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Journal of Fluorine Chemistry 128 (2007) 174–178
JOURNAL OF FLUORINE CHEMISTRY
www.elsevier.com/locate/fluor

Synthesis of γ-butyrolactones containing α,α-difluoromethylenyl bisphosphonate initiated by $Na_2S_2O_4$

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Received 20 October 2006; received in revised form 13 November 2006; accepted 22 November 2006
Available online 25 November 2006

Abstract

Diethyl iododifluoromethylphosphonate (**1**) reacted with 4-pentenoic acids in the presence of $Na_2S_2O_4$ in aqueous acetonitrile solution at ambient temperature to afford various γ-butyrolactones containing α,α-difluoromethylenyl bisphosphonate moiety in moderate to good yields.

Keywords: Fluorinated phosphonate; 4-Pentenoic acids; Difluoromethylene; γ-Butyrolactones

1. Introduction

Phosphorous compounds play an important role in all living organisms and there are a great number of reports on the preparation and biochemical studies on such compounds [1]. The introduction of the *gem*-difluoromethylene (CF_2) moiety into organic compounds has attracted much attention in recent years because this group is usually regarded as an isopolar and isosteric replacement for oxygen [2]. It was suggested that (α,α-difluoroalky)phosphonates could mimic phosphate providing better bioactivities than corresponding phosphonates [3]. Therefore, (α,α-difluoroalky)phosphonates have been investigated as phosphonate analogues [4], enzyme inhibitors [5], and chelating agents [6]. Since γ-lactone represents a significant kind of compounds with biological activity [7], we focus on the synthesis of difluoromethylenated γ-lactones functionalized by bisphosphonate. There are limited reports on the synthesis of γ-lactones containing bisphosphonate [8,9], especially in those containing difluoromethylenyl group [10]. The new synthetic route of such compounds is still interesting and desirable. Here, we report the synthesis of γ-butyrolactones containing difluoromethylenyl bisphosphonate by the reaction of diethyl (iododifluoromethyl)phosphonate (**1**) with 4-pentenoic acids.

2. Results and discussion

Diethyl (iododifluoromethyl) phosphonate (**1**) was synthesized in high yield via iodination of the zinc reagent, $(EtO)_2P(O)CF_2ZnBr$, which was prepared by treating (bromodifluoromethyl)phosphonate (**3**) with activated Zn powder in monoglyme, as known methods [11]. **3** was obtained in excellent yield from triethyl phosphite (**2**) according to literature [12] (Scheme 1).

The addition reaction of **1** to olefins has been completed in the presence of $Pd(PPh_3)_4$ [13–15], Cu [14] or $Na_2S_2O_4$ [16]. We investigated into the reaction of **1** with various 4-pentenoic acids. Different initiators were applied to the reaction (Scheme 2). The details were summarized in Table 1. The results showed that in the presence of Na_2SO_3, the reaction was completed with 85% conversion of **1** and 68% yield of γ-lactone **5c** (Table 1, entry 1). The results were much unsatisfactory when thiourea dioxide or rongalite were used as the initiator (Table 1, entries 4 and 5). When the reaction was carried out in the presence of $NaHSO_3$ or $Na_2S_2O_5$, both the conversions and the yields were very low (Table 1, entries 2 and 3). While treatment of **1** with 2-ethyl-4-pentenoic acid (**4c**) in the presence of $Na_2S_2O_4$ in CH_3CN–H_2O (v/v = 3:1) at 25 °C gave lactone (**5c**) in good yield (81%) (Table 1, entry 6).

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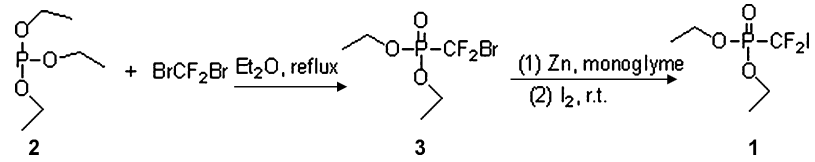
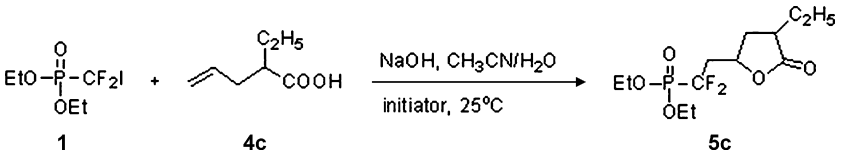
0022-1139/$ – see front matter
doi:10.1016/j.jfluchem.2006.11.009



Scheme 1.



Scheme 2.

Table 1
The reaction of **1** with **4c** in the presence of different initiator[a]

Entry	Initiator	**1**:initiator:$NaHCO_3$	Solvent (CH_3CN/H_2O)	Reaction temperature (°C)	Conversion of **1** (%)	Yield[b] (%)
1	Na_2SO_3	1:2:2	3:1	25	85	68
2	$NaHSO_3$	1:2:2	3:1	25	10	9
3	$Na_2S_2O_5$	1:2:2	3:1	25	14	3
4	Rongalite	1:1.4:2	3:1	25	47	11
5	Thiourea dioxide	1:2.4:2.4	3:1	25	70	20
6	$Na_2S_2O_4$	1:1.4:1.4	3:1	25	100	81

[a] **1**:**4c**:NaOH = 1:1:1 for 8 h.
[b] The yields were based on GC.

It was found that $CH_3CN–H_2O$ (v/v = 3:1) could be used as the solvent in this reaction (Table 2, entry 1). When $CH_3CN–H_2O$ (v/v = 1:1) or $CH_3CN–H_2O$ (v/v = 1:3) were utilized, the yields decreased (Table 2, entries 2 and 3). The temperature variation also affected the reaction. For example, when the reaction of **1** with **4c** took place at 0 °C for 8 h, only 65% yield were given (Table 2, entry 4). The yield was also reduced if the temperature was higher than 25 °C (Table 2, entry 5).

The results of the reaction of **1** with different 4-pentenoic acids **4** were listed in Table 3. It showed that for 2-substituted-4-pentinoic acids (Table 3, entries 2–9), a mixture of *cis*-/*trans*- isomers in ratios of between 1.05:1 and 1:1.83 was obtained. For substituents RCH_2 (R=H, CH_3, C_2H_5, C_3H_7, Ph) on 2-position of 4-pentenoic acids (**4b**–**4f**), *cis*-isomer was formed as the main products. While for group Ph, NHCOPh, $NHCOPhOCH_3$-*p* (**4g**–**4i**), *trans*-lactones dominated in the reaction. We supposed that the major *cis*- or *trans*-isomer resulted from the major configuration of the products: **6** (*exo*-RCH_2 and *exo*-CH_2CF_2P), **7** (*exo*-Ph, *endo*-CH_2CF_2P for the repulsion of large Ph) or **8** (*exo*-CH_2CF_2P, *endo*-NHCOR′ for the hydrogen bond between NH and C=O) (Scheme 3). The purification of the mixture of two isomers was easily achieved by the column chromatograph eluting with the mixture of petroleum and ethyl acetate (Scheme 4).

The mechanism of fluoroalkylation-lactonization has been suggested in our previous publications [15]. Similarly, the reaction of **1** with 4-pentenoic acids **4** to give corresponding γ-butyrolactones 5 may also involve the addition of R_FI to double bond through a mechanism of singe electron transfer (SET)

Table 2
Effect of solvent and temperature on the reaction of **1** with **4c**[a]

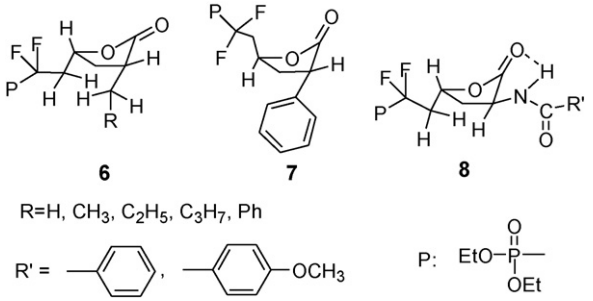
Entry	Solvent (CH_3CN/H_2O)	Reaction temperature (°C)	Conversion of **1** (%)	Yield[b] (%)
1	3:1	25	100	81
2	1:3	25	100	58
3	1:1	25	100	60
4	3:1	0	100	65
5	3:1	45	100	63

[a] **1**:**4c**:$Na_2S_2O_4$:$NaHCO_3$:NaOH = 1:1:1.4:1.4:1 for 8 h.
[b] The yields were based on GC.

Table 3
The reaction of **1** with different unsaturated acids **5a**–**i**[a]

Entry	R_1	R_2	R_3	Product	Yield (%)[b]	*cis*-/*trans*-
1	H (**4a**)	CH_3	CH_3	**5a**	64.0	–
2	CH_3 (**4b**)	H	H	**5b**	60.0	1.05:1
3	C_2H_5 (**4c**)	H	H	**5c**	56.0	1.26:1
4	*n*-C_3H_7 (**4d**)	H	H	**5d**	65.2	1.27:1
5	*n*-C_4H_9 (**4e**)	H	H	**5e**	55.0	1.25:1
6	CH_2Ph (**4f**)	H	H	**5f**	48.6	1.18:1
7	Ph (**4g**)	H	H	**5g**	59.7	1:1.83
8	NHCOPh (**4h**)	H	H	**5h**	40.0	1:1.67
9	$NHCOPhOCH_3$-*p* (**4i**)	H	H	**5i**	39.0	1:1.40

[a] **1**:**4**:NaOH = 1:1:1 in CH_3CN/H_2O = 3:1 (v/v) at 25 °C for 8 h.
[b] Isolated yield.



Scheme 3.

process and then followed by intramolecular S_N2 reaction. The mechnism is illustrated in Fig. 1.

3. Experimental

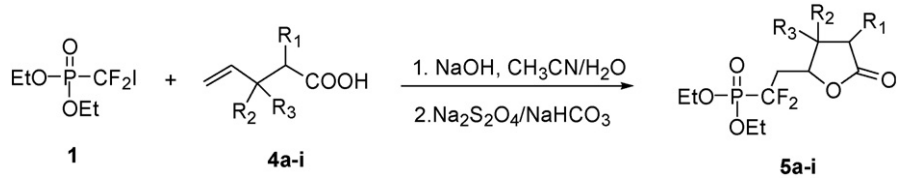
IR spectra were measured on a Nicolet Magna IR-550 spectrometer. High-resolution mass spectra were obtained on a Finnigan GC-MS-4021 spectrometer. NMR spectra were recorded in $CDCl_3$ solution on a Bruker AC-500 spectrometer operating at 500 MHz (^{1}H NMR), 125.8 MHz (^{13}C NMR) and 470.5 MHz (^{19}F NMR). Chemical shifts (δ) are given in ppm relative to TMS for ^{1}H and ^{13}C, and relative to $CFCl_3$ for ^{19}F NMR. Column chromatography was performed using silica gel H, particle size 20–30 μm. Melting points are uncorrected.

3.1. General procedure for the reaction of *1* with 4-pentenoic acids *4*

To the mixture of NaOH (3 mmol, 120 mg), acids **4** (3 mmol), phosphonate **1** (3 mmol, 940 mg), water (3 ml), acetonitrile (9 ml) was added the mixture of $Na_2S_2O_4$ (4.2 mmol, 730 mg) and $NaHCO_3$ (4.2 mmol, 350 mg) in 30 min. After stirring for 8 h, water (ca. 20 ml) was added and then extracted with ethyl ether of 3 × 20 ml. The combined organic layer was washed with saturated brine and dried over anhydrous sodium sulfate. After the evaporation of ethyl ether, the residue was purified by column chromatography eluting with petroleum ether and ethyl acetate to give the corresponding lactones.

3.2. [2-(3,3-Dimethyl-5-oxo-tetrahydro-furan-2-yl)-1,1-difluoro-ethyl]-phosphonic acid diethyl ester (*5a*)

Colorless oil; IR (film, υ_{max}, cm^{-1}): 1784, 1273, 1158, 1022; ^{1}H NMR δ (ppm): 4.53–4.50 (1H, m), 4.35–4.25 (4H, m), 2.32 (1H, AB, J = 16.5 Hz), 2.39 (1H, AB, J = 16.5 Hz), 2.38–2.28 (2H, m), 1.42–1.38 (6H, m), 1.19 (3H, s), 1.04 (3H, s); ^{19}F NMR δ (ppm): −111.17 to −113.66 (2F, m); ^{13}C NMR δ (ppm): 16.9, 17.0, 21.8, 24.7, 34.1–34.6 (m), 40.4, 44.8, 65.4 (d, $J_{P–C}$ = 7.0 Hz), 65.6 (d, $J_{P–C}$ = 6.8 Hz), 81.4–81.5 (m), 117–123 (m, CF_2), 176; HRMS for M^+: $C_{12}H_{21}O_5F_2P$. Calc.: 314.1095; Found: 314.1083.



Scheme 4.

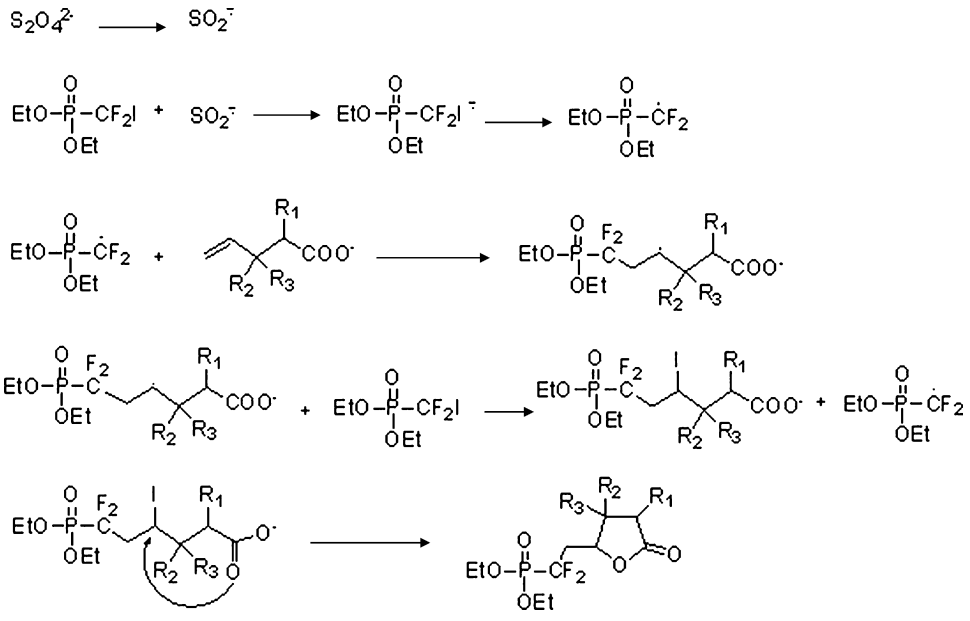


Fig. 1. Mechanism of the reaction of **4** with unsaturated acids.

3.3. [1,1-Difluoro-2-(4-methyl-5-oxo-tetrahydro-furan-2-yl)-ethyl]-phosphonic acid diethyl ester (**5b**)

Colorless oil; IR (film, υ_{max}, cm^{-1}): 1777, 1271, 1167, 1025; ^1H NMR δ (ppm): *cis*-: 4.73–4.75 (1H, m), 4.33–4.27 (4H, m), 2.74–2.60 (2H, stack), 2.60–2.55 (1H, m), 2.40–2.34 (1H, m), 1.69–1.64 (1H, m), 1.40 (6H, t, J = 6.8 Hz), 1.28 (3H, d, J = 6.5 Hz); *trans*-: 4.97–4.94 (1H, m), 4.33–4.27 (4H, m), 2.74–2.60 (1H, m), 2.60–2.55 (1H, m), 2.40–2.34 (1H, m), 2.31–2.25 (1H, m), 2.22–2.13 (1H, m), 1.40 (6H, t, J = 6.8 Hz), 1.31 (3H, d, J = 7.3 Hz); ^{19}F NMR δ (ppm): −110.6 to −112.8 (2F, m); ^{13}C NMR δ (ppm): *cis*-: 15.5, 16.9, 17.0, 36.1, 38.8, 39.9–40.4 (m), 65.5, 65.6, 72.2–72.4 (m), 118–122 (m, CF_2), 179.2; *trans*-: 16.3, 16.9, 17.0, 34.2, 36.7, 38.7–39.9 (m), 65.4, 65.5, 72.2–72.4 (m), 118–122 (m, CF_2), 179.7; HRMS for M^+: $C_{11}H_{19}O_5F_2P$. Calc: 300.0938 Found: 300.0931.

3.4. [2-(4-Ethyl-5-oxo-tetrahydro-furan-2-yl)-1,1-difluoro-ethyl]-phosphonic acid diethyl ester (**5c**)

Colorless oil; IR (film, υ_{max}, cm^{-1}): 1778, 1272, 1167, 1024; ^1H NMR δ (ppm): *cis*-: 4.78–4.74 (1H, m), 4.33–4.26 (4H, m), 2.66–2.55 (3H, stack), 2.41–2.29 (1H, m), 1.88–1.80 (1H, m), 1.68–1.62 (1H, m), 1.60–1.52 (1H, m), 1.40 (6H, t, J = 7.0 Hz), 1.00 (t, 3H, J = 7.5 Hz); *trans*-: 4.93–4.91 (1H, m), 4.33–4.26 (4H, m), 2.66–2.55 (2H, stack), 2.41–2.29 (1H, m), 2.21 (2H, t, J = 7.0 Hz), 1.99–1.90 (1H, m), 1.51–1.42 (1H, m), 1.40 (6H, t, J = 7.0 Hz), 1.03 (3H, t, J = 7.4 Hz); ^{19}F NMR δ (ppm): −110.5 to −112.8; ^{13}C NMR δ (ppm): *cis*-: 11.8, 16.7, 16.8, 23.4, 35.8, 40.6–40.7 (m), 42.3, 65.4, 65.3, 72.3–73.5 (m), 116–124 (m, CF_2), 178.3; *trans*-: 11.9, 16.7, 16.8, 24.2, 34.1, 39.7–40.0 (m), 40.7, 65.2, 65.3, 72.3–72.5 (m), 116–124 (m, CF_2), 178.8; HRMS for M^+: $C_{12}H_{21}O_5F_2P$. Calc: 314.1095; Found: 314.1095.

3.5. [1,1-Difluoro-2-(5-oxo-4-propyl-tetrahydro-furan-2-yl)-ethyl]-phosphonic acid diethyl ester (**5d**)

Colorless oil; IR (film, υ_{max}, cm^{-1}): 1774, 1269, 1165, 1029; ^1H NMR δ (ppm): *cis*-: 4.78–4.75 (1H, m), 4.33–4.26 (4H, m), 2.75–2.50 (3H, stack), 2.45–2.27 (1H, m), 1.82–1.75 (1H, m), 1.70–1.60 (1H, m), 1.50–1.29 (3H, m), 1.38 (6H, t, J = 7.3 Hz), 0.96 (3H, t, J = 7.2 Hz); *trans*-: 4.94–4.92 (1H, m), 4.33–4.26 (4H, m), 2.75–2.50 (2H, stack), 2.45–2.27 (1H, m), 2.21 (t, 2H, J = 7.2 Hz), 1.95–1.85 (1H, m), 1.50–1.29 (3H, m), 1.38 (6H, t, J = 7.3 Hz), 0.95 (t, 3H, J = 7.2 Hz); ^{19}F NMR δ (ppm): −110.6 to −112.9 (2F, m);.^{13}C NMR δ (ppm): *cis*-: 14.3, 17.0, 17.1, 21.1, 32.8, 36.8, 39.8–40.5 (m), 41.0, 65.6, 65.7, 72.6–72.8 (m), 116–122 (m, CF_2), 178.7; *trans*-: 14.4, 17.0, 17.1, 21.1, 33.3, 34.9, 39.4, 39.8–40.5 (m), 65.5, 65.6, 72.6–72.8 (m), 116–122 (m, CF_2), 179.2; HRMS for M^+: $C_{13}H_{23}O_5F_2P$. Calc: 328.1251; Found: 328.1266.

3.6. [2-(4-Butyl-5-oxo-tetrahydro-furan-2-yl)-1,1-difluoro-ethyl]-phosphonic acid diethyl ester (**5e**)

Colorless oil; IR (film, υ_{max}, cm^{-1}): 1777, 1273, 1165, 1022; ^1H NMR δ (ppm): *cis*-: 4.78–4.75 (1H, m), 4.32–4.26 (4H, m), 2.66–2.55 (3H, stack), 2.41–2.31 (1H, m), 1.85–1.81 (1H, m), 1.68–1.60 (1H, m), 1.52–1.46 (1H, m), 1.40 (6H, t, J = 7.1 Hz), 1.38–1.30 (4H, m), 0.92 (3H, t, J = 7.0 Hz); *trans*-: 4.94–4.91 (1H, m), 4.32–4.26 (4H, m), 2.66–2.55 (2H, stack), 2.41–2.31 (1H, m), 2.21 (2H, t, J = 7.0 Hz), 1.95–1.91 (1H, m), 1.40 (6H, t, J = 7.1 Hz), 1.38–1.30 (5H, m), 0.92 (3H, t, J = 7.0 Hz); ^{19}F NMR δ (ppm): −110.6 to −113.1 (2F, m); ^{13}C NMR δ (ppm): *cis*-: 14.5, 17.0, 17.1, 23.1, 30.0, 30.9, 36.8, 41.3, 40.0–40.5 (m), 65.5, 65.6, 72.7–72.8 (m), 116–122 (m, CF_2), 178.7; *trans*-: 14.5, 17.0, 17.1, 23.0, 30.0, 30.5, 34.9, 39.6, 40.0–40.5 (m), 65.4, 65.5, 72.7–72.8 (m, CF_2), 116–122 (m), 179.2; HRMS for M^+: $C_{14}H_{25}O_5F_2P$. Calc: 342.1408; Found: 342.1411.

3.7. [2-(4-Benzyl-5-oxo-tetrahydro-furan-2-yl)-1,1-difluoro-ethyl]-phosphonic acid diethyl ester (**5f**)

Colorless oil; IR (film, υ_{max}, cm^{-1}): 1777, 1272, 1165, 1023; ^1H NMR δ (ppm): *cis*-: 7.32–7.18 (5H, m), 4.75–4.72 (1H, m), 4.29–4.24 (4H, m), 3.18 (1H, ABX, J_1 = 13.8 Hz, J_2 = 4.5 Hz), 2.96–2.92 (2H, stack), 2.74 (1H, ABX, J_1 = 14.0 Hz, J_2 = 9.2 Hz), 2.68–2.50 (1H, m), 2.45–2.20 (1H, m), 1.73–1.67 (1H,m), 1.37 (6H, t, J = 7.0 Hz); *trans*-: 7.32–7.18 (5H, m), 4.75–4.72 (1H, m), 4.29–4.24 (4H, m), 3.29 (1H, ABX, J_1 = 14.0 Hz, J_2 = 4.2 Hz), 2.74 (1H, ABX, J_1 = 14.0 Hz, J_2 = 9.2 Hz), 2.68–2.50 (1H, m), 2.50–2.42 (1H, m), 2.45–2.20 (2H, stack), 2.11–2.05 (1H, m), 1.38 (6H, t, J = 7.0 Hz); ^{19}F NMR δ (ppm): −110.7 to −112.9 (2F, m); ^{13}C NMR δ (ppm): *cis*-: 15.3, 15.4, 32.3, 34.9, 38.2–38.7 (m), 41.4, 63.8, 63.9, 71.0–71.1 (m), 117–122 (m, CF_2), 125.7, 127.7, 127.9, 137.2, 176.2; *trans*-: 15.3, 15.4, 28.6, 34.5, 38.2–38.7 (m), 39.6, 63.7, 63.8, 71.0–71.1 (m), 117–122 (m, CF_2), 125.9, 127.8, 128.0, 136.8, 176.8; HRMS for M^+: $C_{17}H_{23}O_5F_2P$. Calc: 376.1252; Found: 376.1219.

3.8. [1,1-Difluoro-2-(5-oxo-4-phenyl-tetrahydro-furan-2-yl)-ethyl]-phosphonic acid diethyl ester (**5g**)

Colorless oil; IR (film, υ_{max}, cm^{-1}): 1776, 1269, 1161, 1021; ^1H NMR δ (ppm): *cis*-: 7.39–7.26 (5H, m), 4.94–4.91 (1H, m), 4.34–4.27 (4H, m), 3.94–3.89 (1H, m), 2.97–2.92 (1H, m), 2.88–2.55 (1H, m), 2.50–2.39 (1H, m), 2.21–2.15 (1H, m), 1.42–1.29 (6H, m); *trans*-: 7.39–7.26 (5H, m), 5.09–5.04 (1H, m), 4.34–4.27 (4H, m), 3.94–3.89 (1H, m), 2.88–2.55 (2H, stack), 2.58–2.50 (1H, m), 2.50–2.39 (1H, m), 1.42–1.29 (6H, m). ^{19}F NMR δ (ppm): −110.5 to −112.8 (2F, m); ^{13}C NMR δ (ppm): *cis*-: 16.3, 16.4, 37.3, 38.8–39.7 (m), 46.7, 64.9, 65.0, 71.7–71.9 (m), 116–122 (m, CF_2), 127.7, 128.6, 128.9, 135.9, 175.9; *trans*-: 16.3, 16.4, 36.9, 38.8–39.7 (m), 45.2, 65.0, 65.1, 72.2–72.4 (m), 116–122 (m, CF_2), 127.5, 128.0, 129.1, 136.3, 176.3; HRMS for M^+: $C_{16}H_{21}O_5F_2P$. Calc: 362.1095; Found: 362.1096.

3.9. [2-(4-Benzoylamino-5-oxo-tetrahydro-furan-2-yl)-1,1-difluoro-ethyl]-phosphonic acid diethyl ester (**5h**)

White solid; mp. 78–80 °C; IR (KBr, υ_{max}, cm^{-1}): 3332, 1777, 1655, 1292, 1189, 1041; ^1H NMR δ (ppm): *cis*-: 7.81–7.27

(5H, m), 6.86 (1H, d, J = 5.4 Hz), 5.01–4.92 (1H, m), 4.78–4.67 (1H, m), 4.33–4.28 (4H, m), 3.19–3.12 (1H, m), 2.70–2.57 (2H, m), 2.11–2.05 (1H, m), 1.4 (6H, t, J = 7.0 Hz); *trans*-: 7.81–7.27 (5H, m), 6.90 (1H, d, J = 6.0 Hz), 5.25–5.19 (1H, m), 4.66–4.55 (1H, m), 4.33–4.28 (4H, m), 2.79–2.72 (1H, m), 2.70–2.40 (3H, stack), 1.4 (6H, t, J = 7.0 Hz); ^{19}F NMR δ (ppm): −111.3 to −112.3 (2F, m); ^{13}C NMR δ (ppm): *cis*-: 16.9, 17.0, 36.8, 39.8–40.1 (m), 50.9, 65.6, 65.7, 72.3–72.4 (m), 116–123 (m, CF_2), 127.8, 129.2, 132.6, 133.6, 168.21, 175.2; *trans*-: 16.9, 17.0, 35.1, 39.8–40.1 (m), 49.2, 65.5, 65.6, 72.1–72.2 (m), 116–123 (m, CF_2), 127.9, 129.1, 132.6, 133.5, 168.24, 175.6; HRMS for M^+: $C_{17}H_{22}NO_6F_2P$. Calc: 405.1153; Found: 405.1154.

*3.10. 1,1-Difluoro-2-[4-(4-methoxy-benzoylamino)-5-oxo-tetrahydro-furan-2-yl]-ethyl]-phosphonic acid diethyl ester (**5i**)*

Colorless oil; IR (film, υ_{max}, cm^{-1}): 3331, 1786, 1655, 1290, 1180, 1024; ^{1}H NMR δ (ppm): *cis*-: 7.78–6.91 (4H, m), 6.72 (1H, d, J = 5.4 Hz), 4.98–4.91 (1H, m), 4.82–4.76 (1H, m), 4.33–4.28 (4H, m), 3.85 (3H, s), 3.15–3.11 (1H, m), 2.70–2.40 (2H, m), 2.10–2.04 (1H, m), 1.40 (6H, t, J = 7.0 Hz); *trans*-: 7.78–6.91 (4H, m), 6.76 (1H, d, J = 5.9 Hz), 5.22–5.19 (1H, m), 4.71–4.64 (1H, m), 4.33–4.28 (4H, m), 3.85 (3H, s), 2.69–2.61 (1H, m), 2.70–2.40 (3H, stack), 1.40 (6H, t, J = 7.0 Hz). ^{19}F NMR δ (ppm): −111.3 to −112.4 (2F, m); ^{13}C NMR δ (ppm): *cis*-: 16.9, 17.0, 37.0, 39.7–40.1 (m), 50.9, 56.0, 65.6, 65.7, 72.3–72.4 (m), 114.4, 116–122 (m, CF_2), 125.9, 129.7, 129.8, 167.8, 175.4; *trans*-: 16.9, 17.0, 35.2, 39.7–40.1 (m), 49.2, 56.0, 65.5, 65.6, 72.9–73.0 (m), 114.4, 116–122 (m, CF_2), 125.7, 129.8, 163.3, 167.7, 175.8. HRMS for M^+: $C_{18}H_{24}F_2NO_7P$. Calc: 435.1258; Found: 435.1255.

Acknowledgements

We thank the National Natural Science Foundation of China (20672034) and the Shanghai Scientific and Technology Committee (Grant No. 03QB14012) for financial support.

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