $^2J_{PH}$ = 25.1 Hz) for PCH—CH and also a double quartet at $\delta$ = 4.94 ppm ($^3J_{HH}$ = 3.8,$^3J_{PH}$ = 4.0, $^3J_{HH}$ = 10.9 Hz) for other methine proton. NH proton resonance observed at $\delta$ = 4.94 ppm as a doublet with $^3J_{HH}$ = 10.9 Hz. All 13 aromatic protons resonance as a multiplet at $\delta$ = 6.84–7.38 ppm. The vicinal proton–proton coupling constant $^3J_{HH}$ can be obtained from the Karplus equation as a function of the torsion angle [32–36]. Typically, $J_{gauche}$ and $J_{anti}$ configurations give rise to distinct coupling constant, which varies between 1.5 and 10–14, respectively [32–36].

The observation of $^3J_{HH}$ = 3.8 Hz for the two vicinal protons in **4a** confirms a gauche arrangement for such protons. Since compounds **4a** possess two stereogenic centers, two diastereoisomers [(2*R*, 3*S*)-**4a** or (2*S*, 3*R*)-**4a** and (2*S*, 3*S*)-**4a** or (2*R*, 3*R*)-**4a**] with gauche HCCH arrangement are possible (see Scheme 2). Single crystal X-ray diffraction was employed to authenticate the structure of compound **4a**. Prismatic colorless crystal of **4a** was prepared by slow evaporation of a saturated solution of dichloromethane (Fig. 1).




SCHEME 2

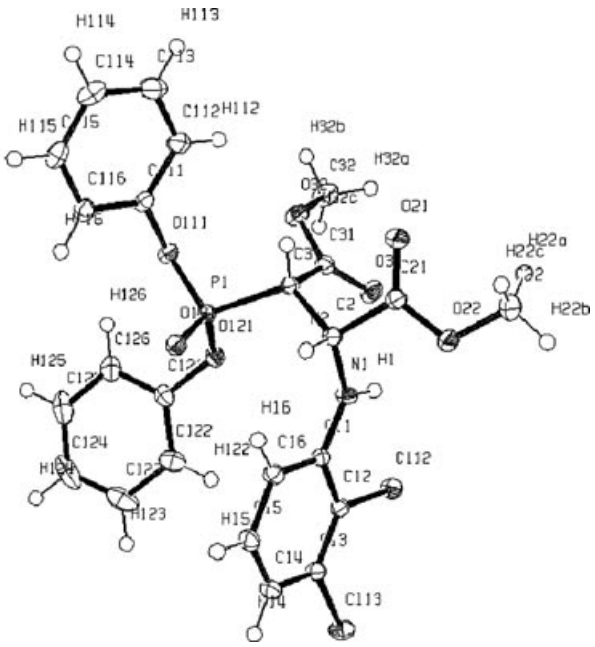



**FIGURE 1** The molecular structure of **4a** with the atom numbering scheme involving ORTEP representation.

Torsion angle between the two hydrogens of the chiral centers (*H*C—C*H*) and other conformational parameters for compound **4a** were extracted from single X-ray crystallographic data and are exhibited in Table 1.

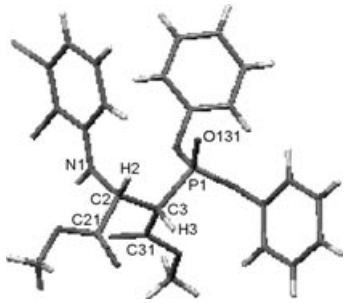
On the basis of the proposed mechanism in the literature [37–41], it is reasonable to assume that the heterocyclic phosphonato ester **4** results from the initial addition of triphenyl phosphite **1** to the acetylenic ester **2** (1:1 adduct or zwitterionic **A**), and subsequent protonation of the 1:1 adduct by the NH-compound **3** to generate intermediate of phosphonium ion **B**, which was followed by the conjugate base ($\mathbf{Z}^-$) to produce ylide **C**. It is converted to **D** in the presence of moisture and subsequent loss of PhOH (see Scheme 3).

In conclusion, the reaction between triphenyl phosphite and dialkyl acetylenedicarboxylates in the presence of aniline derivatives provides a simple one-pot entry into the synthesis of stable phosphonate esters of potential interest. The present procedure offers many advantages, performed under neutral conditions and the used reagents do not require can no any activation or modifications.

## *EXPERIMENTAL*

Melting points and IR spectra were taken on an Electrothermal 9100 apparatus and a JASCO FT-IR spectrometer, respectively. The $^1$H, $^{13}$C, and $^{31}$P NMR spectra were recorded on a Bruker (Rheinstetten, Germany) DRX-500 Avance instrument with $CDCl_3$ as solvent at 500.1, 125.8, and 202.5 MHz, respectively. Elemental analyses for C, H, and N were performed using a Heraeus (Banau, Germany) CHN-O-Rapid analyzer. The mass spectra were recorded on a Shimadzu (Kyoto, Japan) GCMS-QP5050A mass spectrometer operating at an ionization potential of 70 eV. Triphenyl phosphite, dialkyl acetylendicarboxylate, and aniline derivatives were purchased from Merck (Darmstadt, Germany), Fluka (Buchs, Switzerland), and Acros (Geel, Belgium), respectively, and were used without further purifications.

**TABLE 1** Selected Bond Length (Å), Bond Angels (°), and Torsion Angels (°) in Phosphonate Ester Structure **4a**



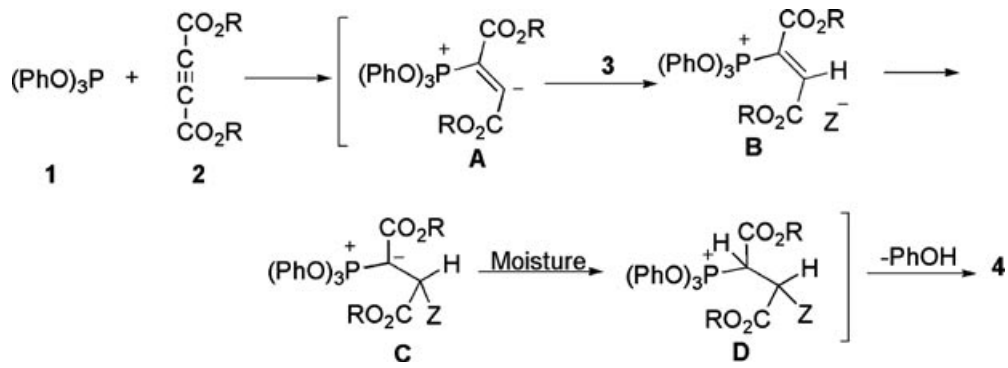

| Entry | Bond length | (Å) |
|---|---|---|
| 1 | C2–C3 | 1.550(2) |
| 2 | P1–C3 | 1.815(1) |
| 3 | C2–H2 | 0.9997(9) |
| 4 | C3–H3 | 0.999(1) |
| 5 | C2–C21 | 1.538(2) |
| 6 | C3–C31 | 1.522(1) |
| 7 | N1–C2 | 1.442(1) |

| Entry | Atom1 | Atom2 | Atom3 | Angle (°) |
|---|---|---|---|---|
| 1 | P1 | C3 | H3 | 106.09(7) |
| 2 | P1 | C3 | C31 | 114.96(7) |
| 3 | P1 | C3 | C2 | 112.01(7) |

| Entry | Atom1 | Atom2 | Atom3 | Atom4 | Angle (°) |
|---|---|---|---|---|---|
| 1 | H2 | C2 | C3 | H3 | 67.1(1) |
| 2 | P1 | C3 | C2 | H2 | −48.3(1) |
| 3 | P1 | C3 | C2 | C21 | −163.34(7) |

### *General Procedure (Exemplified by* **4a***)*

To a stirred solution of 2,3-dichloroaniline (1 mmol) and dimethyl acetylendicarboxylate (1 mmol) in 10 mL $CH_2Cl_2$, a mixture of triphenyl phosphite (1 mmol) in 5 mL $CH_2Cl_2$ at −5°C over 10 min was added drop wise. The mixture was then allowed to warm up to room temperature and was stirred for




SCHEME 3

24 h. The solvent was removed under reduced pressure, and the residue was washed with diethyl ether (2 × 3) mL to afford the product. The product was recrystallized in $CH_2Cl_2$ for generation of pure product.

### *(2S,3S)-Dimethyl 2-(2,3-dichlorophenylamino)-3-(diphenoxyphosphoryl)butandioate (**4a**)*

Colorless crystalline. yield: 95% (0.51 g), mp = 95–98°C. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 3428 (NH), 1722 and 1687 (C=O), 1228 (P=O). MS (*m/z*, %): 539 ($M^+ + 2$, 10), 538 ($M^+ + 1$, 4), 537 ($M^+$, 16), 507 (2), 446 (21), 387 (2), 376 (5), 161 (16), 94 (53), 77 (100). Anal. Calcd for $C_{24}H_{22}Cl_2NO_7P$ (538.31): C, 53.55; H, 4.12; N, 2.60. Found: C, 53.48; H, 4.19; N, 2.51.

$^1$H NMR (500.1 MHz, $CDCl_3$): $\delta_H$ 3.73 and 3.93 (6H, 2s, 2 OC*H*$_3$), 4.22 (1H, dd, $^3J_{HH}$ = 3.8, $^2J_{PH}$ = 25.1 Hz, PC*H*CH), 4.94 (1H, dq, $^3J_{HH}$ = 3.8, $^3J_{PH}$ = 4.0, $^3J_{HH}$ = 10.9 Hz, PCHC*H*), 5.99 (1H, d, $^3J_{HH}$ = 10.9 Hz, PCHCHN*H*), 6.84–7.38 (13H, m, 2 Oph, and 3 $CH_{arom}$).

$^{13}$C NMR (125.8 MHz, $CDCl_3$): $\delta_C$ 47.44 (d, $^1J_{PC}$ = 136.9 Hz, P*C*HCH), 53.10 and 53.33 (2s, 2O*C*H$_3$), 55.32 (d, $^2J_{PC}$ = 3.1 Hz, PCH*C*H), 118.79 and 119.68 (2s, $C_{arom}$ and $CH_{arom}$), 120.32 (d, $^3J_{PC}$ = 4.6 Hz, $2C_{ortho}$), 120.70 (d, $^3J_{PC}$ = 4.4 Hz, $2C_{ortho}$), 125.32 and 125.71 (2s, $2C_{para}$), 127.58 (s, $CH_{arom}$ and $C_{arom}$), 129.50 and 129.91 (2s, $4C_{meta}$), 132.95 (s, $CH_{arom}$), 144.29 (s, $C_{arom}$), 149.88 and 149.93 (2d, $^2J_{PC}$ = 6.3 Hz, $2C_{ipso}$), 167.69 (d, $^3J_{PC}$ = 5.3 Hz, CO), 171.20 (d, $^2J_{PC}$ = 17.2 Hz, CO). $^{31}$P NMR (202.5 MHz, $CDCl_3$): $\delta_P$ 11.70.

### *(2S,3S)-Diethyl 2-(2,3-dichlorophenylamino)-3-(diphenoxyphosphoryl)butandioate (**4b**)*

White powder. yield: 93% (0.53 g), mp = 118–121°C. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 3390 (NH), 1726 and 1681 (C=O), 1218 (P=O). MS (*m/z*, %): 567 ($M^+ + 2$, 13), 566 ($M^+ + 1$, 7), 565 ($M^+$, 20), 520 (2), 519 (5), 494 (66), 492 (94), 473 (2), 331 (36), 94 (41), 77 (100). Anal. Calcd for $C_{26}H_{26}Cl_2NO_7P$ (566.37): C, 55.14; H, 4.63; N, 2.47. Found: C, 55.03; H, 4.71; N, 2.52.

$^1$H NMR (500.1 MHz, $CDCl_3$): $\delta_H$ 1.22 (3H, t, $^3J_{HH}$ = 7.1 Hz, OCH$_2$C*H*$_3$), 1.40 (3H, t, $^3J_{HH}$ = 7.2 Hz, OCH$_2$C*H*$_3$), 4.21 (1H, dd, $^3J_{HH}$ = 3.9, $^2J_{PH}$ = 23.3 Hz, PC*H*CH), 4.14–4.20 (2H, m, $ABX_3$ system, OCH$_2$C*H*$_3$), 4.35–4.44 (2H, m, $ABX_3$ system, OCH$_2$C*H*$_3$), 4.90 (1H, ddd, $^3J_{HH}$ = 3.9, $^3J_{PH}$ = 6.6, $^3J_{HH}$ = 10.9 Hz, PCHC*H*), 5.97 (1H, d, $^3J_{HH}$ = 10.9 Hz, PCHCHN*H*), 6.85–7.38 (13H, m, 2Oph, and 3$CH_{arom}$).

$^{13}$C NMR (125.8 MHz, $CDCl_3$): $\delta_C$ 13.99 and 14.12 (2s, 2OCH$_2$*C*H$_3$), 47.62 (d, $^1J_{PC}$ = 136.7 Hz, P*C*HCH), 55.60 (d, $^2J_{PC}$ = 3.2 Hz, PCH*C*H), 62.21 and 62.65 (2s, 2O*C*H$_2$CH$_3$), 111.35, 118.86, and 119.66 (3s, $2C_{arom}$, and $CH_{arom}$), 120.33 (d, $^3J_{PC}$ = 4.6 Hz, $2C_{ortho}$), 120.77 (d, $^3J_{PC}$ = 4.4 Hz, $2C_{ortho}$), 125.27 and 125.69 (2s, $2C_{para}$), 127.57 (s, $CH_{arom}$), 129.50, and 129.92 (2s, $4C_{meta}$), 132.87 (s, $CH_{arom}$), 144.58 (s, $C_{arom}$), 149.96 (d, $^2J_{PC}$ = 4.7 Hz, $C_{ipso}$), 150.03 (d, $^2J_{PC}$ = 5.4 Hz, $C_{ipso}$), 167.07 (d, $^3J_{PC}$ = 5.4 Hz, CO), 170.67 (d, $^2J_{PC}$ = 17.6 Hz, CO). $^{31}$P NMR (202.5 MHz, $CDCl_3$): $\delta_P$ 12.18.

### *(2S,3S)-Dimethyl 2-(2,4-dichlorophenylamino)-3-(diphenoxyphosphoryl)butandioate (**4c**)*

White powder. yield: 90% (0.49 g), mp = 80–83°C. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 3393 (NH), 1754 and 1718 (C=O), 1224 (P=O). MS (*m/z*, %): 539 ($M^+ + 2$, 38), 538 ($M^+ + 1$, 25), 537 ($M^+$, 49), 507 (2), 506 (1), 505 (4), 478 (63), 412 (3), 376 (12), 161 (38), 94 (30), 77 (100). Anal. Calcd for $C_{24}H_{22}Cl_2NO_7P$ (538.31): C, 53.55; H, 4.12; N, 2.60. Found: C, 53.64; H, 4.23; N, 2.69.

$^1$H NMR (500.1 MHz, $CDCl_3$): $\delta_H$ 3.73 and 3.92 (6H, 2s, 2OC*H*$_3$), 4.21 (1H, dd, $^3J_{HH}$ = 3.8, $^2J_{PH}$ = 25.2 Hz, PC*H*CH), 4.88 (1H, m, PCHC*H*), 5.78 (1H, d, $^3J_{HH}$ = 10.9 Hz, PCHCHN*H*), 6.89 (1H, d, $^3J_{HH}$ = 8.8 Hz, $CH_{arom}$), 7.02 (1H, d, $^3J_{HH}$ = 8.8 Hz, $CH_{arom}$), 7.03–7.39 (11H, m, 2OPh and $CH_{arom}$).

$^{13}$C NMR (125.8 MHz, $CDCl_3$): $\delta_C$ 47.47 (d, $^1J_{PC}$ = 136.5 Hz, P*C*HCH), 53.09 and 53.33 (2s, 2O*C*H$_3$), 55.56 (d, $^2J_{PC}$ = 3.1 Hz, PCH*C*H), 114.21 (s, $CH_{arom}$), 120.39 (d, $^3J_{PC}$ = 4.5 Hz, 2$C_{ortho}$), 120.59 (d, $^3J_{PC}$ = 4.1 Hz, 2 $C_{ortho}$), 121.03 and 123.14 (2s, $CH_{arom,}$ and $C_{arom}$), 125.37 and 125.75 (2s, 2$C_{para}$), 127.73 and 128.82 (2s, $CH_{arom,}$ and $C_{arom}$), 129.75 and 129.86 (2s, 4$C_{meta}$), 141.66 (s, $C_{arom}$), 149.89 (d, $^2J_{PC}$ = 4.7 Hz, $C_{ipso}$), 149.99 (d, $^2J_{PC}$ = 5.6 Hz, $C_{ipso}$), 167.71 (d, $^3J_{PC}$ = 5.6 Hz, CO), 171.23 (d, $^2J_{PC}$ = 17.4 Hz, CO). $^{31}$P NMR (202.5 MHz, $CDCl_3$): $\delta_P$ 11.82.

### *(2S,3S)-Dimethyl 2-(3,4-dichlorophenylamino)-3-(diphenoxyphosphoryl)butandioate (**4d**)*

White powder. yield: 95% (0.51 g), mp = 108–111°C. IR (KBr) ($\nu_{max}$, cm$^{-1}$): 3376 (NH), 1752 and 1726 (C=O), 1219 (P=O). MS (*m/z*, %): 539 ($M^+$ + 2, 14), 538 ($M^+$ + 1, 6), 537 ($M^+$, 16), 505 (2), 480 (39), 479 (10), 478 (55), 446 (41), 376 (19), 161 (65), 94 (42), 77 (100). Anal. Calcd for $C_{24}H_{22}Cl_2NO_7P$ (538.31): C, 53.55; H, 4.12; N, 2.60. Found: C, 53.50; H, 4.23; N, 2.53.

$^1$H NMR (500.1 MHz, $CDCl_3$): $\delta_H$ 3.73 and 3.91 (6H, 2s, 2OC*H*$_3$), 4.18 (1H, dd, $^3J_{HH}$ = 3.9, $^2J_{PH}$ = 25.1 Hz, PC*H*CH), 5.00 (1H, m, PCHC*H*), 6.58 (1H, dd, $^3J_{HH}$ = 8.8,$^4J_{PH}$ = 2.7 Hz, PCHCHN*H*), 6.75 (1H, d, $^3J_{HH}$ = 2.5 Hz, $CH_{arom}$), 7.05 (1H, d, $^3J_{HH}$ = 8.2 Hz, $CH_{arom}$), 7.12–7.32 (11H, m, 2Oph, and $CH_{arom}$).

$^{13}$C NMR (125.8 MHz, $CDCl_3$): $\delta_C$ 47.69 (d, $^1J_{PC}$ = 136.7 Hz, P*C*HCH), 53.05 and 53.32 (2s, 2O*C*H$_3$), 55.57 (d, $^2J_{PC}$ = 3.0 Hz, PCH*C*H), 113.61 (s, $C_{arom}$ and $CH_{arom}$), 115.55 (s, $CH_{arom}$), 120.68 (d, $^3J_{PC}$ = 4.4 Hz, 2$C_{ortho}$), 120.37 (d, $^3J_{PC}$ = 4.3 Hz, 2$C_{ortho}$), 125.41 and 125.73 (2s, 2$C_{para}$), 125.75 (s, $C_{arom}$), 129.64 and 129.95 (2s, 4$C_{meta}$), 132.94 (s, $CH_{arom}$), 145.50 (s, $C_{arom}$), 149.86 (d, $^2J_{PC}$ = 8.3 Hz, $C_{ipso}$), 150.15 (d, $^2J_{PC}$ = 9.0 Hz, $C_{ipso}$), 167.89 (d, $^3J_{PC}$ = 5.3 Hz, CO), 171.41 (d, $^2J_{PC}$ = 17.4 Hz, CO). $^{31}$P NMR (202.5 MHz, $CDCl_3$): $\delta_P$ 11.55.

### *(2S, 3S)-Dimethyl 2-(2-fluorophenylamino)-3-(diphenoxyphosphoryl)butandioate (**4e**)*

White powder. yield: 91% (0.44 g), m.p = 85–88°C. IR (KBr) ($\nu_{max}$, cm$^{-1}$): 3392 (NH), 1764 and 1738 (C=O), 1214 (P=O). MS (*m/z*, %): 489 ($M^+$ + 2, 4), 488 ($M^+$ + 1, 16), 487 ($M^+$, 22), 471 (2), 428 (18), 396 (15), 379 (12), 377 (43), 334 (2), 285 (64), 223 (90), 111 (100), 94 (11), 77 (63). Anal. Calcd for $C_{24}H_{23}FNO_7P$ (487.41): C, 59.14; H, 4.76; N, 2.87. Found: C, 59.22; H, 4.63; N, 2.75.

$^1$H NMR (500.1 MHz, $CDCl_3$): $\delta_H$ 3.73 and 3.89 (6H, 2s, 2 OC*H*$_3$), 4.20 (1H, dd, $^3J_{HH}$ = 4.3, $^2J_{PH}$ = 24.9 Hz, PC*H*CH), 4.92 (1H, br s, PCHC*H*), 5.33 (1H, br d, $^3J_{HH}$ = 8.3 Hz, PCHCHN*H*), 6.70–7.38 (14H, m, 2OPh and 4$CH_{arom}$).

$^{13}$C NMR (125.8 MHz, $CDCl_3$): $\delta_C$ 47.89 (d, $^1J_{PC}$ = 137.2 Hz, P*C*HCH), 52.97 and 53.11 (2s, 2O*C*H$_3$), 55.47 (d, $^2J_{PC}$ = 2.8 Hz, PCH*C*H), 118.74 (d, $^3J_{FC}$ = 7.2 Hz, $CH_{arom}$), 120.50 and 120.68 (2d, $^3J_{PC}$ = 4.5 Hz, 4$C_{ortho}$), 124.48 (d, $^4J_{FC}$ = 3.5 Hz, $CH_{arom}$), 125.30 and 125.67 (2s, 2$C_{para}$), 129.51 (s, 2$C_{meta}$), 129.55 (d, $^3J_{FC}$ = 12.6 Hz, $CH_{arom}$), 129.75 (s, 2$C_{meta}$), 129.85 (d, $^2J_{FC}$ = 18.5 Hz, $CH_{arom}$), 134.9 (d, $^2J_{FC}$ = 11.3 Hz, $C_{arom}$), 150.05 (d, $^2J_{PC}$ = 9.5 Hz, $C_{ipso}$), 150.07 (d, $^2J_{PC}$ = 9.7 Hz, $C_{ipso}$), 152.06 (d, $^1J_{FC}$ = 239.8 Hz, $C_{arom}$), 167.55 (d, $^3J_{PC}$ = 5.7 Hz, CO), 171.63 (d, $^2J_{PC}$ = 16.2 Hz, CO). $^{31}$P NMR (202.5 MHz, $CDCl_3$): $\delta_P$ 11.78.

### *Crystallographic Details for* **4a**

$C_{24}H_{22}Cl_2NO_7P$, $M$ = 538.30, T = 100(2) K, $\lambda$ = 0.71073 Å, triclinic, space group $P\bar{1}$, $a$ = 8.074(5), $b$ = 10.987(5), $c$ = 14.703(5) Å, $\alpha$ = 105.852(5), $\beta$ = 97.302(5), $\gamma$ = 101.379(5)°, V = 1207.2(10) Å$^3$, $Z$ = 2, $D_c$ = 1.481 g cm$^{-3}$, $\mu$ = 0.382 mm$^{-1}$, $F_{000}$ = 556. Colorless slab, 0.42 × 0.28 × 0.16 mm$^3$, $2\theta_{max}$ = 74.6°. 40360 reflections collected, 12,066 unique ($R_{int}$ = 0.0307), GooF = 1.002, $R_1$ = 0.0414, $wR_2$ = 0.1124, $\rho_{max,min}$ = 0.671 , −0.724 e.Å$^{-3}$. Crystallographic data for the structure were collected on an Oxford (Oxford, UK) Diffraction Xcalibur diffractometer fitted with monochromated Mo K$\alpha$ radiation. Following multiscan absorption corrections, the structures were solved and refined using the program SHELXL-97 [42]. CCDC 757969 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

## *REFERENCES*

[1] Bagley, M. C.; Dale, J. W.; Bower, J. Chem Commun 2002, 1682.
[2] Li, Y. X.; Wang, S. H.; Li, Z. M.; Su, N.; Zhao, W. G. Carbohyd Res 2006, 341, 2867.
[3] Tenorio, R. P.; Carvalho, C. S.; Pessanha, C. S.; De Lima, J. G.; De Faria, A. R.; Alves, A. J.; De Melo, E. J. T.; Goes, A. J. S. Bioorg Med Chem Lett 2005, 15, 2575.
[4] Kucukguzel, S. G.; Oruc, E. F.; Rollas, S.; Shahin, F.; Ozbek, A. Eur J Med Chem 2002, 37, 197.
[5] Kato, T.; Ozaki, T.; Tamura, K.; Suzuki, Y.; Akima, M.; Ohi, N. J Med Chem 1999, 42, 3134.
[6] Dömling, A. Chem Rev 2006, 106.
[7] Dömling, A.; Ugi, I. Angew Chem, Int Ed Eng 2000, 39, 3168.
[8] Tozkoparan, B.; Ertan, M.; Kelicen, P.; Demirdamar, R. Il Farmaco 1999, 54, 588.

[9] Jeanneau-Nicolle, E.; Benoit-Guyod, M.; Namil, A.; Leclerc, G. Eur J Med Chem 1992, 27, 115.
[10] Sayed, H. H.; Shamroukh, A. H.; Rashad, A. E. Acta Pharm 2006, 56, 231.
[11] Coburn, R. A.; Glennon, R. A. J Pharm Sci 1973, 62, 1785.
[12] Engel, R. Chem Rev 1977, 77, 349.
[13] Arduago, A. J.; Stewart, C. A. Chem Rev 1994, 94, 1215.
[14] Pietrusiewiewiz, K. M.; Zabloka, M. Chem Rev 1994, 94, 1375.
[15] Bestmann, H. J.; Vostrowsky, O. Top Curr Chem 1983, 109, 85.
[16] Yavari, I.; Alizadeh, A. Tetrahedron 2001, 57, 9873.
[17] Yavari, I.; Adib, M.; Jahani-Moghaddam, F.; Bijanzadeh, H. R. Tetrahedron 2002, 58, 6901.
[18] Balaraman, E.; Kumaraswamy, K. C. Synthesis 2004, 3037.
[19] Kolodiazhnyi, O. I. Tetrahedron 1996, 52, 1855.
[20] Hughes, A. N. Heterocycles 1981, 15, 637.
[21] Ramazani, A.; Kazemizadeh, A. R.; Ahmadi, E.; Noshiranzadeh, N.; Souldozi, A. Curr Org Chem 2008, 12, 59–82.
[22] Maghsoodlou, M. T.; Habibi Khorassani, S. M.; Hazeri, N.; Nassiri, M. Phosphorus Sulfur Silicon 2006, 181, 1363.
[23] Maghsoodlou, M. T.; Hazeri, N.; Habibi-Khorassani, S. M.; Saghatforoush, L.; Rofouei, M. K.; Rezaie, M. Arkivoc 2006, xiii, 117.
[24] Maghsoodlou, M. T.; Habibi-Khorassani, S. M.; Rofouei, M. K.; Adhamdoust, S. R.; Nassiri, M. Arkivoc 2006, xii, 145.
[25] Maghsoodlou, M. T.; Habibi-Khorassani, S. M.; Heydari, R.; Hassankhani, A.; Marandi, G.; Nassiri, M.; Mossadegh, E. Mol Divers 2007, 11, 87.
[26] Maghsoodlou, M. T.; Hazeri, N.; Habibi-Khorassani, S. M.; Nassiri, M.; Marandi, G.; Afshari, G.; Niroumand, U. J Sulfur Chem 2005, 26, 261.
[27] Saghatforoush, L.; Maghsoodlou, M. T.; Aminkhani, A.; Marandi, G.; Kabiri, R. J Sulfur Chem 2006, 27, 583.
[28] Habibi-Khorassani, S. M.; Maghsoodlou, M. T.; Ebrahimi, A.; Zakarianejad, M.; Fattahi, M. J. Solution Chem. 2007, 36, 1117.
[29] Habibi-Khorassani, S. M.; Maghsoodlou, M. T.; Ebrahimi, A.; Roohi, H.; Zakarianejad, M.; Moradian, M. Prog React Kinet Mech 2005, 30, 127.
[30] Habibi-Khorassani, S. M.; Maghsoodlou, M. T.; Zakarianejad, M.; Kazemian, M. A.; Nassiri, M.; Karimi, P. Heteroatom Chem 2008, 19, 723.
[31] Maghsoodlou, M. T.; Heydari, R.; Hazeri, N.; Habibi-Khorassani, S. M.; Nassiri, M.; Ghasemzadeh, M.; Salehzadeh, J.; Gharechaei, Z. Heteroatom Chem 2009, 20, 240.
[32] Yavari, I.; Anary-Abbasinejad, M.; Hossaini, Z. Org Biomol Chem 2003, 1, 560.
[33] Breitmaier, E.; Voelter, W. Carbon-13 NMR Spectroscopy, 3rd ed.; VCH: New York, 1990; pp. 247–254.
[34] Eliel, E. L.; Wilen, S. H. Stereochemistry of Organic Compounds; Wiley: NewYork, 1994.
[35] Karplus, M. J Am Chem Soc 1963, 85, 2870.
[36] Hanoot, A. G.; Leeuw, F. A. M.; Altona, C. Tetrahedron 1980, 36, 783.
[37] Holmes, R. R. Acc Chem Res 2004, 37, 746.
[38] Maryanoff, B. E.; Reitz, A. B. Chem Rev 1989, 89, 863.
[39] Yavari, I.; Kowsari, E. Dyes Pigments 2008, 77, 103.
[40] Rostami Charati, F.; Maghsoodlou, M. T.; Habibi-Khorassani, S. M.; Makha, M. Tetrahedron Lett 2008, 49, 343.
[41] Maghsoodlou, M. T.; Rostami Charati, F.; Habibi-Khorassani, S. M.; Ghasemzadeh, M.; Makha, M. Chem Res 2008, 55.
[42] Sheldrick, G. M. Acta Cryst A 2008, 64, 112.