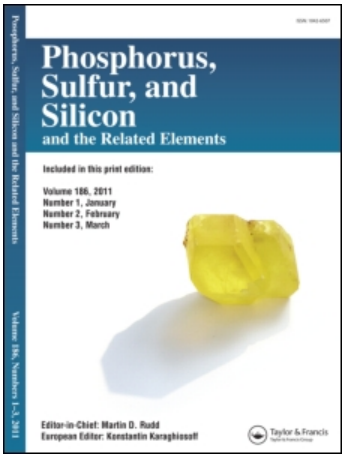

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Synthesis and Biological Activity of O,O'-Dialkyl 5-Aryl-1-Hydroxy-3-Methyl-2E,4E-Pentadienylphosphonates

De Qing Shi[a]; Hui Qing Huang[a]; Ru Yu Chen[a]
[a] Department of Chemistry, Central of China Normal University, Wuhan, Peoples Republic of China

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SYNTHESIS AND BIOLOGICAL ACTIVITY OF O,O′-DIALKYL 5-ARYL-1-HYDROXY-3-METHYL-2E,4E-PENTADIENYLPHOSPHONATES

De Qing Shi, Hui Qing Huang, and Ru Yu Chen
Department of Chemistry, Central of China Normal University, Wuhan 430079, Peoples Republic of China

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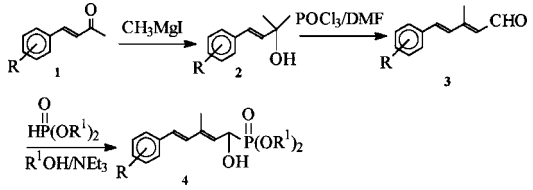
A series of unsaturated α-hydroxy phosphonates were synthesized by the addition reactions of dialkyl phosphites with 5-aryl-3-methyl-2E, 4E-pentadienaldehydes. The structures of all new compounds have been confirmed by ^{1}H NMR, ^{31}P NMR, and IR spectroscopy and by elemental analysis or MS. The bioassays showed that some of these compounds exhibit certain inhibitory activity on the elongation of wheat coleoptile.

Keywords: Plant growth regulator; synthesis; unsaturated hydroxy phosphonates

INTRODUCTION

We have reported the synthesis of several unsaturated phosphonates, some of which exhibit plant growth regulating activity.[1,2] Hydroxyalkylphosphonic acids and their derivatives appear to be very important for their wide biological activities in the inhibition of enzymes,[3,4] fungicides,[5] and plant growth regulation.[6,7] In order to find out new plant growth regulators, we designed and synthesized a number of new title compounds **4**. The synthetic route is shown in Scheme 1.



R=2-Cl, 4-Cl, 4-CH_3, 3, 4-OCH_2O- ; R^1=Me, Et

SCHEME 1

Address correspondence to De Qing Shi, Department of Chemistry, Central of China Normal University, Wuhan 430079, Peoples Republic of China.
E-mail: shidq@public.wh.hb.cn

Preliminary bioassays indicate that some of these compounds have inhibitory activity on the elongation of wheat coleoptile.

RESULTS AND DISCUSSION

Preparation of 5-Aryl-1-hydroxy-3-methyl-2E, 4E-pentadienylphosphonates 4

The reaction of dialkyl phosphites with aldehydes is a convenient method used to synthesize α-hydroxyphosphonates. There are some reports on the synthesis of hydroxyalkenylphosphonates.[8,9] However, there are few reports on the reaction of dialkyl phosphites with dienylaldehydes. Herein we report the reaction of dialkyl phosphites with 5-aryl-3-methyl-2E, 4E-pentadienaldehydes to produce O, O′-dialkyl 5-aryl-1-hydroxy-3-methyl-2E, 4E-pentadienylphosphonates. The reaction under mild conditions (room temperature) resulted in high yields of the products as shown in Scheme 1.

However, the addition of a base (triethylamine) was essential to the addition reaction. Without the use of the triethylamine as a catalyst, the reaction was greatly slowed and the yields were very low too.

The addition reactions show good regioselectivity; the phosphorus atom of dialkyl phosphites attacks only the carbon atom in the carbonyl group of dienals, and no conjugated addition products were found.

The addition reaction of dialkylphosphites with β-ionone did not take place in the presence of triethylamine under reflux for 12 h. It was probably due to the low reactivity of β-ionone.

The Structures of the Title Compounds 4

The molecular structures of all new compounds obtained were confirmed by ^{1}H NMR, ^{31}P NMR, IR spectra, MS and elemental analyses. All results are listed in Table I.

For ^{1}H NMR spectra, when R^1 was Me, the hydrogens of the *O*Me displayed one set of double peaks. The hydrogen of the hydroxyl group of all compounds displayed one wide single peak. The hydrogen of the carbon nearest to the phosphorus atom gave a doublet of doublets, while three hydrogens of the methyl group on the unsaturated carbon side displayed one set of double peaks. If the R group was 3,4-OCH_2O and p-Cl, the hydrogens of the phenyl group displayed one set of multiple peaks. However, if the R group was *o*-Cl and p-CH_3, the hydrogen of the phenyl group showed two sets of peaks. For ^{31}P NMR spectra, the phosphorus atom of all compounds displayed one set of single peak, giving chemical shifts between 24 and 25 ppm.

TABLE I ^{1}H NMR, ^{31}P NMR Data of Compound **4a–h**

No.	^{1}H NMR and ^{31}P NMR (200MHz, $CDCl_3$, ppm)
4a	1.26–1.35 (dt, 6H, $J^{3}_{H-H} = 7.4$ Hz, $2CH_3$), 1.90–1.92 (d, 3H, $J^{4}_{H-H} = 3.1$ Hz,CH_3), 3.76 (sb, 1H, OH), 4.11–4.20 (m, 4H, $2CH_2O$), 4.77–4.87 (dd, 1H, $J^{2}_{P-H} = 9.9$ Hz, $^{3}J_{H-H} = 9.4$ Hz, CH—P), 5.66–5.74 (dd, 1H, $^{3}J_{H-H} = 15.6$Hz, =CH), 6.46–6.54 (d, 1H $^{3}J_{H-H} = 15.9$ Hz, =CH), 6.74–6.82 (d, 1H, $^{3}J_{H-H} = 16.0$ Hz, =CH—Ar), 7.22–7.29 (m, 4H, C_6H_4)
4b	1.91–1.93 (d, 3H, $J^{4}_{H-H} = 3.1$ Hz, CH_3), 3.73 (sb, 1H, OH), 3.76–3.83 (dd, 6H, $J^{3}_{P-H} = 7.4$ Hz, $2CH_3O$), 4.81–4.90 (dd, 1H, $J^{2}_{P-H} = 10.0$ Hz, $^{3}J_{H-H} = 9.6$ Hz, CH—P), 5.67–5.75 (dd, 1H, $^{3}J_{H-H} = 15.8$ Hz, =CH), 6.48–6.56 (d, 1H, $^{3}J_{H-H} = 16.1$ Hz, =CH), 6.73–6.81 (d, 1H, $^{3}J_{H-H} = 16.1$ Hz, =CH—Ar), 7.21–7.33 (m, 4H, C_6H_4), ^{31}P NMR: 24.73
4c	1.27–1.36 (dt, 6H, $J^{3}_{H-H} = 6.8$ Hz, $2CH_3$), 1.90–1.92 (d, 3H, $J^{4}_{H-H} = 3.3$ Hz, CH_3), 2.60 (sb, 1H, OH), 4.12–4.19 (m, 4H, $2CH_2O$), 4.76–4.86 (dd, 1H, $J^{2}_{P-H} = 10.6$ Hz, $^{3}J_{H-H} = 9.4$ Hz, CH—P), 5.58–5.66 (dd, $^{3}J_{H-H}$ =15.6 Hz, 1H, =CH), 5.92 (s, 2H, —OCH_2O—), 6.58–6.66 (d, 2H, $^{3}J_{H-H} = 16.0$ Hz, CH=CH—Ar), 6.68–6.74 (m, 3H, C_6H_3)
4d	1.89–1.91 (d, 3H, $J^{4}_{H-H} = 3.0$ Hz, CH_3), 3.69 (sb, 1H, OH), 3.75–3.83 (dd, 6H, $J^{3}_{P-H} = 7.4$ Hz , $2CH_3O$), 4.80–4.90 (dd, 1H, $J^{2}_{P-H} = 9.9$ Hz, $^{3}J_{H-H} = 9.4$ Hz, CH—P), 5.61–5.69 (dd, 1H, $^{3}J_{H-H} = 15.6$ Hz, =CH), 5.92 (s, 2H, —OCH_2O—), 6.53–6.61 (d, 2H, $^{3}J_{H-H} = 15.8$ Hz, CH=CH—Ar), 6.74–6.92 (m, 3H, C_6H_3), ^{31}P NMR: 24.99
4e	1.28–1.36 (dt, 6H, J^{3}_{H-H} =6.8 Hz , $2CH_3$), 1.96–1.97(d, 3H, $J^{4}_{H-H} = 3.1$ Hz, CH_3), 3.10 (sb, 1H, OH), 4.10–4.21 (m, 4H, $2CH_2O$), 4.79–4.89 (dd, 1H, $J^{2}_{P-H} = 9.9$ Hz, $^{3}J_{H-H} = 9.5$ Hz, CH—P), 5.68–5.75 (dd, $^{3}J_{H-H} = 16.0$ Hz, 1H, =CH), 6.73–6.81(d, 1H, $^{3}J_{H-H} = 16.3$ Hz, =CH), 6.95–7.03 (d, 1H, $^{3}J_{H-H} = 15.9$ Hz, =CH—Ar), 7.17–7.24 (m, 2H, 2H of C_6H_4), 7.24–7.32 (dd, 2H, 2H of C_6H_4)
4f	1.96–1.97 (d, 3H, $J^{4}_{H-H} = 3.1$ Hz, CH_3), 3.50 (sb, 1H, OH), 3.77–3.84 (dd, 6H, $^{3}J_{P-H} = 7.4$ Hz, CH_3O), 4.83–4.93 (dd, 1H, $J^{2}_{P-H} = 10.4$ Hz, $^{3}J_{H-H}$ = 9.9 Hz, CH—P), 5.70–5.78 (dd, 1H, $^{3}J_{H-H} = 15.8$ Hz, =CH), 6.73–6.81 (d, 1H, $^{3}J_{H-H} = 16.1$ Hz, =CH), 6.96–7.04 (d, 1H, $^{3}J_{H-H} = 16.0$ Hz, =CH—Ar), 7.17–7.30 (m, 2H, 2H of C_6H_4), 7.32–7.56 (dd, 2H, 2H of C_6H_4)
4g	1.27–1.36 (dt, 6H, $J^{3}_{H-H} = 6.6$ Hz, $2CH_3$), 1.92–1.93 (d, 3H, $J^{4}_{H-H} = 3.3$ Hz, CH_3), 2.32 (s, 3H, CH_3—Ar), 3.16 (sb, 1H, OH), 4.14–4.19 (m, 4H, $2CH_2O$), 4.78–4.88 (dd, 1H, $J^{2}_{H-H} = 8.6$ Hz, $^{3}J_{H-H} = 9.9$ Hz, CH—P), 5.61–5.69 (dd, 1H, $^{3}J_{H-H} = 15.6$ Hz, =CH), 6.52–6.60 (d, 1H, $^{3}J_{H-H} = 16.4$ Hz, =CH), 6.74–6.83 (d, 1H, $^{3}J_{H-H} = 16.6$ Hz, =CH—Ar), 7.09–7.13 (m, 2H, 2H of C_6H_4), 7.24–7.32 (dd, 2H, 2H of C_6H_4)
4h	1.92–1.95 (d, 3H, $J^{4}_{H-H} = 3.2$ Hz, CH_3), 2.32 (s, 3H, CH_3—Ar), 3.38 (sb, 1H, OH), 3.76–3.84 (dd, 6H, $^{3}J_{P-H} = 7.4$ Hz, $2CH_3O$), 4.80–4.89 (dd, 1H, $J^{2}_{P-H} = 10.4$ Hz, $^{3}J_{H-H} = 9.9$ Hz, CH—P), 5.63–5.71(dd, 1H, $^{3}J_{H-H}$ = 16.0 Hz, =CH), 6.53–6.61 (d, 1H, $^{3}J_{H-H} = 16.8$ Hz, =CH), 6.74–7.82 (d, 1H, $^{3}J_{H-H}$ =15.6 Hz, =CH—Ar), 7.09–7.13 (d, 2H, 2H of C_6H_4), 7.24–7.31 (dd, 2H, 2H of C_6H_4)

TABLE II The Plant Growth Regulating Activities of Compounds **4a–h** (Wheat Coleoptile Tests, Inhibition %)

Compd.	100 ppm (%)	10 ppm (%)
4a	−29.78	−7.11
4b	−21.78	−4.89
4c	−27.97	−11.89
4d	−24.48	−7.69
4e	−48.25	−9.09
4f	−30.77	−9.09
4g	−38.11	−10.84
4h	−46.85	−9.79

The EI mass spectra of all compounds gave the anticipated molecular ion peaks.

The IR spectra of all compounds showed normal stretching absorption bands indicating the existence of the OH (∼3250 cm^{-1}), P═O (∼1180 cm^{-1}), C═C (∼1630 cm^{-1}), and phosphonate diester groups (∼1060, 1000 cm^{-1}).

Plant Growth Regulating Activities

The results of preliminary tests for the plant growth regulating activities indicated that some of the title compounds exhibit inhibitory activity on the elongation of wheat coleoptile. The data for the bioassays are listed in Table II. The substituents R of phenyl group have some effects on the biological activity, while the esters groups have little effect.

EXPERIMENTAL

^1H NMR and ^{31}P NMR spectra were recorded with a BRUKER AC-P200 spectrometer with TMS and 85% H_3PO_4 as the internal and external reference, respectively, and $CDCl_3$ as the solvent, while mass spectra were obtained with a VG ZAB-HS spectrometer using the EI method. IR spectra were measured by a SHIMADZU-435 instrument system. Elemental analyses was performed with a Yanaco —CHN CORDER MT-3 elementary analyzer. Melting Points were determined with a Thomas-Hoover melting point apparatus and the thermometer was uncorrected.

The reagents and solvents were available commercially and purified according to conventional methods before use. 4-Aryl-3-butenones-2 (**1**) were synthesized by aldol condensation of substituted benzaldehydes with acetone according to literature.[10] 4-Aryl-2-methyl-3-butenols-2 (**2**)

were prepared according to literature,[11] yield: 86–95%. Compounds **3** were obtained by Vilsmeier reaction of 4-aryl-2-methyl-3-butenols-2 (**2**) with $POCl_3$ and DMF,[11] yield: 43–65%.

Synthesis of O,O′-Dialkyl-5-aryl-1-hydroxy-2E, 4E-pentadienylphosphonates (4): General Procedure

2 mmol of dienal (**3**), 4 mmol dimethyl phosphite, and 8 mmol of triethylamine in 10 ml anhydrous methanol (diethyl phosphite in ethanol) were added into a 25 ml reaction flask. The mixture was then stirred at room temperature for 8–16 h (see Table III). The phosphite diester was removed under reduced pressure, and the residue was purified by column chromatography on silica gel using petroleum ether-ethyl acetate (1:2–3, V/V) as the eluent. The physical data are listed in Table III, and ^{1}H NMR, ^{31}P NMR data in Table I.

IR and MS for some compounds **4**:

4a (IR, KBr, cm^{-1}) 3250(sb, OH), 3010, 2980, 1630, 1230(s, P=O), 1062(s, C–O–C)

4g (IR, KBr, cm^{-1}) 3258(mb, OH), 3020, 2960, 1634, 1235(s, P=O), 1058(s, C–O–C)

4f (EI-MS, m/s) 316(5%), 318(M^+, 3:1), 207(78%), 191(22%), 156(18%), 109(30%), 95(100%), 81(42%), 65, 39.

TABLE III Reaction Conditions and Experimental Data

							Elemental analysis/ found (cacld.) (%)		
No.	R	R^1	State	m. p. (°C)	Time (h)	Yield (%)	C	H	N
4a	p-Cl	Et	White crystal	90–91	16	86	55.69 (55.73)	6.35 (6.39)	
4b	p-Cl	Me	Colorless Crystal	105–106	12	88	53.24 (53.08)	5.50 (5.69)	
4c	3,4-OCH_2O	Et	Light yellow Solid	116–118	16	85	57.46 (57.63)	6.30 (6.50)	
4d	3,4-OCH_2O	Me	White crystal	108–109	8	75	54.74 (54.21)	5.45 (5.83)	
4e	*o*-Cl	Et	Light yellow Crystal	94–96	16	74	55.65 (55.73)	6.53 (6.39)	
4f	*o*-Cl	Me	Yellow solid	128–130	12	78	53.01 (53.08)	5.57 (5.69)	
4g	p-CH_3	Et	Colorless Crystal	97–98	16	92	62.80 (62.96)	7.59 (7.72)	
4h	p-CH_3	Me	Light yellow Crystal	113–115	8	61	60.83 (60.81)	7.18 (7.09)	

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