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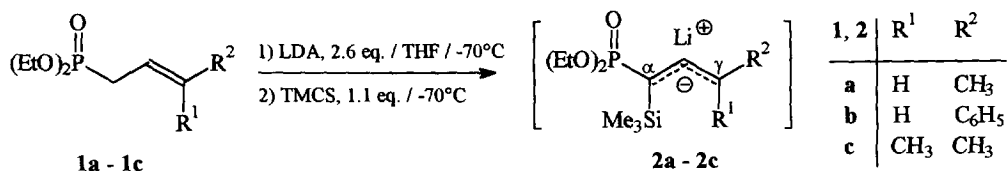
## Unusual and Efficient (*Z*)-Stereoselective Peterson Synthesis of 2-Diethoxyphosphonyl-1-alkoxy-3-methylpenta-1,3-dienes. Their Use in the Diels-Alder Reaction.

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**Abstract** : The lithiated anion of diethyl  $\alpha$ -trimethylsilyl-prenylphosphonate, readily *in situ* generated from diethyl prenylphosphonate, reacts smoothly with various alkyl formates to give the title compounds with exclusive 1-(*Z*)-geometry and in high isolated yield. The [4 + 2] cycloaddition reaction of dienes **3** with electron-deficient dienophiles is described. Copyright © 1996 Published by Elsevier Science Ltd

During the last years, the chemistry of anions derived from allylic-type phosphonates received considerable attention from both structural and synthetic viewpoints.<sup>1-4</sup> In order to control the regioselectivity of these systems, we recently proposed to use the transitory  $\alpha$ -trimethylsilylated carbanions **2** *in situ* generated from the corresponding phosphonates **1** (Scheme 1).<sup>5,6</sup>



Scheme 1

The reactivity and the regioselectivity of the ambident anion **2** toward electrophilic addition are markedly influenced by its own substitution pattern and by the nature as well as the structure of the electrophile. Thus, **2a** showed strict  $\gamma$ -regioselectivity in its reactions with aldehydes,<sup>6</sup> ethyl formate or ethyl chloroformate.<sup>5</sup> In contrast, **2b** reacted with aldehydes at the  $\alpha$ -position only,<sup>6</sup> but was unable to react with ethyl formate. Finally, **2c** added to aromatic aldehydes with exclusive  $\gamma$ -regioselectivity, but reacted both at the  $\gamma$ - and at the  $\alpha$ -position with aliphatic aldehydes.<sup>6</sup> We now report on the reactivity of **2c** toward alkyl formates.

When reacted at  $-70^\circ\text{C}$  with various alkyl formates, carbanion **2c**, quantitatively generated<sup>7</sup> from diethyl prenylphosphonate **1c** as depicted on Scheme 1, behaves as a Peterson reagent, leading to 1-(*Z*)-2-diethoxyphosphonyl-1-alkoxy-3-methylpenta-1,3 dienes **3**, isolated in high yield<sup>8</sup> (Table 1 and Scheme 2).

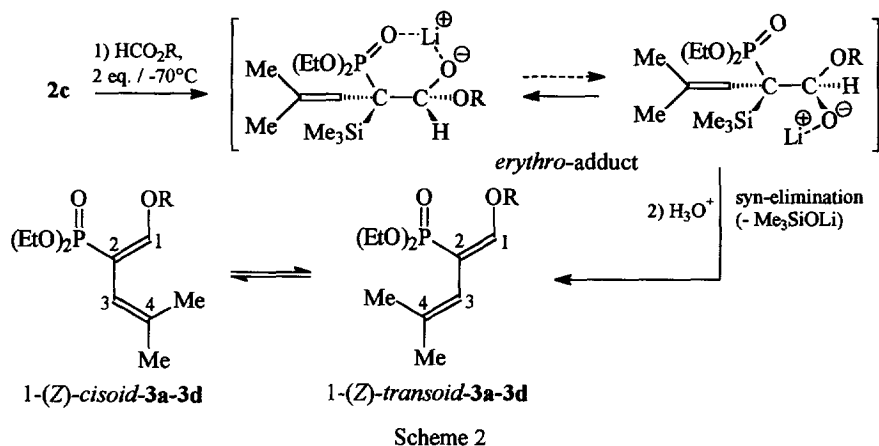
This efficient and strict 1-(*Z*)-stereoselective<sup>9</sup> formation of dienes **3** deserves to be underlined. Indeed, on the one hand, only few reports mention the Peterson reaction with acid derivatives,<sup>10,11</sup> which are in general no good substrates for this olefination process. On the other hand, in the rare examples in which ethyl formate was used to prepare enol ethers by this method, only poor stereoselectivity was observed.<sup>12,13</sup>

In our case, the presence of two methyl groups at the  $\gamma$ -position of **2c** likely determines the  $\alpha$ -regioselectivity of this anion towards the alkyl formate, and favours the fast decomposition of the hindered kinetic *erythro*-adduct,<sup>14</sup> leading to the (*Z*)-enol ether, after *syn*-elimination of the oxophilic silylated moiety, by the Peterson reaction mechanism.<sup>15</sup> Moreover, we noticed that most dienes **3** appeared as a mixture of two isomers. From NMR spectroscopic data, we concluded that we had to deal with a mixture of two conformers, the *cisoid* one being predominant for bulky R groups.<sup>16</sup>

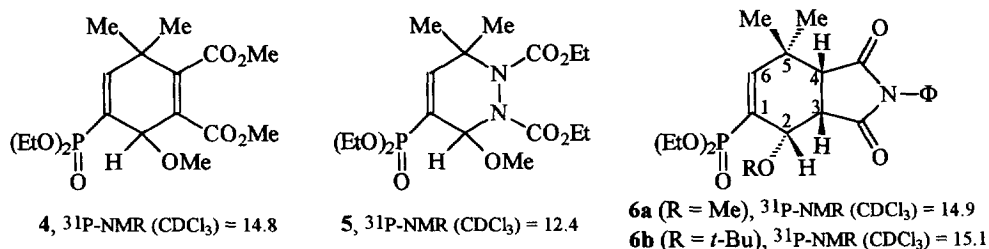
Table 1. Synthesis of Phosphonodienes **3**

Product	R	Yield (a) (%)	% <i>transoid</i> : % <i>cisoid</i> (b)	<sup>31</sup> P NMR (CDCl <sub>3</sub> )	<sup>1</sup> H NMR (CDCl <sub>3</sub> ), for H <sub>1</sub>
				$\delta$ in ppm <i>transoid</i> : <i>cisoid</i>	$\delta$ in ppm ( <sup>3</sup> J <sub>P</sub> H <sub>1</sub> in Hz) <i>transoid</i> : <i>cisoid</i>
<b>3a</b>	Me	92	100 : 0	15.2 : -	6.40 (37.2) : -
<b>3b</b>	Et	89	93 : 7	15.6 : 15.5	6.48 (36.3) : 6.70 (36.4)
<b>3c</b>	<i>i</i> -Pr	72	15 : 85	15.95 : 15.90	6.48 (36.2) : 6.53 (36.5)
<b>3d</b>	<i>t</i> -Bu	84	29 : 71	16.1 : 15.7	6.45 (36.3) : 6.67 (36.7)

(a) Yield in distilled products. All compounds were characterized by <sup>1</sup>H, <sup>13</sup>C NMR spectroscopy, mass spectrometry and C, H elemental microanalysis. (b) Determined by <sup>31</sup>P NMR spectroscopy on crude products.



Then, we used dienes **3** in Diels-Alder cycloaddition reactions. To our knowledge, few examples of Diels-Alder reactions with dienes bearing a phosphonyl group at the C-2 carbon atom have been reported.<sup>17-19</sup> The presence of an electron-donating alkoxide group at the C-1 carbon should favour the reaction. Actually, when dienes **3a** or **3d** were heated with dienophiles as dimethyl acetylenedicarboxylate, diethyl azodicarboxylate or *N*-phenylmaleimide, in a suitable solvent, expected cycloadducts **4**, **5**, **6a** or **6b** (Scheme 3) were obtained in very good yield (76-81%),<sup>20</sup> and with exclusive *endo*-diastereoselectivity in the case of *N*-phenylmaleimide<sup>21</sup> (one enantiomer **6a** or **6b** was represented on Scheme 3).



Scheme 3

In conclusion, we describe, in this communication, an efficient and stereoselective access to new 2-diethoxyphosphonyl-1-alkoxy-3-methyl-1,3-dienes, which proved to be useful Diels-Alder reagents for the synthesis of new attractive cyclic phosphorus compounds.<sup>22</sup>

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7. Formation of **2c** can be monitored by  $^3\text{P}$  NMR spectroscopy [ $\delta$  (THF)  $\sim$  44 ppm].
8. Typical procedure : To a solution of LDA (26 mmol) in THF (25 mL) at  $-70^\circ\text{C}$  was added a solution of **1c** (2.06 g, 10 mmol) in THF (10 mL) over 20 min. A solution of  $\text{Me}_3\text{SiCl}$  (1.3 g, 12 mmol) in THF (10 mL) was added, followed by a solution of *tert*-butyl formate (1.72 g, 20 mmol) in THF (10 mL) and the mixture was stirred for 10 min. at  $-70^\circ\text{C}$ , then hydrolyzed with 4N HCl until pH $\sim$ 2. Usual work-up gave the crude diene **3d**, which was purified by bulb-to-bulb distillation ( $\text{bp}_{0.1} = 115$  to  $122^\circ\text{C}$ , 2.43 g).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 200 MHz) [ $\delta$ ppm, (JHz)] : 1.23, t (7), 6H,  $\text{CH}_3\text{CH}_2\text{O}$ ; 1.29, s, 9H,  $(\text{CH}_3)_3\text{C}$ ; 1.55-1.77, m, 6H,  $(\text{CH}_3)_2\text{C}_4$ ; 3.85-4.1, m, 4H,  $\text{CH}_3\text{CH}_2\text{O}$ ; 5.5-5.65, m, 1H,  $\text{H}_3$ ; 6.45 & 6.67, 2xdd (36.3, 1.4 & 36.7, 1.3), 1H, *transoid*- $\text{H}_1$  & *cisoid*- $\text{H}_1$ .  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ ) [ $\delta$ ppm, (JHz)] : 15.6-16.5, m,  $\text{CH}_3\text{CH}_2\text{O}$ ; 18.1 & 25.1, 2xs, *transoid*- $(\text{CH}_3)_2\text{C}_4$ ; 18.4, d (2.3) & 25.2, s, *cisoid*- $(\text{CH}_3)_2\text{C}_4$ ; 27.5, s,  $(\text{CH}_3)_3\text{C}$ ; 60.7-61.2, m,  $\text{CH}_3\text{CH}_2\text{O}$ ; 73.6, s, *transoid*- $(\text{CH}_3)_3\text{C}$ ; 78.4, s, *cisoid*- $(\text{CH}_3)_3\text{C}$ ; 101.9, d (181.2), *transoid*- $\text{C}_2$ ; 102.0, d (181.6), *cisoid*- $\text{C}_2$ ; 117.7, d (5.9), *transoid*- $\text{C}_3$ ; 118.4, d (6.5), *cisoid*- $\text{C}_3$ ; 134.7, d (11.7), *cisoid*- $\text{C}_4$ ; 134.9, d (11.5), *transoid*- $\text{C}_4$ ; 153.0, d (1), *cisoid*- $\text{C}_1$ ; 158.2, s, *transoid*- $\text{C}_1$ . Moreover, above (*transoid* / *cisoid*)-**3d** mixture was able to be transformed into pure *cisoid*-**3d** by heating at  $120^\circ\text{C}$  for 4-5 h.
9. The *Z*-configuration of  $\text{C}_1=\text{C}_2$  bond in **3** was unambiguously determined by the measurement of  $^3\text{J}_{\text{P-H}_1}$  ( $\sim$  37 Hz) in the  $^1\text{H}$  NMR spectra.  $^3\text{J}_{\text{P-H}}$  values of  $\sim$ 10 Hz were observed for similar dienes of 1-(*E*)-configuration; see Ref. 4.
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14. As proved by monitoring the reaction by  $^{31}\text{P}$  NMR spectroscopy, we were unable to detect any signal corresponding to the adduct, even at  $-70^\circ\text{C}$ .
15. The predominant formation of the *erythro*-adduct could result from a chelation control by the phosphonyl group during the addition of **2c** to the formate. For a discussion of the Peterson reaction mechanism, see for example : Bassindale, A.R.; Ellis, R.J.; Lau, J.C.-Y.; Taylor, P.G. *J. Chem. Soc. Perkin Trans. II*, **1986**, 593-597 and Ref. cited.
16. The attribution of the *cisoid* conformation to the predominant conformer of **3d** resulted from the measurement of a NOE effect of about 4% on H1 upon irradiation of the methyl groups of the prenyl moiety. By analogy with **3d**, the *cisoid* conformers in **3b** and **3c** were assigned to the ones showing the lowest chemical shift in  $^{31}\text{P}$  NMR spectroscopy and the highest chemical shift for H1 in  $^1\text{H}$  NMR spectroscopy. Any NOE effect could not be detected when **3a** was subjected to a similar experiment : the *transoid* conformation was assigned to this structure. For other examples in a related series, see : Brel', V.K.; Komarov, V. Ya.; Ionin, B.I.; Petrov, A.A. *Zh. Obshch. Khim.* **1983**, *53*, 66-75.
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20. Yields in purified products. All compounds were characterized by  $^1\text{H}$ ,  $^{13}\text{C}$ -NMR spectroscopy, mass spectrometry and C, H elemental microanalysis.  
 Typical procedure : A mixture of **3a** (1.24 g, 5 mmol), *N*-phenylmaleimide (1.3 g, 7.5 mmol) and a few mg of 2,6-di-*t*-butyl-4-methylphenol in toluene (20 mL) was boiled for 28 h under argon (progress of the reaction was monitored by  $^{31}\text{P}$ -NMR spectroscopy). Evaporation of the solvent under reduced pressure gave quantitatively the crude product as a sole diastereoisomer. Further purification by column chromatography over  $\text{SiO}_2$  (eluent : ether, then MeOH) led to the pure cycloadduct **6a** as an oil (1.7 g, 81% yield).  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ , 200 MHz) [ $\delta$ ppm, (JHz)] : 1.3, t (7), 6H,  $\text{CH}_3\text{CH}_2\text{O}$ ; 1.4 & 1.5, 2xs, 6H,  $(\text{CH}_3)_2\text{Cs}$ ; 2.95, d (10.6), 1H,  $\text{H-C}_4$ ; 3.2, dd (10.6, 5.0), 1H,  $\text{H-C}_3$ ; 3.4, s, 3H,  $\text{CH}_3\text{O}$ ; 4.0-4.3, m, 4H,  $\text{CH}_3\text{CH}_2\text{O}$ ; 4.6, dd (8.9, 5.0), 1H,  $\text{H-C}_2$ ; 6.95, d (20.5), 1H,  $\text{H-C}_6$ ; 7.2-7.5, m, 5H,  $\text{H}_{\text{arom}}$ .  $^{13}\text{C}\{^1\text{H}\}$ -NMR ( $\text{CDCl}_3$ ) [ $\delta$ ppm, (JHz)] : 16.1 & 16.2, 2xd (6.0 & 6.4),  $\text{CH}_3\text{CH}_2\text{O}$ ; 24.8, d (3.2),  $\text{CH}_3$ -Cs; 32.2, s,  $\text{CH}_3$ -Cs; 34.4, d (15.5), Cs; 46.2, d (7.6), C3; 46.7, d (2.2), C4; 58.5, s,  $\text{CH}_3\text{O}$ ; 61.8 & 62.0, 2xd (6.0 & 5.9),  $\text{CH}_3\text{CH}_2\text{O}$ ; 70.3, d (13.4), C2; 127.5, d (187.0), C1; 126.3, s, *m*-Carom; 128.1, s, *p*-Carom; 129.0, s, *o*-Carom; 131.7, s, *i*-Carom; 158.8, d (8.4), C6; 174.8, d (1.8), C=O; 176.0, s, C=O. MS (70 eV) : 421 (M+); 406 (M-15); 391, 376, 243, 187, 91, 77, 29.
21. The *endo*-configuration was readily assigned from the  $^1\text{H}$ -NMR spectra of **6a** and **6b**, by the measurement of the coupling constants  $^3J_{\text{H}_2\text{H}_3}$  ( $\sim 5$  Hz), which reflects a *cis* arrangement for H2 and H3. See, for example : Barluenga, J.; Tomas, M.; Ballesteros, A.; Lopez, L.A. *Synthesis*, **1995**, 985-988.
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