Hetero-Diels–Alder reactions of α-carbonylated styrylphosphonates with enol ethers. High-pressure influence on reactivity and diastereoselectivity

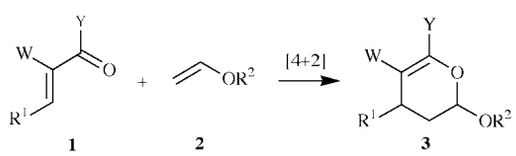
Hashim Al-Badri,[a] Jacques Maddaluno,[b] Serge Masson[c] and Noël Collignon*[a]

[a] *Laboratoire d'Hétérochimie Organique de l'IRCOF, UPRES-A 6014 CNRS, INSA de Rouen, Place E. Blondel, BP 08, 76131 Mont-Saint-Aignan Cedex, France*
[b] *Laboratoire des Fonctions Azotées et Oxygénées Complexes de l'IRCOF, UPRES-A 6014 CNRS, Université de Rouen, 76821 Mont-Saint-Aignan Cedex, France*
[c] *Laboratoire de Chimie Moléculaire et Thioorganique, UMR 6507 CNRS, Université de Caen et ISMRA, 6 Boulevard du Maréchal Juin, 14050 Caen Cedex, France*

Received (in Cambridge) 18th May 1999, Accepted 23rd June 1999

Variously substituted α-carbonylated styrylphosphonates **5** were easily prepared by Knoevenagel-type syntheses, and used as oxadienes in hetero-Diels–Alder [4 + 2] cycloadditions with enol ethers, to give new phosphonylated 3,4-dihydro-2*H*-pyrans **6**. It was confirmed that the reactivity , as well as the *trans*-diastereoselectivity of the reaction, was significantly enhanced by the use of high-pressure conditions, particularly in the presence of Bu^{t}OH as a co-solvent. Moreover, a one-pot synthesis of **6** *via* a tandem-sequence Knoevenagel and hetero-Diels–Alder reactions was achieved.

The hetero-Diels–Alder reaction of α,β-unsaturated carbonyl compounds **1** with electron-rich alkenes such as vinyl ethers **2**, has seen an impressive development during the last decade;[1,2] this inverse-electron-demand [4 + 2] cycloaddition reaction provides a direct access to variously substituted 3,4-dihydro-2*H*-pyrans **3**, which are useful synthetic precursors of carbohydrates and natural products[3] (Scheme 1).



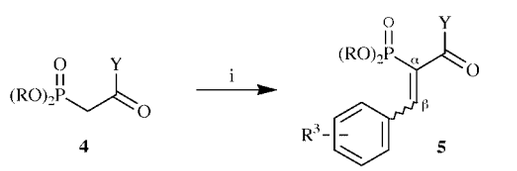
Scheme 1 Hetero-Diels–Alder reaction of 1-oxa-1,3-dienes **1**.

The presence of electron-withdrawing substituents (Y, W) greatly enhances the reactivity of the diene by lowering the energy of its LUMO, and consequently favours the dominant $\{LUMO_{diene} \Leftrightarrow HOMO_{dienophile}\}$ interaction which controls the formation of the cycloadduct π bond.[2,4] For the first time, very recently, 1-oxa-1,3-dienes bearing a phosphonate group on the carbon-1 [**1**, Y = P(O)(OR)$_2$; W = H] have been used as heterodienes in cycloaddition reactions with some enol ethers.[5,6] Our current interest in phosphonodienes synthesis,[7–10] and their use as Diels–Alder reagents,[11] prompts us to publish our results concerning the hetero-Diels–Alder reactions of 1-oxa-1,3-dienes bearing a phosphonate group at position 3 and variously substituted at positions 2 and 4 [**1**, W = P(O)(OR)$_2$; R^1 = aryl; Y = alkyl, aryl or functional group], leading to a new class of 5-phosphono-3,4-dihydro-2*H*-pyrans with promising synthetic potential.

Results and discussion

Synthesis of starting phosphonates 5

First, in this study, we synthesized some new α-carbonylated styrylphosphonates **5a**–**j**, in the series ketones (Y = Me or Ph), keto ester (Y = CO$_2$Et) and keto amide (Y = CONEt$_2$), by Knoevenagel-type reactions (Scheme 2) of the corresponding α-functional methylenephosphonates **4**† with aromatic aldehydes using conventional conditions[13] (method I), or with their bis-morpholino aminal derivatives (method II) following the conditions described by Sakoda *et al.*[14] The results of the synthesis of phosphonates **5** and their characteristics are collected in Table 1. Most of the isolated products were obtained as pure (*E*)-isomers, while for **5j** the isolated product was enriched at more than 95% in its (*E*)-isomer. Moreover, in the case of **5d**,



4	R	Y
4a	Me	Me
4b	Me	Ph
4c	Et	Me
4d	iPr	Me
4e	Me	CO_2Et
4f	Me	$CONEt_2$

5	R	Y	R^3
5a	Me	Me	H
5b	Me	Me	4-NO_2
5c	Me	Me	4-MeO
5d	Me	Me	2-NO_2
5e	Me	Me	2-CF_3
5f	Me	Ph	4-NO_2
5g	Et	Me	4-NO_2
5h	iPr	Me	4-NO_2
5i	Me	CO_2Et	4-NO_2
5j	Me	$CONEt_2$	4-NO_2

Scheme 2 *Reagents and conditions*: i, ArCHO (1 mol equiv.), piperidine (catalytic), PhH (solvent), reflux [Method I][13] or ArCH(morpholino)$_2$ (1 mol equiv.), $ClCH_2CO_2H$ (2 mol equiv.), toluene (solvent), 20 °C [Method II].[14]

† Phosphonates **4** are either commercially available (**4a**,**b**), or easily prepared (**4c**–**f**) by metallation–functionalization of the corresponding methylphosphonate[12] (the synthesis of the new product **4f** is described in the Experimental section as a typical procedure).

Table 1 Synthesis, physical and analytical data of phosphonates **5**

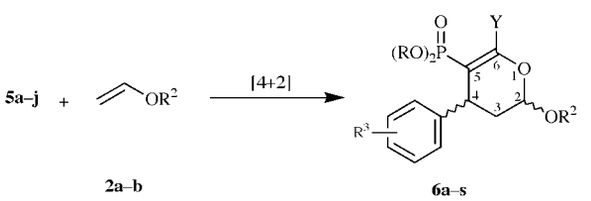
Product	Method	$E:Z$ ratio[a] in the crude mixture	^{31}P ($CDCl_3$), δ (ppm) E; Z	Yield (%)[b] (configuration)	Mp (T/°C)
5a	II	>97:3	18.0; 16.9	86 (E)	[c]
5b	II	96:4	16.1; 12.7	90 (E)	117
5c	II	96:4	18.8; 17.9	83 (E)	[c]
5d	II	78:22	16.7; 15.6	52 (E)[d]	89
5e	II	96:4	16.3; 15.5	80 (E)	90
5f	I	>98:2	16.4; 13.8	86 (E)	114
5g	II	100:0	13.2;	88 (E)	65[e]
5h	II	>98:2	11.1; 9.8	78 (E)	[c]
5i	I	92:8	15.1; 12.0	65[f] (E)	88
5j	II[g]	80:20	16.4; 14.2	70 ($E:Z$ > 95:5)	112

[a] Determined by ^{31}P and/or ^{1}H NMR integration measurements. [b] Product purified by crystallization from *tert*-butyl methyl ether or by flash chromatography over silica gel (eluent: Et_2O) and characterized by ^{1}H and ^{13}C NMR spectroscopy. Satisfactory microanalysis or HRMS (**5f**) was obtained. [c] Oily product. [d] A fraction (9% yield), enriched in the Z-isomer ($Z:E$ > 98:2), was isolated as an oily product. [e] Lit.,[14] 70–72 °C. [f] Product **5i** has to be kept dry and was not able to be purified by chromatography. [g] A mixture (in a ≈ 60:40 ratio) of **5j** and of the corresponding Wittig–Horner product was obtained by using method I.

we were able to separate, besides (*E*)-**5d**, a fraction enriched at more than 98% in (*Z*)-**5d**.‡

Hetero-Diels–Alder reactions of phosphonates 5 with enol ethers 2

The present work describes the cycloaddition of phosphonates **5a**–**j** with commercially available vinyl ethers **2a** and **2b**, under different conditions of temperature and pressure, leading to new 5-dialkoxyphosphoryl-3,4-dihydro-2*H*-pyrans **6a**–**s**, isolated as a mixture of *trans*- and *cis*-diastereomers (Scheme 3



2	R^2
2a	Et
2b	Bu^t

6	R	Y	R^2	R^3
6a	Me	Me	Et	4-NO_2
6b	Me	Me	Bu^t	4-NO_2
6c	Et	Me	Et	4-NO_2
6d	Et	Me	Bu^t	4-NO_2
6e	Pr^i	Me	Et	4-NO_2
6f	Me	Me	Et	H
6g	Me	Me	Bu^t	H
6h	Me	Me	Et	4-MeO
6i	Me	Me	Bu^t	4-MeO
6j	Me	Me	Et	2-NO_2
6k	Me	Me	Bu^t	2-NO_2
6l	Me	Me	Et	2-CF_3
6m	Me	Me	Bu^t	2-CF_3
6n	Me	Me	Et	4-NO_2
6o	Me	Me	Bu^t	4-NO_2
6p	Me	Me	Et	4-NO_2
6q	Me	Me	Bu^t	4-NO_2
6r	Me	Me	Et	4-NO_2
6s	Me	Me	Bu^t	4-NO_2

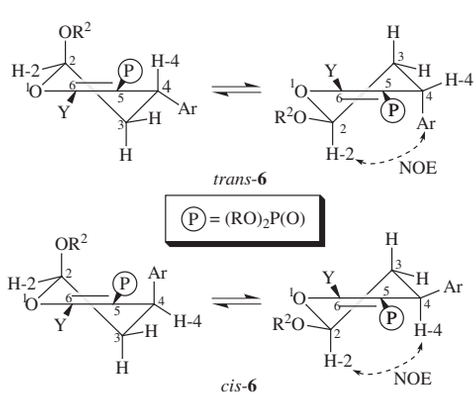
Scheme 3 Hetero-Diels–Alder reaction of phosphonates **5** with vinyl ethers **2**.

and Table 2). The progress of the reaction was monitored by ^{31}P NMR spectroscopy and, generally, the dienophile was used in large excess (5 to 10 mol equiv.) and also served as the reaction solvent.

‡ The (*E*)- and *Z*-geometry of the C^{α}=C^{β} double bond in **5** was assigned by $^{3}J_{PH\beta}$ coupling-constant measurements in ^{1}H NMR spectra.[15,16]

Cycloaddition reactions in the ketone series. The main part of this study (entries 1 to 31, Table 2) was concerned with the hetero-Diels–Alder reaction of keto phosphonates **5a**–**h** with enol ethers **2**. In this series, we started our investigations with the electron-poor diene (*E*)-**5b**, which should have shown good reactivity in the inverse-electron-demand cycloaddition process. Surprisingly, when this diene was allowed to react with ethyl vinyl ether **2a** in refluxing toluene, no cycloadduct was formed, even after 6 days. However, the cycloaddition was complete after only 2 hours at 130 °C in sealed tube without additional solvent (method A), giving a crude mixture containing two phosphorus species [^{31}P NMR $\delta(CDCl_3)$ = 25.68 and 25.67], in the ratio 56:44 (entry 1, Table 2). Flash chromatography over silica gel (eluent: diethyl ether) furnished the purified product **6a** in 94% yield, without altering the ratio of the two components. Moreover, we were able to separate them thoroughly, by using mixtures of diethyl ether and hexane as eluent. Related ^{1}H and ^{13}C NMR spectra unambiguously established their expected dihydropyran structure, while ^{1}H–^{1}H NOESY experiments allowed us to attribute the relative configuration of each isomer. Actually, an NOE effect was observed between the anomeric proton H-2 and the *ortho*-aromatic protons for the major component, establishing its *trans*-configuration (*t*-**6a**); in contrast, for the minor component, both the absence of the above effect and the observation of an NOE coupling interaction between the anomeric proton H-2 and the proton H-4 confirmed its relative *cis*-configuration (*c*-**6a**), each diastereomer being in conformational equilibrium, and assumed to exist in the well accepted rapidly interconverting half-chair forms[17–19] (Scheme 4§).

At this stage it was ascertained that starting oxadiene (*E*)-**5b**,



Scheme 4 Relative configurations and conformations of cycloadducts **6**.

§ One enantiomer of each conformation is represented.

Table 2 Conditions, selectivities and yields of the hetero-Diels–Alder reactions of **5** and **2**

Entry	Diene	Dienophile	Method[a]	Temperature (T/°C)	Time (t/h)	Products[b]	Selectivity[c] *trans*/*cis*	Yield (%)[d]
1	(*E*)-**5b**	**2a**	A	130	2	*t*-**6a**/*c*-**6a**	56:44	94
2			B	20	24		75:25	95
3			C	20	24		92:8	95
4	(*E*)-**5b**	**2b**	A	130	1.5	*t*-**6b**/*c*-**6b**	25:75	96
5			C	20	24		50:50	95
6	(*E*)-**5g**	**2a**	A	130	5	*t*-**6c**/*c*-**6c**	55:45	95
7	(*E*)-**5g**	**2b**	A	130	4	*t*-**6d**/*c*-**6d**	27:73	93
8	(*E*)-**5h**	**2a**	A	130	24	*t*-**6e**/*c*-**6e**	61:39	94
9			B	20	24		84:16	95
10	(*E*)-**5a**	**2a**	A	130	12	*t*-**6f**/*c*-**6f**	54:46	87
11			B	45	48		60:40	92
12			C	45	48		85:15	91
13	(*E*)-**5a**	**2b**	A	130	24	*t*-**6g**/*c*-**6g**	19:81	96
14			B	45	72		17:83	92
15	(*E*)-**5c**	**2a**	A	130	28	*t*-**6h**/*c*-**6h**	52:48	92
16			B	20	26		76:24	93
17	(*E*)-**5c**	**2b**	A	130	28	*t*-**6i**/*c*-**6i**	19:81	89
18			B	20	26		20:80	92
19	(*E*)-**5d**	**2a**	A	130	30	*t*-**6j**/*c*-**6j**	56:44	88
20			B	45	72		91:9	94
21	(*Z*)-**5d**[e]	**2a**	A	130	5		24:76	91
22	(*E*)-**5d**	**2b**	A	130	30	*t*-**6k**/*c*-**6k**	64:36	86
23			B	45	72		56:44	94
24	(*E*)-**5e**	**2a**	A	130	170	*t*-**6l**/*c*-**6l**	69:31	93
25			C	45	190		91:9	95
26	(*E*)-**5e**	**2b**	A	130	144	*t*-**6m**/*c*-**6m**	53:47	87
27			B	45	190		60:40	91
28			C	45	60		85:15	89
29	(*E*)-**5f**	**2a**	A	130	144	*t*-**6n**/*c*-**6n**	50:50	40[f]
30			B	45	72		64:36	93
31			C	45	60		82:18	91
32	(*E*)-**5f**	**2b**	B	20	95	*t*-**6o**/*c*-**6o**	24:76	92
33	(*E*)-**5i**	**2a**	A	20	15	*t*-**6p**/*c*-**6p**	70:30	90
34			B	20	3		72:28	93
35			C	20	3		76:24	89
36	(*E*)-**5i**	**2b**	A	20	15	*t*-**6q**/*c*-**6q**	20:80	88
37			B	20	3		20:80	88
38	(*E*)-**5j**[g]	**2a**	A	20	10	*t*-**6r**/*c*-**6r**	20:80	91
39			B	20	1		33:67	92
40	(*E*)-**5j**[g]	**2b**	A	60	3	*t*-**6s**/*c*-**6s**	25:75	87
41			B	20	3		16:84	93

[a] A: reaction in sealed tube, without additional solvent; B: reaction under 10 kbar, without additional solvent; C: reaction under 10 kbar, in the presence of Bu^{t}OH (1 mol equiv.). [b] Products isolated as a mixture of *trans*- and *cis*-diastereomers. [c] Determined on the crude mixtures, by ^{31}P and/or ^{1}H NMR integration measurements. [d] Yield of purified oily products. Purification by flash chromatography (eluent Et_2O). Purity checked and structures established by ^{1}H and ^{13}C NMR spectroscopy. Satisfactory microanalysis or HRMS was obtained. [e] Diene enriched in the *Z*-isomer ($Z:E > 98:2$). [f] Partial decomposition occurred during the reaction. [g] Diene enriched in the *E*-isomer ($E:Z > 95:5$).

as well as each of the separated pure diastereomeric cycloadducts *t*-**6a** and *c*-**6a**, did not undergo any isomerization, nor decomposition, under the conditions of the reaction. Consequently, it has been assumed afterwards that the [4 + 2] cycloadditions of **5** with **2** were kinetically controlled, and that, when starting from the (*E*)-isomeric oxadiene, the *trans* or the *cis* diastereomers of **6** are formed *via* an *endo-anti* (path a) or an *exo-syn* (path b) transition structure, respectively (Scheme 5). Conversely, the same *trans* and *cis* diastereomers could be obtained by reaction of **2** with the related oxadiene **5** of *Z*-configuration, *via* the corresponding *exo-anti* (path c) and *endo-syn* (path d) transition states, respectively.

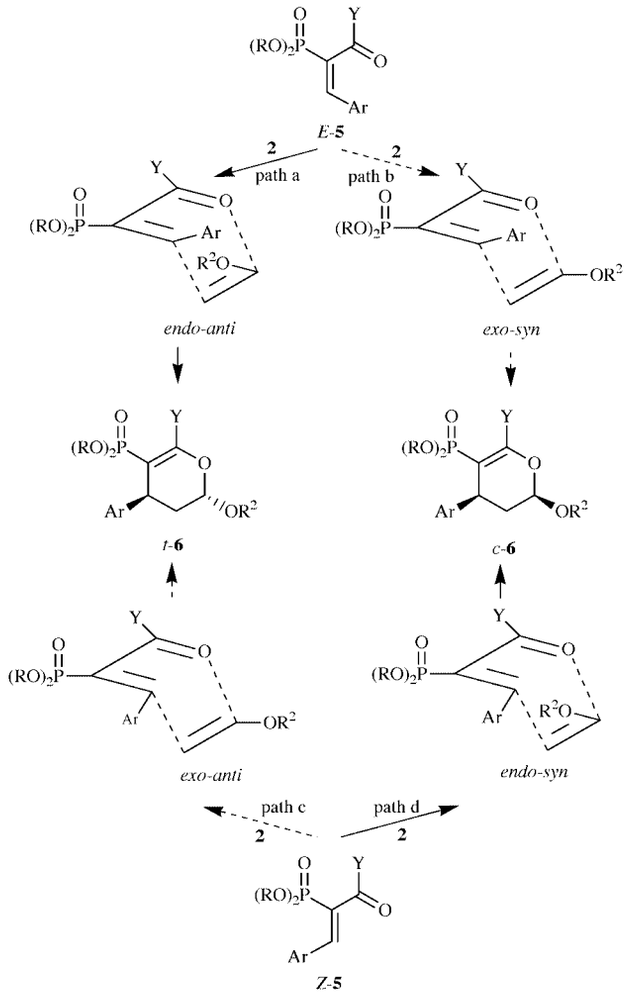
Since poor diastereoselectivity was obtained for the pair of reagents (*E*)-**5b**–**2a** in sealed tubes, we decided to test the reaction at high pressure and we noticed that the amount of the *trans*-product increased significantly under 10 kbar¶ (method B), while the reaction went to completion at 20 °C (entry 2). Moreover, excellent *trans*-diastereoselectivity (de = 84%, entry 3) was attained under the same conditions (10 kbar; 20 °C), but in the presence of one mole equivalent of Bu^{t}OH as a protic co-solvent (method C). These results seem to be in accordance with the well established rule that high pressure favours the more compact transition state,[20–22] namely the *endo-anti* one in this case (path a, Scheme 5). Moreover, the presence of Bu^{t}OH‖ likely favours the *endo*-approach of the reagents too, by simultaneous interaction between the acidic proton of the alcohol with the oxygen atoms of the carbonyl group and of the ether.

Additional insight into the effect of the steric bulkiness of the substituent at the dienophile, was gained by studying the cycloaddition of diene (*E*)-**5b** with *tert*-butyl vinyl ether **2b**. In a sealed tube (entry 4), the *cis* product *c*-**6b** predominated, probably because of the bulky Bu^t group, which allows the *exo-syn* approach (path b, Scheme 5) to be more favourable.[23] With method C (entry 5) lack of diastereoselectivity was an expected consequence of the high-pressure effect, which just compensated for the steric hindrance effect in this case.

We evaluated, at this stage, the effect of the nature of the R group in the phosphonic moiety, by using (*E*)-**5g** (R = Et) and (*E*)-**5h** (R = Pr^i) as dienes (entries 6–9). The results obtained were closely comparable to those of the methyl ester series,

¶ 1 bar = 10^5 Pa.

‖ Using MeOH instead of Bu^{t}OH gave rise to a Michael addition reaction of the alcohol with the oxadiene.



Scheme 5 Transition structures for the formation of *t*-**6** and *c*-**6** cycloadducts.

under the same conditions (compare entries 1 and 6, 4 and 7, for example).

Then, we examined the influence of the nature of the substituent R^3 at the aromatic ring of the diene. As expected, in the absence of an electron-withdrawing group on the benzene ring the diene (*E*)-**5a** was significantly less reactive than was (*E*)-**5b**, as confirmed by times and temperatures required to obtain complete reactions; however, diastereoselectivities of the cycloadditions with **2a** or **2b**, under high pressure or not, were nearly identical with those obtained with diene (*E*)-**5b** (entries 10–14). For diene (*E*)-**5c**, substituted at the *para*-position of the benzene ring by an electron-donating group (MeO), the results were comparable (entries 15–18) to those for the unsubstituted diene (*E*)-**5a**. For these two last dienes, whereas high-pressure conditions increased the *trans*-selectivity of the cycloadditions with **2a** (entries 11, 12, 16), curiously, with **2b** these conditions did not alter the *cis*-selectivity of the cycloaddition (entries 14, 18).

Moreover, we studied the influence of the position of the substituent at the aromatic ring by using dienes **5d** and **5e**, substituted at the *ortho*-position by an electron-withdrawing group: the NO_2 and the CF_3 group, respectively. Examination of the data of the cycloaddition of dienes (*E*)-**5d** and (*E*)-**5e** (entries 19–28) reveals several interesting features. First, the observed diastereoselectivities were very similar and comparable to those obtained with the *para*-nitro-substituted diene (*E*)-**5b**; in particular an excellent *trans*-selectivity was attained, under high-pressure conditions, with dienophile **2a** (entries 20 and 25). Secondly, these *ortho*-substituted dienes showed significant lower reactivities than did diene (*E*)-**5b** : the reactions were slower and required external heating, even under high-pressure conditions. More precisely, as a consequence of combined steric and electronic effects, the facility of cycloaddition of dienes **5** decreases in the following order according to the nature of the R^3 substituent on the benzene ring: *p*-NO_2 > *o*-NO_2 > *o*-CF_3. Moreover, in one example, we confirmed the expected inversion in the *trans* : *cis* ratio of the cycloadduct **6j**, by using a diene of *Z*-configuration [(*Z*)-**5d**] in place of (*E*)-**5d** (compare entries 19 and 21). Finally, when the methyl substituent at the carbonyl group was replaced by a phenyl one, we found that the related diene (*E*)-**5f** was unexpectedly unstable and part decomposed at high temperature in a sealed tube (entry 29). Unquestionably, in this case, the use of high-pressure conditions was very effective and allowed the cycloaddition to proceed at lower temperature with excellent yields, whichever dienophile **2a** or **2b** was employed (entries 30–32). However, the diastereoselectivities of the corresponding reactions remained moderate.

Cycloaddition reactions in the α-keto ester and α-keto amide series. The presence of an electron-withdrawing substituent such as an ester[24–27] or an amide[27–29] group at the 2-position of 1-oxa-1,3-dienes is well known to accelerate the 4π participation of the α,β-unsaturated carbonyl system in [4 + 2] cycloaddition reactions with electron-rich dienophiles. To the best of our knowledge, no such functionalized 1-oxa-1,3-diene, bearing, in addition, a phosphonate group at the 3-position, has been used in hetero-Diels–Alder reactions. As expected, the corresponding phosphono(benzylidene)pyruvic ester (*E*)-**5i** and amide (*E*)-**5j** expressed a better reactivity than did their keto analogs. Generally the cycloaddition reactions with **2a** or **2b** proceeded at room temperature and atmospheric pressure in high yield (entries 33, 36, 38, 40). As in the keto series, reaction of the pyruvic ester (*E*)-**5i** was *trans*-diastereoselective with **2a** (entry 33) and *cis*-diastereoselective with **2b** (entry 36), but to a moderate extent. Unexpectedly, however, the pyruvic amide (*E*)-**5j** gave a comparable *cis*-selective cycloaddition with both **2b** (entry 40) and **2a** (entry 38): in this last case, the steric hindrance of the bulky ethyl substituents at nitrogen very likely destabilized the *endo*-approach of the reagents. Moreover, under high-pressure, whereas the reactions were completed very quickly at 20 °C, in contrast to the keto series, very low changes in the diastereoselectivity were observed under these conditions, even in the presence of the protic co-solvent (entry 35). Possibly, the higher rate of the reaction, as well as the change in electronic distribution caused by the functional substituent might explain the absence of a solvation effect.

Use of a sequential Knoevenagel–hetero-Diels–Alder reaction. Sequential chemical transformations which involve a series of reaction steps without the isolation of any intermediate, and therefore which greatly enhance the efficiency of organic synthesis, have been reviewed.[30] Among them, tandem Knoevenagel–hetero-Diels–Alder reactions have been successfully used in order to synthesize several natural products.[31] We were interested in developing such a sequence, particularly in the case of phosphono(benzylidene)pyruvic ester **5i**, which underwent some decomposition during its purification and which had to be stored dry.** Thus, we decided to realize the sequence represented in Scheme 6, allowing the direct synthesis of cycloadducts **6p** or **6r** from a three-component system including *p*-nitrobenzaldehyde, ethyl vinyl ether **2a** and phosphonopyruvate **4e** or phosphonopyruvamide **4f**, respectively.

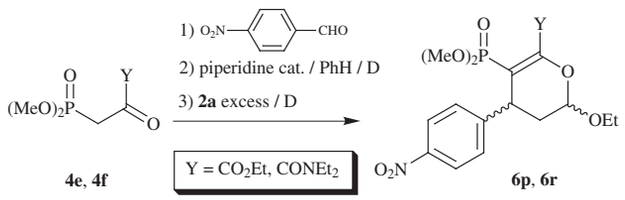
The reagents were introduced into a reactor equipped with a Dean–Stark separator, the progress of the reaction being monitored by ^{31}P NMR spectroscopy. In the case of the phosphonopyruvate **4e**, the dienophile **2a** had to be added after the complete formation of the intermediate Knoevenagel

** See footnote *f*, Table 1.

Table 3 Synthesis of **6p** and **6r** by a tandem-sequence Knoevenagel–hetero-Diels–Alder reaction

Entry	Product	Time (*t*/h)[a]	Selectivity[b] *trans*/*cis*	Yield (%)[c] (Calc. yield)[d]
1	*t*-**6p**/*c*-**6p**	16	24:76	87 (58.5)
2	*t*-**6r**/*c*-**6r**	4.5	22:78	91 (63.7)

[a] Time for the overall sequence. [b] Determined on the crude mixture, by ^{31}P and ^{1}H integration measurements. [c] Yield of isolated products, purified by flash chromatography (eluent Et_2O). [d] Calculated overall yield for the sequence in two separate reactions.



Scheme 6 Tandem-sequence Knoevenagel–hetero-Diels–Alder reactions.

product in order to avoid the growth of a non-identified phosphorus by-product. On the other hand, in the case of the phosphonopyruvamide **4f** the concomitant addition of the three components of the reaction is recommended: it avoided the formation of the troublesome Wittig–Horner product.†† As shown in Table 3, the yields of isolated cycloadducts were excellent and much higher than the overall yields calculated for the corresponding sequences in two separate reactions. The *trans*:*cis* ratio obtained for the cycloadduct **6r** by the tandem-sequence (entry 2, Table 3) was comparable to that observed in the corresponding separate reactions (entry 38, Table 2), confirming the *exo*-selectivity of the cycloaddition of the pair of reagents (*E*)-**5j–2a**. In contrast, the *trans*:*cis* ratio of the cycloadduct **6p** directly prepared from **4e** (entry 1, Table 3), was roughly the inverse of that obtained in the separate-cycloadditions method (entry 33, Table 2). Obviously, the change in the reaction medium, and especially the presence of the piperidine in the sequential method, might be the cause of the inversion of the diastereoselectivity. This hypothesis was confirmed by the following experiment: upon heating of (*E*)-**5i** with **2a**, in benzene and in the presence of a catalytic amount of piperidine, cycloadduct **6p** was obtained in a 25:75 *trans*:*cis* ratio, very close to that obtained by the sequential method. In order to explain the role played by the piperidine in the selectivity of the reaction, we separated the two diastereomers *t*-**6p** and *c*-**6p** by column chromatography, and we heated them separately, in the presence of piperidine, under conditions similar to those of the corresponding sequential reaction. Each diastereomer was recovered unchanged after these attempts, confirming the absence of any isomerization reaction due to the basic medium. Another explanation of the role of the piperidine during the cycloaddition process might be the transient formation of an ionic adduct resulting from 1,4-addition of the nucleophilic amine to the oxadiene, leading to a dominating dipolar cycloaddition mechanism. In such a process, the development of a negative charge at the oxygen atom of the diene should be unfavourable to the *endo*-approach of the reagents, because of the repelling interaction between their respective oxygen sites.

Additional remarks on the spectroscopic data of phosphonodihydropyrans 6. In some cases, relative configuration and predominant conformation of substituted 3,4-dihydro-2*H*-pyrans have been previously established from the related ^{1}H NMR spectra, by measuring the coupling constants of the anomeric H-2 proton.[17–19] Having determined the *trans*- or *cis*-configuration of the 5-dialkoxyphosphoryl-3,4-dihydro-2*H*-pyrans **6**, as a result of NOESY experiments realized on the separated diastereomers (for **6a**, **6b**, **6c**, **6k**, **6n**, **6o**, **6p**, **6r** and **6s**) or on their mixture (for the others), we have collected in Table 4 some characteristic values abstracted from the detailed NMR data (given in the Experimental section). These values are concerned with the ^{31}P NMR chemical shift and with the ^{1}H, as well as the ^{13}C NMR, data of the anomeric H-2 and C-2 nuclei.‡‡ From Table 4, it seems, first, that ^{31}P NMR chemical shift cannot be used as a criterion for the stereochemical assignment of phosphonodihydropyrans **6**; secondly, although the ^{1}H chemical shift of the anomeric H-2 proton of the *trans*-diastereomer is found to be systematically lower than that of its *cis*-counterpart, sometimes the very slight difference of chemical shifts between the two isomers (lower than 0.05 ppm for **6k**, **6m** and **6o**, for example) makes the corresponding assignment risky; moreover, the variable coupling patterns (doublet of doublet or superficial triplet) of the related signals, as well as the observed coupling constants, indicate that the preferential conformation having the C-2 alkoxy group in an axial or in an equatorial position (Scheme 4) of each diastereomer is variable from one product to another. Consequently, these ^{1}H NMR data cannot be used as criteria of assignment. Finally, the most outstanding feature is the ^{13}C NMR chemical shift of the C-2 anomeric carbon, which varies in the range 91–100 ppm and which is found to be systematically lower by from 1 ppm (**6a**) up to more than 3 ppm (**6o**) for the *trans*-diastereomer, in comparison with the *cis*-one. Relying on the about twenty examples studied in this work, we think, therefore, that the relationship $\delta_{C\text{-}2}{}^{trans} < \delta_{C\text{-}2}{}^{cis}$ can be securely used as a criterion for the relative configurational assignment of the phosphonodihydropyrans of type **6**, in particular when the results of NOE experiments are of questionable value in this regard.

Conclusions

In this work we studied the hetero-Diels–Alder reaction of easily available α-carbonylated styrylphosphonates in the ketone, ester and amide series, with enol ethers, leading to new 5-phosphonylated 3,4-dihydro-2*H*-pyrans. Although the yields were generally quantitative in a sealed tube at 130 °C, we showed that the use of high-pressure conditions not only allowed the reaction to proceed at lower temperature, but significantly enhanced the *trans*-diastereoselectivity of the cycloaddition, particularly by the use of Bu^{t}OH as a co-solvent. Moreover, we achieved, in two examples, the synthesis of the heterodiene and its subsequent cycloaddition, in a sole reactor, by a tandem-sequence Knoevenagel–hetero-Diels–Alder reaction. Finally, we have proposed a useful criterion for the stereochemical assignment of the cycloadducts, based on the chemical shift of the anomeric carbon of the dihydropyran ring. Further investigations, into the use of Lewis acid catalysts in an enantioselective version of the studied reaction, are now in progress.

Experimental

General

Solvents were purified by conventional methods prior to use. Reagents were purchased from common commercial suppliers. Metallation experiments were performed under an atmosphere of dry argon. High-pressure cycloaddition reactions were performed in a Unipress piston-cylinder apparatus for pressures up to 14 kbar. TLC was performed on Merck 60F-254 silica gel plates and column chromatography over silica gel SI 60 (230–

†† See footnote *g*, Table 1.

‡‡ For numbering of the proton and carbon atoms of the dihydropyran ring, see Scheme 4.

Table 4 Characteristic NMR data of cycloadducts **6**

	^{31}P NMR ($CDCl_3$) δ/ppm		^{1}H NMR ($CDCl_3$) for H-2 δ/ppm, multiplicity (J/Hz)		^{13}C NMR ($CDCl_3$) for C-2 δ/ppm	
Product	*trans*	*cis*	*trans*	*cis*	*trans*	*cis*
6a	25.68	25.67	4.85, dd (7.9, 2.6)	5.0, t (2.8)	96.73	97.73
6b	26.04	26.12	5.06, dd (7.8, 2.7)	5.28, t (3.2)	91.29	92.68
6c	22.63	22.77	4.85, dd (8.2, 2.6)	5.05, t (2.8)	96.42	97.68
6d	22.98	23.14	5.05, dd (7.9, 2.6)	5.25, t (3.1)	91.22	92.60
6e	22.63	22.77	4.75, dd (8.1, 2.6)	5.0, t (2.6)	96.51	98.87
6f	26.64	26.36	4.80, t (6.5)	4.96, dd (6.3, 2.4)	97.33	98.93
6g	27.0	26.74	5.07, dd (8.8, 2.5)	5.17, dd (7.0, 2.1)	91.85	93.98
6h	26.79	26.51	4.77, t (6.2)	4.95, dd (6.3, 2.3)	97.32	98.93
6i	27.03	26.74	5.05, dd (8.8, 2.6)	5.12, dd (7.1, 2.2)	91.71	93.80
6j	25.12	25.17	4.93, dd (7.6, 2.6)	5.01, dd (5.2, 2.6)	97.0	98.45
6k	25.43	25.60	5.19, dd (7.6, 2.7)	5.22, dd (5.9, 2.6)	91.66	93.42
6l	25.38	25.39	4.90, dd (8.3, 2.8)	4.96, dd (6.2, 2.4)	96.82	98.63
6m	25.71	25.82	5.15, dd (8.3, 2.6)	5.18, dd (6.4, 2.6)	91.41	93.65
6n	23.52	23.59	5.15, t (3.1)	5.20, dd (6.7, 2.7)	96.80	99.66
6o	23.94	23.88	5.38, dd (4.7, 2.5)	5.39, dd (7.6, 2.0)	91.80	95.04
6p	20.46	20.55	5.10, dd (4.8, 2.4)	5.16, t (3.4)	97.35	98.86
6q	21.05	21.02	5.33, t (2.2)	5.38, t (2.0)	92.50	94.39
6r	20.95	21.01	4.98, dd (6.8, 2.7)	5.15, t (2.8)	97.42	98.53
6s	21.38	21.42	4.71, dd (7.7, 2.7)	5.41, t (2.9)	92.45	93.48

400 mesh). Gas–liquid chromatography (GLC) was performed on a Varian 3300 chromatograph equipped with a 15 m Megabore OV 101 column. Mps were taken on a Kofler apparatus and are uncorrected. Elemental microanalyses were carried out on a Carlo Erba EA 1110 analyser. HRMS measurements were performed under electronic impact at 70 eV on a JEOL AX 500 spectrometer. NMR spectra were recorded on a Bruker DXP 300 spectrometer operating at 300 MHz for proton, 75.4 MHz for carbon, and 121.5 MHz for phosphorus; chemical shifts (δ) are expressed in ppm relative to TMS for ^{1}H and ^{13}C nuclei and to H_3PO_4 for ^{31}P nucleus; coupling constants (J) are given in Hz; coupling multiplicities are reported using conventional abbreviations.

Typical procedure for the synthesis of phosphonate 4f

A mixture of BuLi in hexane (6.6 cm^3, 10 mmol) and THF (30 cm^3) under argon was cooled to −70 °C. Dimethyl methylphosphonate (1.24 g, 10 mmol) in THF (10 cm^3) was added dropwise with stirring for about 15 min, after which a solution of ethyl *N*,*N*-diethyloxamate (1.73 g, 10 mmol) in THF (10 cm^3) was added dropwise. The temperature was not allowed to exceed −70 °C during the addition. The reaction mixture was stirred for 60 min; then, the reaction was quenched at −70 °C, using 4 mol dm^{-3} aq. HCl until pH ≈ 1. Diethyl ether (10 cm^3) was then added and the organic phase was separated. The aqueous phase was extracted with methylene dichloride (3 × 15 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure to give the crude product which was purified by chromatography over silica gel and elution with (1 : 1) Et_2O–CH_2Cl_2 to yield the pure product. 3-(*Dimethoxyphosphoryl*)-N,N-*diethyl*-2-*oxopropanamide* **4f** was obtained as a liquid (2.25 g, 90%), bp 120 °C/0.03 mmHg (Found: C, 42.93; H, 7.26; N, 5.78. $C_9H_{18}N_2O_5P$ requires C, 43.02; H, 7.17; N, 5.57%); δ_P 22.9; δ_H 1.13 and 1.17 (6H, 2 t, J 7.0, CH_3CH$_2$N), 3.28 and 3.35 (4H, 2 q, J 7.0, CH$_3$CH_2N), 3.6 (2H, d, J 23.3, PCH_2O), 3.73 (6H, d, J 11.3, CH_3OP); δ_C 11.9 and 13.72 (2 s, CH$_3$CH$_2$N), 37.56 (d, J 88.75, PCH$_2$CO), 39.58 and 41.85 (2 s, CH$_3$$CH_2$N), 52.63 (d, J 6.26, CH$_3$OP), 164.28 (s, NCO), 190.66 (d, J 4.83, CO).

General procedure for the synthesis of α-carbonylated styryl-phosphonates 5 (method I)

In a 100 cm^3 flask equipped with a Dean–Stark separator and a reflux condenser were placed a mixture of equimolar amounts (10 mmol) of phosphonate **4** and the appropriate aldehyde in benzene (30 cm^3) and a few drops of piperidine. The reaction mixture was refluxed for 24 h, then the benzene was removed by distillation under reduced pressure. The crude product was then purified as indicated in Table 1 to give the pure oxadiene **5**.

General procedure for the synthesis of α-carbonylated styryl-phosphonates 5 (method II)

To a solution of phosphonate **4** (10 mmol) and chloroacetic acid (1.85 g, 20 mmol) in toluene (15 cm^3) was added the appropriated bis(morpholino) aldehyde aminal§§ (10 mmol). The mixture was stirred at 20 °C for several hours, the reaction being monitored by ^{31}P NMR spectroscopy. The reaction mixture was then hydrolysed by water (20 cm^3) and the residue obtained after the usual work-up was purified as indicated in Table 1, leading to pure oxadiene **5**.

(*E*)-3-Dimethoxyphosphoryl-4-phenylbut-3-en-2-one (*E*)-5a. *Oily product*, bp 135 °C/0.04 mmHg, purified by chromatography over silica gel and elution with diethyl ether (Found: C, 56.46; H, 5.78. $C_{12}H_{15}O_4P$ requires C, 56.69; H, 5.90%); δ_P 18.0; δ_H 2.18 (3H, s, CH_3CO), 3.77 (6H, d, J 11.1, CH_3OP), 7.25–7.36 (5H, m, H$_{arom}$), 7.55 (1H, d, J 25.47, H-4); δ_C 31.17 (d, J 2.34, CH$_3$CO), 52.78 (d, J 5.68, CH$_3$OP), 128.65, 129.0 and 130.2 (3 s, *o*, *m, p*-C$_{arom}$), 132.8 (d, J 161.5, C-3), 133.2 (d, J 21.6, *i*-C$_{arom}$), 145.6 (d, J 5.88, C-4), 202.68 (d, J 8.5, CO).

(*E*)-3-Dimethoxyphosphoryl-4-(4-nitrophenyl)but-3-en-2-one (*E*)-5b. *Yellow solid*, purified by crystallization from *tert*-butyl methyl ether (Found: C, 48.25; H, 4.47; N, 4.78. $C_{12}H_{14}NO_6P$ requires C, 48.16; H, 4.68; N, 4.68%); δ_P 16.1; δ_H 2.25 (3H, s, CH_3CO), 3.82 (6H, d, J 11.2, CH_3OP), 7.52 and 8.23 (4H, 2 d, J 8.8, H$_{arom}$), 7.52 (1H, d, J 25.2, H-4); δ_C 31.0 (s, CH$_3$CO), 53.5 (d, J 5.7, CH$_3$OP), 124.0 and 130.0 (2 s, *o*, *m*-C$_{arom}$), 137.5 (d, J 169.3, C-3), 139.5 (d, J 21.9, *i*-C$_{arom}$), 142.8 (d, J 6.0, C-4), 148.8 (s, *p*-C$_{arom}$), 202.0 (d, J 8.5, CO).

(*E*)-3-Dimethoxyphosphoryl-4-(4-methoxyphenyl)but-3-en-2-one (*E*)-5c. *Oily product*, purified by chromatography over silica gel and elution with diethyl ether (Found: C, 54.92; H, 5.78. $C_{13}H_{17}O_5P$ requires C, 54.92; H, 5.98%); δ_P 18.8; δ_H 2.21 (3H, s, CH_3CO), 3.74 (6H, d, J 11.2, CH_3OP), 3.8 (3H, s, OCH_3), 6.81

§§ The required aminals were prepared from the corresponding aldehydes according to ref. 14.

and 7.25 (4H, 2 d, *J* 8.8, H_{arom}), 7.5 (1H, d, *J* 25.7, H-4); δ_C 31.03 (d, *J* 2.5, *C*H_3CO), 52.9 (d, *J* 5.7, *C*H_3OP), 55.4 (s, O*C*H_3), 114.4 and 131.4 (2 s, *o*, *m*-C_{arom}), 126.0 (d, *J* 22.0, *i*-C_{arom}), 129.5 (d, *J* 173.0, C-3), 145.85 (d, *J* 6.3, C-4), 161.5 (s, *p*-C_{arom}), 203.5 (d, *J* 8.8, CO).

(*E*)-3-Dimethoxyphosphoryl-4-(2-nitrophenyl)but-3-en-2-one (*E*)-5d. *Yellow solid*, separated by chromatography over silica gel and elution with (5:100) hexane–diethyl ether (Found: C, 48.18; H, 4.69; N, 4.65. $C_{12}H_{14}NO_6P$ requires C, 48.16; H, 4.68; N, 4.68%); δ_P 16.7; δ_H 1.92 (3H, s, C*H*$_3$CO), 3.7 (6H, d, *J* 11.25, C*H*$_3$OP), 7.25 (1H, d, *J* 7.35, H_{arom}), 7.4–7.59 (2H, m, H_{arom}), 7.88 (1H, d, *J* 23.93, H-4), 8.18 (1H, d, *J* 8.77, H_{arom}); δ_C 31.0 (d, *J* 0.83, *C*H_3CO), 53.28 (d, *J* 5.66, *C*H_3OP), 125.1, 130.3, 130.7 and 134.0 (4 s, *o*-, *m*-, *p*-C_{arom}), 131.0 (d, *J* 21.8, *i*-C_{arom}), 134.6 (d, *J* 171.1, C-3), 145.0 (d, *J* 7.5, C-4), 146.8 (s, *o*-C_{arom}), 199.8 (d, *J* 10.64, CO).

(*Z*)-3-Dimethoxyphosphoryl-4-(2-nitrophenyl)but-3-en-2-one (*Z*)-5d. *Yellow oil*, separated by chromatography over silica gel and elution with (5:100) hexane–diethyl ether (Found: C, 48.26; H, 4.71; N, 4.63. $C_{12}H_{14}NO_6P$ requires C, 48.16; H, 4.68; N, 4.68%); δ_P 15.6; δ_H 2.5 (3H, s, C*H*$_3$CO), 3.5 (6H, d, *J* 10.8, C*H*$_3$OP), 7.25 (1H, d, *J* 7.35, H_{arom}), 7.45–7.7 (2H, m, H_{arom}), 8.18 (1H, d, *J* 8.75, H_{arom}), 8.3 (1H, d, *J* 44.2, H-4); δ_C 28.0 (d, *J* 2.57, *C*H_3CO), 52.74 (d, *J* 6.26, *C*H_3OP), 125.5, 128.2, 130.8 and 134.0 (4 s, *o*-, *m*-, *p*-C_{arom}), 131.8 (d, *J* 17.96, *i*-C_{arom}), 133.5 (d, *J* 190.2, C-3), 146.1 (s, *o*-C_{arom}), 151.15 (d, *J* 3.5, C-4), 197.36 (d, *J* 11.1, CO).

(*E*)-3-Dimethoxyphosphoryl-4-[2-(trifluoromethyl)phenyl]but-3-en-2-one (*E*)-5e. *Colourless solid*, purified by crystallization from *tert*-butyl methyl ether (Found: C, 48.32; H, 4.26. $C_{13}H_{14}F_3O_4P$ requires C, 48.44; H, 4.34%); δ_P 16.3; δ_H 1.93 (3H, s, C*H*$_3$CO), 3.8 (6H, d, *J* 10.3, C*H*$_3$OP), 7.3–7.72 (4H, m, H_{arom}), 7.9 (1H, d, *J* 24.4, H-4); δ_C 30.93 (d, *J* 2.62, *C*H_3CO), 53.22 (d, *J* 5.66, *C*H_3OP), 124.0 (q, *J* 273.8, Ar*C*F_3), 126.2 (q, *J* 6.0, *C*CF_3), 127.9 (q, *J* 30.56, *C*F_3), 129.65, 130.3 and 132.11 (3 s, *o*-, *m*-, *p*-C_{arom}), 133.2 (d, *J* 22.0, *i*-C_{arom}), 136.85 (d, *J* 169.7, C-3), 143.1 (d, *J* 6.56, C-4), 201.15 (d, *J* 9.2, CO).

(*E*)-2-Dimethoxyphosphoryl-3-(4-nitrophenyl)-1-phenylprop-2-en-1-one (*E*)-5f. *Yellow solid*, purified by crystallization from *tert*-butyl methyl ether [HRMS required for $C_{17}H_{16}NO_6P$ (*M*): 361.0715. Found: M^+, 361.0711]; δ_P 16.4; δ_H 3.74 (6H, d, *J* 12.0, C*H*$_3$OP), 7.2–7.45 and 7.65–7.78 (7H, 2 m, H_{arom}), 7.58 (1H, d, *J* 26.4, H-4), 7.95 (2H, d, *J* 8.78, H_{arom}); δ_C 53.3 (d, *J* 5.9, *C*H_3OP), 123.7, 128.6, 129.3, 130.1, 134.5 and 134.7 (6 s, *o*-, *m*-, *p*-C_{arom}), 134.6 (d, *J* 170.7, C-2), 139.3 (d, *J* 21.96, *i*-C_{arom}), 143.5 (d, *J* 6.0, C-3), 148.0 (s, *p*-C_{arom}), 194.4 (d, *J* 7.7, CO).

(*E*)-3-Diethoxyphosphoryl-4-(4-nitrophenyl)but-3-en-2-one (*E*)-5g. *Yellow solid*, purified by crystallization from *tert*-butyl methyl ether (Found: C, 51.25; H, 5.42; N, 4.16. $C_{14}H_{18}NO_6P$ requires C, 51.37; H, 5.50; N, 4.28%); δ_P 13.2; δ_H 2.4 (6H, t, *J* 7.1, C*H*$_3$CH$_2$OP), 2.3 (3H, s, C*H*$_3$CO), 4.25 (4H, q, *J* 7.1, CH$_3$C*H*$_2$OP), 7.52 and 8.25 (4H, 2 d, *J* 8.8, H_{arom}), 7.6 (1H, d, *J* 24.27, H-4); δ_C 16.15 (d, *J* 6.4, *C*H$_3$CH$_2$OP), 31.2 (d, *J* 0.9, *C*H$_3$CO), 63.08 (d, *J* 5.77, CH$_3$*C*H$_2$OP), 123.9 and 129.8 (2 s, *o*-, *m*-C_{arom}), 138.32 (d, *J* 168.97, C-3), 139.74 (d, *J* 21.88, *i*-C_{arom}), 141.72 (d, *J* 6.0, C-4), 148.26 (s, *p*-C_{arom}), 200.1 (d, *J* 8.67, CO).

(*E*)-3-Diisopropoxyphosphoryl-4-(4-nitrophenyl)but-3-en-2-one (*E*)-5h. *Yellow oil*, purified by chromatography over silica gel and elution with diethyl ether (Found: C, 53.93; H, 6.06; N, 3.82. $C_{16}H_{22}NO_6P$ requires C, 54.08; H, 6.19; N, 3.94%); δ_P 11.1; δ_H 1.27 and 1.3 {12H, 2 d, *J* 6.2, [(C*H*$_3$)$_2$CHO]$_2$P}, 2.23 (3H, s, C*H*$_3$CO), 4.55 {2H, m, [(CH$_3$)$_2$C*H*O]$_2$P}, 7.45 and 8.15 (4H, 2 d, *J* 8.77, H_{arom}), 7.51 (1H, d, *J* 24.86, H-4); δ_C 23.5–23.78 {m, [(*C*H$_3$)$_2$CHO]$_2$P}, 31.14 (s, *C*H$_3$CO), 72.0 {d, *J* 6.2, [(CH$_3$)$_2$-*C*HO]$_2$P}, 123.8 and 129.7 (2 s, *o*-, *m*-C_{arom}), 139.3 (d, *J* 21.8, *i*-C_{arom}), 140.0 (d, *J* 162.7, C-3), 140.75 (d, *J* 6.7, C-4), 148.1 (s, *p*-C_{arom}), 201.87 (d, *J* 8.5, CO).

(*E*)-Ethyl 3-dimethoxyphosphoryl-4-(4-nitrophenyl)-2-oxobut-3-enoate (*E*)-5i. *Yellow solid*, purified by crystallization from *tert*-butyl methyl ether; HRMS required for $C_{14}H_{16}NO_8P$ (*M*): 357.0613. Found: M^+, 357.0601; δ_P 15.1; δ_H 1.1 (3H, t, *J* 7.1, C*H*$_3$CH$_2$O), 3.8 (6H, d, *J* 11.4, C*H*$_3$OP), 4.08 (2H, q, *J* 7.1, CH$_3$C*H*$_2$O), 7.4 and 8.2 (4H, 2 d, *J* 8.7, H_{arom}), 8.0 (1H, d, *J* 23.8, H-4); δ_C 13.57 (s, *C*H$_3$CH$_2$O), 53.46 (d, *J* 5.66, *C*H$_3$OP), 63.0 (s, CH$_3$*C*H$_2$O), 124.0 and 130.0 (2 s, *o*-, *m*-C_{arom}), 132.2 (d, *J* 174.4, C-3), 139.39 (d, *J* 20.3, *i*-C_{arom}), 148.4 (s, *p*-C_{arom}), 149.21 (d, *J* 5.8, C-4), 159.65 (d, *J* 5.58, CO), 186.29 (d, *J* 7.8, CO).

3-(Dimethoxyphosphoryl)-*N*,*N*-diethyl-4-(4-nitrophenyl)-2-oxobut-3-enamide (*E*)-5j. *Yellow solid*, purified by chromatography over silica gel and elution with diethyl ether (Found: C, 49.91; H, 5.36; N, 7.13. $C_{16}H_{21}N_2O_7P$ requires C, 50.00; H, 5.46; N, 7.29%); δ_P 16.4; δ_H 1.04 and 1.22 (6H, 2 t, *J* 7.0, C*H*$_3$CH$_2$N), 3.29 and 3.38 (4H, 2 q, *J* 7.0, CH$_3$C*H*$_2$N), 3.8 (6H, d, *J* 12.0, C*H*$_3$OP), 7.6 and 8.15 (4H, 2 d, *J* 8.77, H_{arom}), 7.8 (1H, d, *J* 23.94, H-4); δ_C 12.0 and 13.9 (2 s, *C*H$_3$CH$_2$N), 40.6 and 41.9 (2 s, CH$_3$*C*H$_2$N), 53.2 (d, *J* 5.3, *C*H$_3$OP), 123.74 and 128.8 (2 s, *o*-, *m*-C_{arom}), 133.8 (d, *J* 171.8, C-3), 139.8 (d, *J* 20.37, *i*-C_{arom}), 148.47 (s, *p*-C_{arom}), 149.6 (d, *J* 6.26, C-4), 164.4 (s, CO), 189.51 (d, *J* 12.75, CO).

General procedure for the synthesis of phosphonopyrans 6 in a sealed tube (method A)

A solution of oxadiene **5** (2 mmol) in an excess of dienophile **2** (5–10 equiv.) was placed in a sealed tube and heated at a temperature and for a time as indicated in Table 2, the reaction being monitored by ^{31}P NMR spectroscopy. The excess of dienophile was then evaporated under reduced pressure and the residue was purified by flash chromatography over silica gel and elution with diethyl ether to give the cycloadduct **6**. All the products exhibited ^1H NMR, ^{13}C NMR and microanalysis or HRMS data in agreement with the assigned structures.

General procedure for the synthesis of phosphonopyrans 6 by the pressure-promoted hetero-Diels–Alder reaction (methods B and C)

A solution of oxadiene **5** (1 mmol) in an excess of dienophile **2** (5–10 equiv.), and possibly containing 1 equiv. of Bu^{t}OH (Method C), was introduced in a pressure vessel, then put in the high-pressure apparatus, and left under 10 kbar at a temperature and for a time indicated in Table 2. Then, after release of pressure, further work-up and purification were carried out as above, giving the pure product **6**.

5-(Dimethoxyphosphoryl)-2-ethoxy-3,4-dihydro-6-methyl-4-(4-nitrophenyl)-2*H*-pyran 6a. *Viscous product* purified by flash column chromatography over silica gel and elution with diethyl ether (Found: C, 51.88; H, 6.15; N, 3.82. $C_{16}H_{22}NO_7P$ requires C, 51.75; H, 5.92; N, 3.77%), isolated as a mixture of diastereomers, which have been separated.

***t*-6a.**—Viscous product, separated by column chromatography over silica gel and elution with hexane–diethyl ether in gradient (100:0 to 0:100); δ_P 25.68; δ_H 1.1 (3H, t, *J* 7.2, C*H*$_3$CH$_2$O), 1.7–1.98 and 2.0–2.12 (2H, 2 m, H$_2$-3), 2.2 (3H, d, *J* 1.1, C*H*$_3$-6), 3.3 and 3.55 (6H, 2 d, *J* 11 and 11.1, C*H*$_3$OP), 3.4–3.5 (1H, m, CH$_3$C*H*O), 3.7–3.93 (2H, m, CH$_3$C*H*O and H-4), 4.85 (1H, dd, *J* 7.9 and 2.6, H-2), 7.35 and 8.14 (4H, 2 d, *J* 8.7, H_{arom}); δ_C 15.1 (s, *C*H$_3$CH$_2$O), 20.05 (d, *J* 2.3, *C*H$_3$-6), 35.42 (d, *J* 8.8, C-3), 38.0 (d, *J* 7.5, C-4), 51.86 and 51.9 (2 d, *J* 5.2 and 7.7, *C*H$_3$OP), 64.86 (s, CH$_3$*C*H$_2$O), 95.4 (d, *J* 200.4,

C-5), 96.73 (s, C-2), 123.6 and 128.68 (2 s, *o*-, *m*-C_{arom}), 146.63 (s, *i*-C_{arom}), 152.54 (s, *p*-C_{arom}), 164.5 (d, *J* 26.6, C-6).

c-6a.—Viscous product, separated by column chromatography over silica gel and elution with hexane–diethyl ether in gradient; δ_P 25.668; δ_H 0.96 (3H, t, *J* 7.2, CH_3CH$_2$O), 1.9–2.06 and 2.13–2.2 (2H, 2 m, H_2-3), 2.2 (3H, d, *J* 1.11, CH_3-6), 3.32 and 3.5 (6H, 2 d, *J* 11 and *J* 11.1, CH_3OP), 3.66–3.76 (2H, 2 m, CH$_3$CH_2O), 3.78–3.83 (1H, m, H-4), 5.0 (1H, 2 t, *J* 2.8, H-2), 7.35 and 8.04 (4H, 2 d, *J* 8.7, H_{arom}); δ_C 14.85 (s, *C*H$_3$CH$_2$O), 20.3 (d, *J* 2.7, *C*H$_3$-6), 34.9 (d, *J* 9.1, C-3), 37.3 (d, *J* 7.2, C-4), 52.0 and 52.1 (2 d, *J* 6.2 and 6.1, *C*H$_3$OP), 64.3 (s, CH$_3$*C*H$_2$O), 97.0 (d, *J* 201.4, C-5), 97.73 (s, C-2), 122.9 and 129.1 (2 s, *o*-, *m*-C_{arom}), 146.2 (s, *i*-C_{arom}), 152.6 (s, *p*-C_{arom}), 164.0 (d, *J* 25.6, C-6).

2-*tert*-Butoxy-5-(dimethoxyphosphoryl)-3,4-dihydro-6-methyl-4-(4-nitrophenyl)-2*H*-pyran 6b. *Viscous product* purified by flash column chromatography over silica gel and elution with diethyl ether (Found: C, 53.79; H, 6.95; N, 3.32. $C_{18}H_{26}NO_7P$ requires C, 54.13; H, 6.51; N, 3.50%), isolated as a mixture of diastereomers, which have been separated.

t-6b.—Viscous product, separated by column chromatography over silica gel and elution with hexane–diethyl ether in gradient; δ_P 26.04; δ_H 1.12 [9H, s, (CH_3)$_3$C], 1.69–1.72 and 1.92–2.06 (2H, 2 m, H_2-3), 2.15 (3H, d, *J* 1.43, CH_3-6), 3.3 and 3.6 (6H, 2 d, *J* 11.1 and 11.2, CH_3OP), 3.8–3.9 (1H, m, H-4), 5.06 (1H, dd, *J* 7.8 and 2.7, H-2), 7.35 and 8.1 (4H, 2 d, *J* 8.7, H_{arom}); δ_C 20.3 (d, *J* 2.5, *C*H$_3$-6), 28.45 [s, (*C*H$_3$)$_3$C], 36.7 (d, *J* 9.0, C-3), 38.24 (d, *J* 7.8, C-4), 51.64 and 51.87 (2 d, *J* 5.7 and 6.0, *C*H$_3$OP), 76.05 [s, (CH$_3$)$_3$*C*], 91.29 (s, C-2), 94.39 (d, *J* 200.8, C-5), 123.5 and 128.5 (2 s, *o*-, *m*-C_{arom}), 146.52 (s, *i*-C_{arom}), 152.99 (s, *p*-C_{arom}), 164.8 (d, *J* 26.3, C-6).

c-6b.—Viscous product, separated by column chromatography over silica gel and elution with hexane–diethyl ether in gradient; δ_P 26.12; δ_H 1.08 [9H, s, (CH_3)$_3$C], 1.88–2.0 and 2.08–2.18 (2H, 2 m, H_2-3), 2.27 (3H, d, *J* 1.21, CH_3-6), 3.35 and 3.55 (6H, 2 d, *J* 11.0 and 11.2, CH_3OP), 3.75–3.92 (1H, m, H-4), 5.28 (1H, 2 t, *J* 3.2, H-2), 7.4 and 8.03 (4H, 2 d, *J* 8.7, H_{arom}); δ_C 20.6 (d, *J* 2.5, *C*H$_3$-6), 28.36 [s, (*C*H$_3$)$_3$C], 36.28 (d, *J* 9.0, C-3), 37.6 (d, *J* 7.3, C-4), 52.0 and 52.08 (2 d, *J* 5.88 and 5.51, *C*H$_3$OP), 75.78 [s, (CH$_3$)$_3$*C*], 92.68 (s, C-2), 96.31 (d, *J* 201.7, C-5), 122.8 and 129.1 (2 s, *o*-, *m*-C_{arom}), 146.1 (s, *i*-C_{arom}), 153.0 (s, *p*-C_{arom}), 164.35 (d, *J* 25.6, C-6).

5-(Diethoxyphosphoryl)-3,4-dihydro-2-ethoxy-6-methyl-4-(4-nitrophenyl)-2*H*-pyran 6c. *Viscous product* purified by flash column chromatography over silica gel and elution with diethyl ether (Found: C, 53.96; H, 6.54; N, 3.51. $C_{18}H_{26}NO_7P$ requires C, 54.13; H, 6.51; N, 3.50%), isolated as a mixture of diastereomers, which have been separated.

t-6c.—Viscous product, separated by column chromatography over silica gel and elution with hexane–diethyl ether in gradient; δ_P 22.63; δ_H 0.95 (3H, t, *J* 7.0, CH_3CH$_2$O), 1.2 and 1.25 (6H, 2 t, *J* 7.1, CH_3CH$_2$OP), 1.82–2.1 (2H, m, H_2-3), 2.25 (3H, d, *J* 0.95, CH_3-6), 3.45 (1H, q, *J* 7.1, CH$_3$C*H*OP), 3.62–3.96 (6H, m, CH$_3$C*H*OP, CH$_3$CH_2OP, CH$_3$CH_2O and H-4), 4.85 (1H, dd, *J* 8.0 and 2.56, H-2), 7.32 and 8.1 (4H, 2 d, *J* 8.78, H_{arom}); δ_C 15.0 (s, *C*H$_3$CH$_2$O), 16.0 and 16.03 (2 d, *J* 6.6, *C*H$_3$CH$_2$OP), 20.0 (d, *J* 2.45, *C*H$_3$-6), 35.0 (d, *J* 8.77, C-3), 38.0 (d, *J* 7.5, C-4), 60.05 and 60.08 (2 d, *J* 5.3 and 5.55, CH$_3$*C*H$_2$OP), 64.5 (s, CH$_3$*C*H$_2$O), 96.0 (d, *J* 200.57, C-5), 96.42 (s, C-2), 123.5 and 128.8 (2 s, *o*-, *m*-C_{arom}), 146.45 (s, *i*-C_{arom}), 150.8 (s, *p*-C_{arom}), 163.6 (d, *J* 26.5, C-6).

c-6c.—Viscous product, separated by column chromatography over silica gel and elution with hexane–diethyl ether in gradient; δ_P 22.77; δ_H 1.0 (3H, t, *J* 7.0, CH_3CH$_2$O), 1.1 and 1.17 (6H, 2 t, *J* 7.1, CH_3CH$_2$OP), 1.91–2.03 and 2.1–2.19 (2H, 2 m, H_2-3), 2.2 (3H, d, *J* 1.26, CH_3-6), 3.35 (1H, q, *J* 7.1, CH$_3$C*H*OP), 3.5–3.94 (6H, m, CH$_3$C*H*OP, CH$_3$CH_2OP, CH$_3$CH_2O and H-4), 5.05 (1H, 2 t, *J* 2.85, H-2), 7.37 and 8.05 (4H, 2 d, *J* 8.6, H_{arom}); δ_C 14.9 (s, *C*H$_3$CH$_2$O), 16.0 and 16.02 (2 d, *J* 6.5, *C*H$_3$CH$_2$OP), 20.02 (d, *J* 2.67, *C*H$_3$-6), 34.5 (d, *J* 9.0, C-3), 36.5 (d, *J* 7.17, C-4), 61.5 and 61.52 (2 d, *J* 6.08 and 5.83, CH$_3$*C*H$_2$OP), 64.2 (s, CH$_3$*C*H$_2$O), 98.0 (d, *J* 200.8, C-5), 97.68 (s, C-2), 123.0 and 129.3 (2 s, *o*-, *m*-C_{arom}), 146.1 (s, *i*-C_{arom}), 152.8 (s, *p*-C_{arom}), 163.5 (d, *J* 25.7, C-6).

2-*tert*-Butoxy-5-(diethoxyphosphoryl)-3,4-dihydro-6-methyl-4-(4-nitrophenyl)-2*H*-pyran 6d. *Viscous product* purified by flash column chromatography over silica gel and elution with diethyl ether (Found: C, 55.92; H, 7.12; N, 3.16. $C_{20}H_{30}NO_7P$ requires C, 56.20; H, 7.02; N, 3.27%), isolated as a mixture of diastereomers, which were not separated.

t-6d.—δ_P 22.98; δ_H 0.96 and 1.17 (6H, 2 t, *J* 7.0, CH_3-CH$_2$OP), 1.14 [9H, s, (CH_3)$_3$C], 1.7–1.8 and 1.96–2.05 (2H, 2 m, H_2-3), 2.18–2.23 (3H, m, CH_3-6), 3.54–3.95 (5H, m, CH$_3$-CH_2OP and H-4), 5.05 (1H, dd, *J* 7.9 and 2.6, H-2), 7.35 and 8.13 (4H, 2 d, *J* 8.66, H_{arom}); δ_C 15.9 (d, *J* 6.0, *C*H$_3$CH$_2$OP), 20.4 (s, *C*H$_3$-6), 36.8 (d, *J* 9.04, C-3), 37.66 (d, *J* 7.1, C-4), 61.1 (d, *J* 6.3, CH$_3$*C*H$_2$OP), 76.0 [s, (CH$_3$)$_3$*C*], 91.22 (s, C-2), 95.7 (d, *J* 200.5, C-5), 122.7 and 128.7 (2 s, *o*-, *m*-C_{arom}), 146.5 (s, *i*-C_{arom}), 153.25 (s, *p*-C_{arom}), 163.9 (d, *J* 26.0, C-6).

c-6d.—δ_P 23.14; δ_H 0.97 and 1.18 (6H, 2 t, *J* 7.1, CH_3-CH$_2$OP), 1.05 [9H, s, (CH_3)$_3$C], 1.75–1.95 and 2.05–2.15 (2H, 2 m, H_2-3), 2.27 (3H, d, *J* 1.21, CH_3-6), 3.54–3.95 (5H, m, CH$_3$CH_2OP and H-4), 5.25 (1H, t, *J* 3.1, H-2), 7.38 and 8.03 (4H, 2 d, *J* 8.7, H_{arom}); δ_C 16.0 and 16.2 (2 d, *J* 6.5 and 7.5, *C*H$_3$CH$_2$OP), 20.6 (d, *J* 2.7, *C*H$_3$-6), 28.4 [s, (*C*H$_3$)$_3$C], 36.3 (d, *J* 9.0, C-3), 37.7 (d, *J* 7.1, C-4), 61.2 and 61.23 (2 d, *J* 5.8 and 6.1, CH$_3$*C*H$_2$OP), 76.0 [s, (CH$_3$)$_3$*C*], 92.6 (s, C-2), 97.6 (d, *J* 201.1, C-5), 123.1 and 129.0 (2 s, *o*-, *m*-C_{arom}), 146.0 (s, *i*-C_{arom}), 153.4 (s, *p*-C_{arom}), 163.7 (d, *J* 25.9, C-6).

5-(Diisopropoxyphosphoryl)-2-ethoxy-3,4-dihydro-6-methyl-4-(4-nitrophenyl)-2*H*-pyran 6e. Viscous product purified by flash column chromatography over silica gel and elution with diethyl ether (Found: C, 56.03; H, 7.23; N, 3.04. $C_{20}H_{30}NO_7P$ requires C, 56.20; H, 7.02; N, 3.27%), isolated as a mixture of diastereomers, which were not separated.

t-6e.—δ_P 22.63; δ_H 0.92 and 1.02 [12H, 2 d, *J* 6.1, (CH_3)$_2$C], 1.1–1.2 (3H, m, CH_3CH$_2$O), 1.8–2.08 (2H, m, H_2-3), 2.22 (3H, d, *J* 1.68, CH_3-6), 3.37–3.48 (1H, m, CH$_3$C*H*HO), 3.78–3.92 (2H, m, CH$_3$CH*H*O and H-4), 4.33–4.43 [2H, m, (CH$_3$)$_2$C*H*], 4.75 (1H, dd, *J* 8.1 and 2.6, H-2), 7.32 and 8.12 (4H, 2 d, *J* 8.55, H_{arom}); δ_C 14.95 (s, *C*H$_3$CH$_2$O), 19.9 (d, *J* 1.0, *C*H$_3$-6), 23.71 [d, *J* 4.68, (*C*H$_3$)$_2$C], 35.5 (d, *J* 8.8, C-3), 38.29 (d, *J* 7.5, C-4), 64.7 (s, CH$_3$*C*H$_2$O), 69.68 and 69.89 [2d, *J* 6.26 and 6.03, (CH$_3$)$_2$*C*], 96.51 (s, C-2), 98.9 (d, *J* 201.72, C-5), 123.3 and 128.87 (2 s, *o*-, *m*-C_{arom}), 146.41 (s, *i*-C_{arom}), 152.96 (s, *p*-C_{arom}), 163.5 (d, *J* 26.2, C-6).

c-6e.—δ_P 22.77; δ_H 0.98 and 1.1 [12H, 2 d, *J* 6.0, (CH_3)$_2$C], 1.1–1.2 (3H, m, CH_3CH$_2$O), 1.85–2.19 (2H, m, H-3), 2.22 (3H, d, *J* 1.68, CH_3-6), 3.29–3.35 (1H, m, CH$_3$C*H*HO), 3.63–3.78 (1H, m, CH$_3$CH*H*O), 3.8–3.92 (1H, m, H-4), 4.33–4.43 [2H, m, (CH$_3$)$_2$C*H*], 5.0 (1H, 2 t, *J* 2.65, H-2), 7.34 and 8.15 (4H, 2 d, *J* 8.6, H_{arom}); δ_C 14.76 (s, *C*H$_3$CH$_2$O), 20.2 (d, *J* 1.6, *C*H$_3$-6), 23.58 [d, *J* 4.37, (*C*H$_3$)$_2$C], 34.9 (d, *J* 9.0, C-3), 37.6 (d, *J* 7.3, C-4), 64.1 (s, CH$_3$*C*H$_2$O), 69.68 and 69.89 [2d, *J* 6.26 and 6.03, (CH$_3$)$_2$*C*], 98.87 (s, C-2), 97.2 (d, *J* 202.0, C-5), 122.56 and 129.29 (2 s, *o*-, *m*-C_{arom}), 145.99 (s, *i*-C_{arom}), 152.96 (s, *p*-C_{arom}), 163.1 (d, *J* 25.3, C-6).

5-(Dimethoxyphosphoryl)-2-ethoxy-3,4-dihydro-6-methyl-4-phenyl-2*H*-pyran 6f. *Viscous product* purified by flash column chromatography over silica gel and elution with diethyl ether (Found: C, 58.61; H, 7.11. $C_{16}H_{23}O_5P$ requires C, 58.89; H, 7.05), isolated as a mixture of diastereomers, which were not separated.

t-6f.—δ_P 26.64; δ_H 1.12 (3H, t, *J* 7.2, CH_3CH$_2$O), 1.87–1.98 and 2.15–2.2 (2H, 2 m, H_2-3), 2.23 (3H, br s, CH_3-6), 3.2 and 3.52 (6H, 2 d, *J* 10.9 and 11.3, CH_3OP), 3.51–4.0 (3H, m,

CH_3CH_2O and H-4), 4.8 (1H, t, *J* 6.5, H-2), 7.05–7.3 (5H, m, H_{arom}); δ_C 15.42 (s, *C*H_3CH$_2$O), 19.91 (d, *J* 1.0, *C*H_3-6), 35.49 (d, *J* 9.0, C-3), 38.3 (d, *J* 7.6, C-4), 51.8 and 52.1 (2 d, *J* 6.0 and 5.4, *C*H_3OP), 64.77 (s, CH_3CH_2O), 95.75 (d, *J* 201.0, C-5), 97.33 (s, C-2), 126.5, 127.9 and 128.3 (3 s, *o*-, *m, p*-C_{arom}), 144.6 (s, *i*-C_{arom}), 164.0 (d, *J* 27.5, C-6).

c-6f.—δ_P 26.36; δ_H 1.08 (3H, t, *J* 7.0, CH_3CH_2O), 1.87–1.98 and 2.15–2.2 (2H, 2 m, H_2-3), 2.18 (3H, br s, C*H*$_3$-6), 3.18 and 3.45 (6H, 2 d, *J* 11.0 and 10.8, C*H*$_3$OP), 3.51–4.0 (3H, m, CH_3CH_2O and H-4), 4.96 (1H, dd, *J* 6.3 and *J* 2.4, H-2), 7.05–7.3 (5H, m, H_{arom}); δ_C 14.9 (s, *C*H_3CH$_2$O), 20.3 (d, *J* 1.0, *C*H_3-6), 36.9 (d, *J* 9.6, C-3), 38.85 (d, *J* 7.5, C-4), 51.8 and 52.1 (2 d, *J* 6.0 and 5.4, *C*H_3OP), 64.3 (s, CH_3CH_2O), 98.93 (s, C-2), 98.88 (d, *J* 200.36, C-5), 126.1, 127.8 and 128.1 (3 s, *o*-, *m, p*-C_{arom}), 144.3 (s, *i*-C_{arom}), 163.36 (d, *J* 26.7, C-6).

2-*tert*-Butoxy-5-(dimethoxyphosphoryl)-3,4-dihydro-6-methyl-4-phenyl-2*H*-pyran 6g. *Viscous product* purified by flash column chromatography over silica gel and elution with diethyl ether [HRMS: required for $C_{18}H_{27}O_5P$ (*M*), 354.1596. Found: M^+, 354.1613], isolated as a mixture of diastereomers, which were not separated.

t-6g.—δ_P 27.0; δ_H 1.1 [9H, s, (C*H*$_3$)$_3$C], 1.7–2.12 (2H, m, H_2-3), 2.24 (3H, d, *J* 2.1, C*H*$_3$-6), 3.24 and 3.53 (6H, 2 d, *J* 11.1 and 11.0, C*H*$_3$OP), 3.62–3.8 (1H, m, H-4), 5.07 (1H, dd, *J* 8.8 and *J* 2.5, H-2), 7.05–7.3 (5H, m, H_{arom}); δ_C 20.68 (d, *J* 1.9, *C*H_3-6), 28.7 [s, (*C*H$_3$)$_3$C], 38.72 (d, *J* 9.5, C-3), 39.66 (d, *J* 7.47, C-4), 51.3 and 51.6 (2 d, *J* 5.7 and 6.0, *C*H_3OP), 76.57 [s, (CH$_3$)$_3$*C*], 91.85 (s, C-2), 96.7 (d, *J* 200.4, C-5), 126.5, 127.88 and 128.28 (3 s, *o*-, *m*-, *p*-C_{arom}), 145.0 (s, *i*-C_{arom}), 164.81 (d, *J* 26.1, C-6).

c-6g.—δ_P 26.74; δ_H 1.13 [9H, s, (C*H*$_3$)$_3$C], 1.7–2.12 (2H, m, H_2-3), 2.14 (3H, d, *J* 21.4, C*H*$_3$-6), 3.2 and 3.45 (6H, 2 d, *J* 11.18 and 11.2, C*H*$_3$OP), 3.62–3.8 (1H, m, H-4), 5.17 (1H, dd, *J* 7.0 and 2.1, H-2), 7.05–7.3 (5H, m, H_{arom}); δ_C 20.7 (d, *J* 2.0, *C*H_3-6), 28.6 [s, (*C*H$_3$)$_3$C], 38.72 (d, *J* 9.5, C-3), 39.66 (d, *J* 7.47, C-4), 51.7 and 51.8 (2 d, *J* 5.9 and 5.5, *C*H_3OP), 75.72 [s, (CH$_3$)$_3$*C*], 93.98 (s, C-2), 98.73 (d, *J* 200.36, C-5), 126.05, 127.8 and 128.13 (3 s, *o*-, *m*-, *p*-C_{arom}), 144.57 (s, *i*-C_{arom}), 164.3 (d, *J* 26.79, C-6).

5-(Dimethoxyphosphoryl)-2-ethoxy-3,4-dihydro-4-(4-methoxyphenyl)-6-methyl-2*H*-pyran 6h. *Viscous product* purified by flash column chromatography over silica gel and elution with diethyl ether (Found: C, 56.92; H, 7.28. $C_{17}H_{25}O_6P$ requires C, 57.30; H, 7.02%), isolated as a mixture of diastereomers, which were not separated.

t-6h.—δ_P 26.79; δ_H 1.13 (3H, t, *J* 7.0, C*H*$_3$CH$_2$O), 1.8–1.9 (2H, m, H_2-3), 2.21 (3H, d, *J* 1.8, C*H*$_3$-6), 3.25 and 3.52 (6H, 2 d, *J* 11.0 and 11.2, C*H*$_3$OP), 3.32–3.41 (1H, m, CH$_3$C*H*HO), 3.6–4.1 (2H, m, CH$_3$CH*H*O and H-4), 3.7 (3H, s, OC*H*$_3$), 4.77 (1H, t, *J* 6.2, H-2), 6.75 and 7.08 (4H, 2 d, *J* 8.7, H_{arom}); δ_C 15.05 (s, *C*H$_3$CH$_2$O), 19.87 (d, *J* 2.5, *C*H$_3$-6), 35.6 (d, *J* 9.2, C-3), 37.5 (d, *J* 7.63, C-4), 51.77 and 52.1 (2 d, *J* 5.9 and *J* 5.6, *C*H$_3$OP), 55.12 (s, OCH$_3$), 64.78 (s, CH$_3$CH$_2$O), 95.7 (d, *J* 200.85, C-5), 97.32 (s, C-2), 113.6 and 128.8 (2 s, *o*-, *m*-C_{arom}), 136.55 (s, *i*-C_{arom}), 158.07 (s, *p*-C_{arom}), 163.75 (d, *J* 27.6, C-6).

c-6h.—δ_P 26.51; δ_H 1.08 (3H, t, *J* 7.0, C*H*$_3$CH$_2$O), 1.8–1.9 (2H, m, H_2-3), 2.15 (3H, d, *J* 1.9, C*H*$_3$-6), 3.19 and 3.42 (6H, 2 d, *J* 11.0 and 11.2, C*H*$_3$OP), 3.32–3.41 (1H, m, CH$_3$C*H*HO), 3.6–4.1 (2H, m, CH$_3$CH*H*O and H-4), 3.68 (3H, s, OC*H*$_3$), 4.95 (1H, dd, *J* 6.3 and 2.3, H-2), 6.7 and 7.1 (4H, 2 d, *J* 8.7, H_{arom}); δ_C 14.9 (s, *C*H$_3$CH$_2$O), 20.26 (d, *J* 2.7, *C*H$_3$-6), 36.55 (d, *J* 9.5, C-3), 38.0 (d, *J* 7.6, C-4), 51.7 and 52.0 (2 d, *J* 6.3 and 6.2, *C*H$_3$OP), 55.05 (s, OCH$_3$), 64.34 (s, CH$_3$CH$_2$O), 98.93 (s, C-2), 99.2 (d, *J* 199.9, C-5), 113.1 and 129.0 (2 s, *o*, *m*-C_{arom}), 136.2 (s, *i*-C_{arom}), 157.4 (s, *p*-C_{arom}), 163.07 (d, *J* 26.7, C-6).

2-*tert*-Butoxy-5-(dimethoxyphosphoryl)-3,4-dihydro-4-(4-methoxyphenyl)-6-methyl-2*H*-pyran 6i. *Viscous product* purified by flash column chromatography over silica gel and elution with diethyl ether (Found: C, 59.39; H, 7.54. $C_{19}H_{29}O_6P$ requires C, 59.37; H, 7.55%), isolated as a mixture of diastereomers, which were not separated.

t-6i.—δ_P 27.03; δ_H 1.18 [9H, s, (C*H*$_3$)$_3$C], 1.7–2.1 (2H, m, H_2-3), 2.2 (3H, br s, C*H*$_3$-6), 3.25 and 3.5 (6H, 2 d, *J* 11.0 and 11.1, C*H*$_3$OP), 3.52–3.6 (1H, m, H-4), 3.7 (3H, s, OC*H*$_3$), 5.05 (1H, dd, *J* 8.8 and 2.6, H-2), 6.78 and 7.05 (4H, 2 d, *J* 8.6, H_{arom}); δ_C 20.0 (s, *C*H$_3$-6), 30.9 [s, (*C*H$_3$)$_3$C], 36.0 (d, *J* 8.9, C-3), 37.7 (d, *J* 7.7, C-4), 51.5 and 51.65 (2 d, *J* 6.2 and 5.8, *C*H$_3$OP), 54.9 (s, OCH$_3$), 75.66 [s, (CH$_3$)$_3$*C*], 91.71 (s, C-2), 95.0 (d, *J* 199.6, C-5), 113.2 and 128.5 (2 s, *o*-, *m*-C_{arom}), 136.8 (s, *i*-C_{arom}), 157.9 (s, *p*-C_{arom}), 163.9 (d, *J* 26.7, C-6).

c-6i.—δ_P 26.74; δ_H 1.15 [9H, s, (C*H*$_3$)$_3$C], 1.7–2.1 (2H, m, H_2-3), 2.11 (3H, br s, C*H*$_3$-6), 3.2 and 3.43 (6H, 2 d, *J* 11.0 and 11.1, C*H*$_3$OP), 3.52–3.6 (1H, m, H-4), 3.65 (3H, s, OC*H*$_3$), 5.12 (1H, dd, *J* 7.1 and 2.2, H-2), 6.8 and 7.1 (4H, 2 d, *J* 8.6, H_{arom}); δ_C 20.5 (s, *C*H$_3$-6), 28.3 [s, (*C*H$_3$)$_3$C], 38.6 (d, *J* 10.9, C-3), 38.7 (d, *J* 7.15, C-4), 51.5 and 51.65 (2 d, *J* 6.2 and 5.8, *C*H$_3$OP), 54.9 (s, OCH$_3$), 75.5 [s, (CH$_3$)$_3$*C*], 93.8 (s, C-2), 98.8 (d, *J* 199.7, C-5), 112.9 and 128.9 (2 s, *o*-, *m*-C_{arom}), 136.3 (s, *i*-C_{arom}), 157.6 (s, *p*-C_{arom}), 163.5 (d, *J* 26.6, C-6).

5-(Dimethoxyphosphoryl)-2-ethoxy-3,4-dihydro-6-methyl-4-(2-nitrophenyl)-2*H*-pyran 6j. *Viscous product* purified by flash column chromatography over silica gel and elution with diethyl ether (Found: C, 51.48; H, 5.78; N, 3.52. $C_{16}H_{22}NO_7P$ requires C, 51.75; H, 5.92; N, 3.77%), isolated as a mixture of diastereomers, which were not separated.

t-6j.—δ_P 25.12; δ_H 1.16 (3H, t, *J* 7.0, C*H*$_3$CH$_2$O), 1.98–2.18 (2H, m, H_2-3), 2.23 (3H, d, *J* 1.1, C*H*$_3$-6), 3.3 and 3.5 (6H, 2 d, *J* 10.9 and 11.4, C*H*$_3$OP), 3.4–3.49 and 3.78–3.42 (2H, 2 m, CH$_3$C*H*$_2$O), 4.15–4.26 (1H, m, H-4), 4.93 (1H, dd, *J* 7.65 and 2.65, H-2), 7.31 (1H, t, *J* 8.25, H_{arom}), 7.38 (1H, d, *J* 7.7, H_{arom}), 7.51 (1H, t, *J* 7.7, H_{arom}), 7.79 (1H, d, *J* 8.2, H_{arom}); δ_C 15.04 (s, *C*H$_3$CH$_2$O), 20.0 (d, *J* 2.68, *C*H$_3$-6), 33.56 (d, *J* 6.9, C-4), 34.21 (d, *J* 8.5, C-3), 51.6 and 51.99 (2 d, *J* 5.85 and 6.12, *C*H$_3$OP), 64.69 (s, CH$_3$CH$_2$O), 96.3 (d, *J* 201.26, C-5), 97.0 (s, C-2), 124.39, 127.33, 130.47 and 132.33 (4 s, *o*-, *m*-, *p*-C_{arom}), 139.0 (s, *i*-C_{arom}), 149.26 (s, *o*-C_{arom}), 164.1 (d, *J* 27.17, C-6).

c-6j.—δ_P 25.17; δ_H 1.06 (3H, t, *J* 7.0, C*H*$_3$CH$_2$O), 1.98–2.18 (2H, m, H_2-3), 2.23 (3H, d, *J* 1.1, C*H*$_3$-6), 3.3 and 3.5 (6H, 2 d, *J* 10.9 and 11.4, C*H*$_3$OP), 3.4–3.49 and 3.78–3.42 (2H, 2 m, CH$_3$C*H*$_2$O), 4.15–4.26 (1H, m, H-4), 5.01 (1H, dd, *J* 5.2 and 2.6, H-2), 7.25 (1H, t, *J* 8.1, H_{arom}), 7.43 (1H, d, *J* 7.4, H_{arom}), 7.54 (1H, t, *J* 7.4, H_{arom}), 7.74 (1H, d, *J* 8.1, H_{arom}); δ_C 14.85 (s, *C*H$_3$CH$_2$O), 20.28 (d, *J* 2.7, *C*H$_3$-6), 33.5 (d, *J* 6.8, C-4), 34.24 (d, *J* 8.6, C-3), 51.6 and 51.99 (2 d, *J* 5.85 and 6.12, *C*H$_3$OP), 64.45 (s, CH$_3$CH$_2$O), 98.45 (s, C-2), 98.7 (d, *J* 201.1, C-5), 123.7, 126.94, 130.0 and 131.8 (4 s, *o*-, *m*-, *p*-C_{arom}), 138.2 (s, *i*-C_{arom}), 149.26 (s, *o*-C_{arom}), 163.7 (d, *J* 27.0, C-6).

2-*tert*-Butoxy-5-(dimethoxyphosphoryl)-3,4-dihydro-6-methyl-4-(2-nitrophenyl)-2*H*-pyran 6k. *Viscous product* purified by flash column chromatography over silica gel and elution with diethyl ether (Found: C, 53.98; H, 6.22; N, 3.34. $C_{18}H_{26}NO_7P$ requires C, 54.13; H, 6.51; N, 3.50%), isolated as a mixture of diastereomers, which have been separated.

t-6k.—Viscous product, separated by column chromatography over silica gel and elution with (0.5 : 100) methanol–diethyl ether; δ_P 25.43; δ_H 1.15 [9H, s, (C*H*$_3$)$_3$C], 1.88–2.0 and 2.08–2.18 (2H, 2 m, H_2-3), 2.17 (3H, d, *J* 2.67, C*H*$_3$-6), 3.16 and 3.47 (6H, 2 d, *J* 10.99 and 11.4, C*H*$_3$OP), 4.12–4.23 (1H, m, H-4), 5.19 (1H, dd, *J* 7.6 and 2.7, H-2), 7.3 (1H, t, *J* 8.2, H_{arom}), 7.41 (1H, d, *J* 7.8, H_{arom}), 7.52 (1H, t, *J* 8.2, H_{arom}), 7.78 (1H, d, *J* 7.8, H_{arom}); δ_C 20.4 (d, *J* 2.7, *C*H$_3$-6), 28.65 [s, (*C*H$_3$)$_3$C], 33.7 (d, *J* 6.77, C-4), 35.5 (d, *J* 8.5, C-3), 51.65 and 52.0 (2 d, *J* 6.06 and 6.3, *C*H$_3$OP), 75.95 [s, (CH$_3$)$_3$*C*], 91.66 (s, C-2), 96.1 (d, *J* 201.18, C-5), 124.4, 127.3, 130.4 and 132.4 (4 s, *o*-, *m*-, *p*-C_{arom}), 139.5 (s, *i*-C_{arom}), 149.35 (s, *o*-C_{arom}), 164.77 (d, *J* 26.42, C-6).

c-6k.—Viscous product, separated by column chromatography over silica gel and elution with (0.5:100) methanol–diethyl ether; δ_P 25.6; δ_H 1.12 [9H, s, $(CH_3)_3C$], 1.86–2.02 and 2.25–2.38 (2H, 2 m, H_2-3), 2.15 (3H, d, *J* 1.95, CH_3-6), 3.17 and 3.46 (6H, 2 d, *J* 11.0 and 11.2, CH_3OP), 4.12–4.23 (1H, m, H-4), 5.22 (1H, dd, *J* 5.87 and 2.62, H-2), 7.22 (1H, t, *J* 8.1, H_{arom}), 7.41 (1H, t, *J* 8.1, H_{arom}), 7.55 (1H, d, *J* 8.0, H_{arom}), 7.72 (1H, d, *J* 8.1, H_{arom}); δ_C 20.67 (d, *J* 2.8, CH_3-6), 28.46 [s, $(CH_3)_3C$], 33.7 (d, *J* 6.77, C-4), 36.0 (d, *J* 8.74, C-3), 51.91 and 52.17 (2 d, *J* 6.12 and 6.37, CH_3OP), 75.98 [s, $(CH_3)_3C$], 93.42 (s, C-2), 97.59 (d, *J* 202.2, C-5), 123.7, 126.9, 131.7 and 131.9 (4 s, *o*-, *m*-, *p*-C_{arom}), 139.4 (s, *i*-C_{arom}), 149.4 (s, *o*-C_{arom}), 164.75 (d, *J* 26.4, C-6).

5-(Dimethoxyphosphoryl)-2-ethoxy-3,4-dihydro-6-methyl-4-[2-(trifluoromethyl)phenyl]-2*H*-pyran 6l. *Viscous product* purified by flash column chromatography over silica gel and elution with diethyl ether (Found: C, 51.44; H, 5.47. $C_{17}H_{22}F_3O_5P$ requires C, 51.77; H, 5.58), isolated as a mixture of diastereomers, which were not separated.

t-6l.—δ_P 25.38; δ_H 1.18 (3H, t, *J* 7.0, CH_3CH_2O), 1.81–1.92 and 2.0–2.13 (2H, 2 m, H_2-3), 2.29–2.3 (3H, m, CH_3-6), 3.12 and 3.52 (6H, 2 d, *J* 11.2 and 11.2, CH_3OP), 3.42–3.49 and 3.78–3.42 (2H, 2 m, CH_3CH_2O), 4.06–4.15 (1H, m, H-4), 4.9 (1H, dd, *J* 8.3 and 2.8, H-2), 7.25 (1H, t, *J* 7.25, H_{arom}), 7.34 (1H, d, *J* 7.25, H_{arom}), 7.45 (1H, t, *J* 7.25, H_{arom}), 7.6 (1H, d, *J* 7.25, H_{arom}); δ_C 15.08 (s, CH_3CH_2O), 20.03 (d, *J* 2.6, CH_3-6), 34.26 (d, *J* 6.95, C-4), 34.64 (d, *J* 8.4, C-3), 51.6 and 51.86 (2 d, *J* 5.87 and 6.06, CH_3OP), 64.77 (s, CH_3CH_2O), 96.41 (d, *J* 201.72, C-5), 96.82 (s, C-2), 125.5 (q, *J* 279.23, CF_3), 128.0 (q, *J* 29.88, CCF_3), 126.5 (q, *J* 6.0, *m*-$CCCF_3$), 126.5, 129.57 and 131.5 (3 s, *o*-, *m*-, *p*-C_{arom}), 143.51 (s, *i*-C_{arom}), 164.39 (d, *J* 27.92, C-6).

c-6l.—δ_P 25.39; δ_H 1.1 (3H, t, *J* 7.0, CH_3CH_2O), 1.81–1.92 and 2.0–2.13 (2H, 2 m, H_2-3), 2.26–2.28 (3H, m, CH_3-6), 3.12 and 3.52 (6H, 2 d, *J* 11.2 and 11.2, CH_3OP), 3.42–3.49 and 3.78–3.42 (2H, 2 m, CH_3CH_2O), 4.0–4.05 (1H, m, H-4), 4.96 (1H, dd, *J* 6.2 and 2.41, H-2), 7.2 (1H, t, *J* 7.9, H_{arom}), 7.37 (1H, d, *J* 7.9, H_{arom}), 7.43 (1H, t, *J* 7.9, H_{arom}), 7.52 (1H, d, *J* 7.9, H_{arom}); δ_C 14.92 (s, CH_3CH_2O), 20.38 (d, *J* 3.0, CH_3-6), 34.25 (d, *J* 6.9, C-4), 36.37 (d, *J* 8.7, C-3), 51.6 and 51.86 (2 d, *J* 5.87 and 6.06, CH_3OP), 64.49 (s, CH_3CH_2O), 98.63 (s, C-2), 98.77 (d, *J* 201.65, C-5), 125.3 (q, *J* 279.0, CF_3), 127.0 (q, *J* 29.8, CCF_3), 125.5 (q, *J* 6.1, *m*-$CCCF_3$), 126.56, 130.5 and 131.2 (3 s, *o*-, *m*-, *p*-C_{arom}), 143.17 (s, *i*-C_{arom}), 164.13 (d, *J* 26.94, C-6).

2-*tert*-Butoxy-5-(dimethoxyphosphoryl)-3,4-dihydro-6-methyl-4-[2-(trifluoromethyl)phenyl]-2*H*-pyran 6m. *Viscous product* purified by flash column chromatography over silica gel and elution with diethyl ether [HRMS: required for $C_{19}H_{26}F_3O_5P$ (*M*): 422.1470. Found: M^+, 422.1473], isolated as a mixture of diastereomers, which were not separated.

t-6m.—δ_P 25.71; δ_H 1.13 [9H, s, $(CH_3)_3C$], 1.68–1.75 and 1.82–2.08 (2H, 2 m, H_2-3), 2.26 (3H, br s, CH_3-6), 3.1 and 3.53 (6H, 2 d, *J* 10.9 and 11.3, CH_3OP), 4.03–4.15 (1H, m, H-4), 5.15 (1H, dd, *J* 8.3 and 2.6, H-2), 7.24 (1H, t, *J* 7.4, H_{arom}), 7.35 (1H, d, *J* 7.8, H_{arom}), 7.45 (1H, t, *J* 7.4, H_{arom}), 7.6 (1H, d, *J* 7.8, H_{arom}); δ_C 20.4 (d, *J* 2.8, CH_3-6), 28.56 [s, $(CH_3)_3C$], 34.55 (d, *J* 7.5, C-4), 36.13 (d, *J* 8.1, C-3), 51.5 and 51.86 (2 d, *J* 6.9 and 6.01, CH_3OP), 75.9 [s, $(CH_3)_3C$], 91.41 (s, C-2), 96.0 (d, *J* 201.2, C-5), 125.3 (q, *J* 278.23, CF_3), 127.75 (q, *J* 29.88, CCF_3), 126.22 (q, *J* 6.1, *m*-$CCCF_3$), 126.3, 129.26 and 131.25 (3 s, *o*-, *m*-, *p*-C_{arom}), 144.13 (s, *i*-C_{arom}), 164.8 (d, *J* 27.7, C-6).

c-6m.—δ_P 25.82; δ_H 1.18 [9H, s, $(CH_3)_3C$], 1.68–1.75 and 1.82–2.08 (2H, 2 m, H_2-3), 2.2 (3H, d, *J* 1.39, CH_3-6), 3.08 and 3.48 (6H, 2 d, *J* 11.0 and 11.25, CH_3OP), 4.03–4.15 (1H, m, H-4), 5.18 (1H, dd, *J* 6.4 and 2.6, H-2), 7.2 (1H, t, *J* 7.5, H_{arom}), 7.38 (1H, d, *J* 7.84, H_{arom}), 7.48 (1H, t, *J* 7.5, H_{arom}), 7.55 (1H, d, *J* 7.84, H_{arom}); δ_C 20.78 (d, *J* 2.9, CH_3-6), 28.51 [s, $(CH_3)_3C$], 35.2 (d, *J* 6.9, C-4), 37.0 (d, *J* 8.5, C-3), 51.5 and 51.86 (2 d, *J* 6.9 and 6.01, CH_3OP), 75.96 [s, $(CH_3)_3C$], 93.66 (s, C-2), 97.5 (d, *J* 201.0, C-5), 125.1 (q, *J* 279.1, CF_3), 126.75 (q, *J* 29.82, CCF_3), 125.25 (q, *J* 6.1, *m*-$CCCF_3$), 126.2, 130.31 and 131.0 (3 s, *o*-, *m*-, *p*-C_{arom}), 143.6 (s, *i*-C_{arom}), 164.4 (d, *J* 26.9, C-6).

5-(Dimethoxyphosphoryl)-2-ethoxy-3,4-dihydro-4-(4-nitrophenyl)-6-phenyl-2*H*-pyran 6n. *Viscous product* purified by flash column chromatography over silica gel and elution with diethyl ether [HRMS: required for $C_{21}H_{24}NO_7P$ (M), 433.1291. Found; M^+, 433.1281], isolated as a mixture of diastereomers, which have been separated.

t-6n.—Viscous product, separated by column chromatography over silica gel and elution with diethyl ether: δ_P 23.52; δ_H 1.22 (3H, t, *J* 7.1, CH_3CH_2O), 1.82–1.98 and 2.11–2.27 (2H, 2 m, H_2-3), 3.05 and 3.12 (6H, 2 d, *J* 11.1 and 11.3, CH_3OP), 3.53–3.7 and 3.84–3.96 (2H, 2 m, CH_3CH_2O), 4.0–4.08 (1H, m, H-4), 5.15 (1H, t, *J* 3.1, H-2), 7.31–7.42 and 7.55–7.65 (5H, 2 m, H_{arom}), 7.45 and 8.15 (4H, 2 d, *J* 8.68, H_{arom}); δ_C 14.99 (s, CH_3CH_2O), 36.32 (d, *J* 8.52, C-3), 37.4 (d, *J* 7.2, C-4), 51.48 and 51.89 (2 d, *J* 5.97 and *J* 6.7, CH_3OP), 64.58 (s, CH_3CH_2O), 96.8 (s, C-2), 99.62 (d, *J* 201.95, C-5), 123.47, 127.67, 128.9 and 129.1 (4 s, *o*-, *m*-, *p*-C_{arom}), 136.6 (d, *J* 3.3, *i*-C_{arom}), 146.65 (s, *i*-C_{arom}), 151.8 (s, *p*-C_{arom}), 162.77 (d, *J* 23.67, C-6).

c-6n.—Viscous product, separated by column chromatography over silica gel and elution with diethyl ether: δ_P 23.59; δ_H 1.11 (3H, t, *J* 7.1, CH_3CH_2O), 2.0–2.03 and 2.2–2.33 (2H, 2 m, H_2-3), 3.05 and 3.12 (6H, 2 d, *J* 11.1 and 11.3, CH_3OP), 3.41–3.55 and 3.8–3.9 (2H, 2 m, CH_3CH_2O), 4.0–4.08 (1H, m, H-4), 5.2 (1H, dd, *J* 6.7 and 2.67, H-2), 7.31–7.42 and 7.55–7.65 (5H, 2 m, H_{arom}), 7.45 and 8.15 (4H, 2 d, *J* 8.68, H_{arom}); δ_C 14.82 (s, CH_3CH_2O), 36.95 (d, *J* 9.08, C-3), 39.7 (d, *J* 7.5, C-4), 51.69 and 51.99 (2 d, *J* 6.05 and *J* 8.7, CH_3OP), 64.65 (s, CH_3CH_2O), 99.66 (s, C-2), 99.74 (d, *J* 203.68, C-5), 123.14, 129.1, 129.9 and 129.96 (4 s, *o*-, *m*-, *p*-C_{arom}), 135.3 (d, *J* 3.47, *i*-C_{arom}), 146.4 (s, *i*-C_{arom}), 151.5 (s, *p*-C_{arom}), 163.66 (d, *J* 23.32, C-6).

2-*tert*-Butoxy-5-(dimethoxyphosphoryl)-3,4-dihydro-4-(4-nitrophenyl)-6-phenyl-*H*-pyran 6o. *Viscous product* purified by flash column chromatography over silica gel and elution with diethyl ether (Found: C, 59.66; H, 5.98; N, 2.96. $C_{23}H_{28}NO_7P$ requires C, 59.86; H, 6.07; N, 3.03%), isolated as a mixture of diastereomers, which have been separated.

t-6o.—Viscous product, separated by column chromatography over silica gel and elution with (1:100) methanol–diethyl ether; δ_P 23.94; δ_H 1.25 [9H, s, $(CH_3)_3C$], 1.8–1.92 and 2.02–2.18 (2H, 2 m, H_2-3), 3.09 and 3.15 (6H, 2 d, *J* 11.17 and 11.3, CH_3OP), 4.01–4.15 (1H, m, H-4), 5.38 (1H, dd, *J* 4.7 and 2.51, H-2), 7.3–7.4 and 7.6–7.68 (5H, 2 m, H_{arom}), 7.5 and 8.16 (4H, 2 d, *J* 8.7, H_{arom}); δ_C 28.37 [s, $(CH_3)_3C$], 37.72 (d, *J* 6.8, C-4), 37.82 (d, *J* 8.3, C-3), 51.6 and 51.9 (2 d, *J* 5.91 and 6.5, CH_3OP), 76.1 [s, $(CH_3)_3C$], 91.8 (s, C-2), 98.97 (d, *J* 201.72, C-5), 123.6, 123.7, 127.76, 128.6, 128.9, 129.1, 129.14, 129.53 and 129.94 (9 s, *o*-, *m*-, *p*-C_{arom}), 136 and 146.65 (2 s, *i*-C_{arom}), 152.55 (s, *p*-C_{arom}), 163.5 (d, *J* 23.54, C-6).

c-6o.—Viscous product, separated by column chromatography over silica gel and elution with (1:100) methanol–diethyl ether; δ_P 23.88; δ_H 1.21 [9H, s, $(CH_3)_3C$], 1.92–2.08 and 2.2–2.34 (2H, 2 m, H_2-3), 3.08 and 3.12 (6H, 2 d, *J* 11.2 and 11.1, CH_3OP), 4.01–4.18 (1H, m, H-4), 5.39 (1H, dd, *J* 7.65 and 2.05, H-2), 7.28–7.45 and 7.52–7.6 (5H, 2 m, H_{arom}), 7.5 and 8.1 (4H, 2 d, *J* 8.5, H_{arom}); δ_C 28.58 [s, $(CH_3)_3C$], 38.86 (d, *J* 9.13, C-3), 40.7 (d, *J* 7.47, C-4), 51.72 and 52.1 (2 d, *J* 6.03 and 6.7, CH_3OP), 76.38 [s, $(CH_3)_3C$], 95.04 (s, C-2), 99.69 (d, *J* 203.38, C-5), 123.32, 127.78, 128.9, 129.22, 129.24 and 130.04 (6 s, *o*-, *m*-, *p*-C_{arom}), 135.6 and 146.54 (2 s, *i*-C_{arom}), 151.9 (s, *p*-C_{arom}), 164.51 (d, *J* 23.54, C-6).

5-(Dimethoxyphosphoryl)-2-ethoxy-6-ethoxycarbonyl-3,4-dihydro-4-(4-nitrophenyl)-2*H*-pyran 6p. *Viscous product* purified by flash column chromatography over silica gel and elution with

diethyl ether (Found: C, 50.48; H, 5.72; N, 3.38. $C_{18}H_{24}NO_9P$ requires C, 50.34; H, 5.59; N, 3.26%), isolated as a mixture of diastereomers, which have been separated.

t-6p.—Viscous product, separated by column chromatography over silica gel and elution with (1 : 100) methanol–diethyl ether; δ_P 20.46; δ_H 1.19 (3H, t, *J* 7.0, CH_3CH$_2$O), 1.33 (3H, t, *J* 7.1, CH_3CH$_2$O), 1.96–2.03 and 2.12–2.23 (2H, 2 m, H_2-3), 3.38 and 3.45 (6H, 2 d, *J* 11.6 and 11.3, CH_3OP), 3.5–3.6 (1H, m, CH$_3$CH*H*O), 3.83–3.98 (2H, m, CH$_3$C*H*HO and H-4), 4.22–4.37 (2H, m, CH$_3$CH_2O), 5.1 (1H, dd, *J* 4.8 and 2.4, H-2), 7.37 and 8.12 (4H, 2 d, *J* 8.6, H_{arom}); δ_C 13.56 and 14.75 (2 s, *C*H$_3$CH$_2$O), 35.5 (d, *J* 8.4, C-3), 36.27 (d, *J* 5.48, C-4), 52.1 and 53.0 (2 d, *J* 6.0 and 7.2, *C*H$_3$OP), 62.35 and 64.95 (2 s, CH$_3$*C*H$_2$O), 97.35 (s, C-2), 100.0 (d, *J* 197.2, C-5), 123.48 and 129.1 (2 s, *o*-, *m*-C_{arom}), 146.8 (s, *i*-C_{arom}), 150.17 (s, *p*-C_{arom}), 155.1 (d, *J* 22.94, C-6), 163.1 (d, *J* 4.3, C=O).

c-6p.—Viscous product, separated by column chromatography over silica gel and elution with (1 : 100) methanol–diethyl ether; δ_P 20.55; δ_H 1.02 (3H, t, *J* 7.0, CH_3CH$_2$O), 1.35 (3H, t, *J* 7.1, CH_3CH$_2$O), 2.0–2.1 and 2.2–2.31 (2H, 2 m, H_2-3), 3.4–3.95 (7H, m, CH_3OP and CH$_3$C*H*O), 3.75–3.95 (2H, m, CH$_3$CH*H*O and H-4), 4.23–4.38 (2H, m, CH$_3$CH_2O), 5.16 (1H, t, *J* 3.4, H-2), 7.38 and 8.08 (4H, 2 d, *J* 8.7, H_{arom}); δ_C 13.8 and 14.8 (2 s, *C*H$_3$CH$_2$O), 34.61 (d, *J* 8.3, C-3), 36.56 (d, *J* 5.58, C-4), 52.2 and 53.1 (2 d, *J* 6.1 and 7.58, *C*H$_3$OP), 62.4 and 65.0 (2 s, CH$_3$*C*H$_2$O), 98.86 (s, C-2), 100.85 (d, *J* 198.55, C-5), 122.94 and 131.8 (2 s, *o*-, *m*-C_{arom}), 146.6 (s, *i*-C_{arom}), 150.1 (s, *p*-C_{arom}), 155.4 (d, *J* 23.0, C-6), 163.0 (d, *J* 4.37, C=O).

2-*tert*-Butoxy-5-(dimethoxyphosphoryl)-6-ethoxycarbonyl-3,4-dihydro-4-(4-nitrophenyl)-2*H*-pyran 6q. *Viscous product* purified by flash column chromatography over silica gel and elution with (1 : 10) methanol–diethyl ether (Found: C, 52.32; H, 6.12; N, 3.32. $C_{20}H_{28}NO_9P$ requires C, 52.51; H, 6.12; N, 3.06%), isolated as a mixture of diastereomers, which were not separated.

t-6q.—δ_P 21.05; δ_H 1.22 [9H, s, (CH_3)$_3$C], 1.3 (3H, t, *J* 7.1, CH_3CH$_2$O), 1.8–2.06 and 2.15–2.3 (2H, 2 m, H_2-3), 3.4 and 3.49 (6H, 2 d, *J* 11.28 and 11.3, CH_3OP), 4.92 (1H, q, *J* 6.8, H-4), 4.19–3.5 (2H, m, CH$_3$CH_2O), 5.33 (1H, t, *J* 2.22, H-2), 7.38 and 8.15 (4H, 2 d, *J* 8.54, H_{arom}); δ_C 13.73 (s, *C*H$_3$CH$_2$O), 28.47 [s, (*C*H$_3$)$_3$C], 36.8 (d, *J* 8.45, C-3), 37.13 (d, *J* 5.5, C-4), 52.26 and 52.6 (2 d, *J* 5.13 and 5.6, *C*H$_3$OP), 76.57 [s, (CH$_3$)$_3$*C*], 92.5 (s, C-2), 100.65 (d, *J* 197.5, C-5), 123.45 and 128.89 (2 s, *o*-, *m*-C_{arom}), 146.8 (s, *i*-C_{arom}), 150.56 (s, *p*-C_{arom}), 155.89 (d, *J* 22.86, C-6), 163.06 (d, *J* 4.2, C=O).

c-6q.—δ_P 21.02; δ_H 1.11 [9H, s, (CH_3)$_3$C], 1.3 (3H, t, *J* 7.1, CH_3CH$_2$O), 1.8–2.06 and 2.15–2.3 (2H, 2 m, H_2-3), 3.45 and 3.5 (6H, 2 d, *J* 11.22 and 11.3, CH_3OP), 4.92 (1H, q, *J* 6.8, H-4), 4.19–3.5 (2H, m, CH$_3$CH_2O), 5.38 (1H, t, *J* 2.02, H-2), 7.38 and 8.07 (4H, 2 d, *J* 8.54, H_{arom}); δ_C 13.78 (s, *C*H$_3$CH$_2$O), 28.3 [s, (*C*H$_3$)$_3$C], 36.1 (d, *J* 8.67, C-3), 37.13 (d, *J* 5.5, C-4), 52.26 and 52.6 (2 d, *J* 5.13 and 5.6, *C*H$_3$OP), 76.57 [s, (CH$_3$)$_3$*C*], 94.39 (s, C-2), 100.56 (d, *J* 197.4, C-5), 122.86 and 129.45 (2 s, *o*-, *m*-C_{arom}), 146.48 (s, *i*-C_{arom}), 150.4 (s, *p*-C_{arom}), 155.87 (d, *J* 22.8, C-6), 163.06 (d, *J* 4.2, C=O).

6-(Diethylcarbamoyl)-5-(dimethoxyphosphoryl)-2-ethoxy-3,4-dihydro-4-(4-nitrophenyl)-2*H*-pyran 6r. *Viscous product* purified by flash column chromatography over silica gel and elution with diethyl ether (Found: C, 52.54; H, 6.56; N, 6.16. $C_{20}H_{29}N_2O_8P$ requires C, 52.63; H, 6.40; N, 6.14%), isolated as a mixture of diastereomers, which have been separated.

t-6r.—Viscous product, separated by column chromatography over silica gel and elution with (0.5 : 100) methanol–diethyl ether; δ_P 20.95; δ_H 1.05–1.23 [9H, m, CH_3CH$_2$O and N(CH$_2$CH_3)$_2$], 1.95–2.05 and 2.06–2.2 (2H, 2 m, H_2-3), 3.25–3.55 [12H, m, CH$_3$C*H*O, (CH_3OP)$_2$, N(CH_2CH$_3$)$_2$ and H-4], 3.82–3.95 (1H, m, CH$_3$CH*H*O), 4.98 (1H, dd, *J* 6.77 and 2.7, H-2), 7.4 and 8.15 (4H, 2 d, *J* 8.7, H_{arom}); δ_C 11.87 and 13.46 [2 s, N(CH$_2$*C*H$_3$)$_2$], 14.78 (s, *C*H$_3$CH$_2$O), 35.0 (d, *J* 10.0, C-3), 36.4 (d, *J* 6.2, C-4), 38.5 and 42.7 [2 s, N(*C*H$_2$CH$_3$)$_2$], 51.9 and 52.3 (2 d, *J* 6.2 and 5.6, *C*H$_3$OP), 65.1 (s, CH$_3$*C*H$_2$O), 97.4 (d, *J* 200.2, C-5), 97.42 (s, C-2), 123.4 and 128.95 (2 s, *o*-, *m*-C_{arom}), 146.7 (s, *i*-C_{arom}), 150.5 (s, *p*-C_{arom}), 159.1 (d, *J* 25.6, C-6), 163.4 (d, *J* 3.5, C=O).

c-6r.—Viscous product, separated by column chromatography over silica gel and elution with (0.5 : 100) methanol–diethyl ether; δ_P 21.01; δ_H 0.98 and 1.15 [6H, 2 t, *J* 7.1 and *J* 7.2, N(CH$_2$CH_3)$_2$], 1.22 (3H, t, *J* 7.1, CH_3CH$_2$O), 2.04–2.15 and 2.21–2.31 (2H, 2 m, H_2-3), 3.34–3.52 [11H, m, CH$_3$C*H*HO, N(CH_2CH$_3$)$_2$ and (CH_3OP)$_2$], 3.75–3.85 (1H, m, CH$_3$CH*H*O), 3.86–3.94 (1H, m, H-4), 5.15 (1H, t, *J* 2.85, H-2), 7.46 and 8.13 (4H, 2 d, *J* 8.8, H_{arom}); δ_C 12.0 and 13.67 [2 s, N(CH$_2$*C*H$_3$)$_2$], 14.7 (s, *C*H$_3$CH$_2$O), 34.45 (d, *J* 8.6, C-3), 36.17 (d, *J* 6.0, C-4), 38.6 and 41.8 [2 s, N(*C*H$_2$CH$_3$)$_2$], 52.08 and 52.15 (2 d, *J* 6.1 and 6.0, *C*H$_3$OP), 64.86 (s, CH$_3$*C*H$_2$O), 98.5 (d, *J* 199.5, C-5), 98.53 (s, C-2), 122.8 and 129.5 (2 s, *o*-, *m*-C_{arom}), 146.47 (s, *i*-C_{arom}), 150.8 (s, *p*-C_{arom}), 158.7 (d, *J* 25.35, C-6), 163.6 (d, *J* 3.5, C=O).

2-*tert*-Butoxy-6-(diethylcarbamoyl)-5-(dimethoxyphosphoryl)-3,4-dihydro-4-(4-nitrophenyl)-2*H*-pyran 6s. *Viscous product* purified by flash column chromatography over silica gel and elution with diethyl ether (Found: C, 54.41; H, 6.95; N, 5.68. $C_{22}H_{33}N_2O_8P$ requires C, 54.54; H, 6.87; N, 5.78%), isolated as a mixture of diastereomers, which have been separated.

t-6s.—Viscous product, separated by column chromatography over silica gel and elution with (0.5 : 100) methanol–diethyl ether; δ_P 21.38; δ_H 1.13 [9H, s, (CH_3)$_3$C], 1.15 and 1.22 [6H, 2 t, *J* 7.1, N(CH$_2$CH_3)$_2$], 1.83–1.95 and 2.0–2.11 (2H, 2 m, H_2-3), 3.38 [4H, q, *J* 7.1, N(CH_2CH$_3$)$_2$], 3.46 (6H, d, *J* 11.9, CH_3OP), 3.88–3.96 (1H, m, H-4), 4.71 (1H, dd, *J* 7.7 and *J* 2.7, H-2), 7.4 and 8.13 (4H, 2 d, *J* 8.7, H_{arom}); δ_C 12.08 and 13.16 [2 s, N(CH$_2$*C*H$_3$)$_2$], 27.5 [s, (*C*H$_3$)$_3$C], 36.35 (d, *J* 8.5, C-3), 37.05 (d, *J* 6.34, C-4), 38.59 and 42.86 [2 s, N(*C*H$_2$CH$_3$)$_2$], 52.16 and 52.45 (2 d, *J* 6.0 and 5.58, *C*H$_3$OP), 76.3 [s, (CH$_3$)$_3$*C*], 92.45 (s, C-2), 96.49 (d, *J* 200.66, C-5), 123.6 and 129.05 (2 s, *o*, *m*-C_{arom}), 146.9 (s, *i*-C_{arom}), 151.1 (s, *p*-C_{arom}), 159.94 (d, *J* 25.58, C-6), 163.68 (d, *J* 3.1, C=O).

c-6s.—Viscous product, separated by column chromatography over silica gel and elution with (0.5 : 100) methanol–diethyl ether; δ_P 21.42; δ_H 1.03 [9H, s, (CH_3)$_3$C], 1.15 and 1.23 [6H, 2 t, *J* 7.1, N(CH$_2$CH_3)$_2$], 1.88–1.09 and 2.19–2.26 (2H, 2 m, H_2-3), 3.41 [4H, q, *J* 7.1, N(CH_2CH$_3$)$_2$), 3.45 and 3.5 (6H, 2 d, *J* 11.5, CH_3OP), 3.82–3.93 (1H, m, H-4), 5.41 (1H, t, *J* 2.86, H-2), 7.4 and 8.06 (4H, 2 d, *J* 8.78, H_{arom}); δ_C 12.06 and 13.66 [2 s, N(CH$_2$*C*H$_3$)$_2$], 28.28 [s, (*C*H$_3$)$_3$C], 35.79 (d, *J* 8.54, C-3), 36.22 (d, *J* 5.89, C-4), 38.45 and 42.81 [2 s, N(*C*H$_2$CH$_3$)$_2$], 52.19 and 52.53 (2 d, *J* 5.98 and 5.66, *C*H$_3$OP), 76.45 [s, (CH$_3$)$_3$*C*], 93.48 (s, C-2), 97.52 (d, *J* 200.1, C-5), 122.75 and 129.55 (2 s, *o*-, *m*-C_{arom}), 146.37 (s, *i*-C_{arom}), 151.27 (s, *p*-C_{arom}), 159.24 (d, *J* 25.35, C-6), 163.6 (d, *J* 3.54, C=O).

Typical procedure for the one-pot synthesis of phosphonopyran 6r

To a 100 cm^3 flask equipped with a Dean–Stark trap and a reflux condenser were added a mixture of phosphonate **4f** (2.51 g, 10 mmol), 4-nitrobenzaldehyde (1.51 g, 10 mmol), and ethyl vinyl ether (7.2 g, 100 mmol) in benzene (50 cm^3) and a few drops of piperidine were introduced. The reaction mixture was refluxed for 4 h, then the benzene was removed by distillation under reduced pressure. Further work-up and purification were carried out as above, giving the pure product **6r** (Table 3).

Acknowledgements

We warmly thank Dr X. Pannecoucke, who conducted the NOE experiments. This work was supported by the Réseau Interrégional Normand de Chimie Organique Fine (Contrat de

Plan Etat-Bassin Parisien-Régions Haute-Normandie et Basse-Normandie), which is gratefully acknowledged, especially for delivering a post-doctoral fellowship to H. Al-Badri.

References

1 L. F. Tietze and G. Kettschau, *Top. Curr. Chem.*, 1997, **189**, 1.
2 L. F. Tietze, G. Kettschau, J. A. Gewert and A. Schuffenhauer, *Curr. Org. Chem.*, 1998, **2**, 19.
3 A. Ichihara and Oikawa, *Curr. Org. Chem.*, 1998, **2**, 365.
4 K. N. Houk, *J. Am. Chem. Soc.*, 1973, **95**, 4092.
5 L. A. Telan, C.-D. Poon and S. A. Evans, Jr., *J. Org. Chem.*, 1996, **61**, 7455.
6 D. A. Evans and J. S. Johnson, *J. Am. Chem. Soc.*, 1998, **120**, 4895.
7 H. Al-Badri, E. About-Jaudet and N. Collignon, *Synthesis*, 1994, 1072.
8 H. Al-Badri, E. About-Jaudet, J.-C. Combret and N. Collignon, *Synthesis*, 1995, 1401.
9 H. Al-Badri, E. About-Jaudet and N. Collignon, *J. Chem. Soc., Perkin Trans. 1*, 1996, 931.
10 F. Chevalier, H. Al-Badri and N. Collignon, *Bull. Soc. Chim. Fr.*, 1997, **134**, 801.
11 H. Al-Badri, E. About-Jaudet and N. Collignon, *Tetrahedron Lett.*, 1996, **37**, 2951.
12 E. Aboujaoude, N. Collignon and P. Savignac, *J. Organomet. Chem.*, 1984, **264**, 9.
13 A. N. Pudovik, G. E. Yasterbova and V. I. Nikitina, *J. Gen. Chem. USSR* (*Engl. Transl.*), 1967, **37**, 480.
14 R. Sakoda, H. Matsumoto and K. Seto, *Synthesis*, 1993, 705.
15 G. L. Kenyon and F. H. Westheimer, *J. Am. Chem. Soc.*, 1966, **88**, 3557.
16 C. Benezra, S. Niec and G. Ourisson, *Bull. Soc. Chim. Fr.*, 1967, 1140.
17 M. J. Cook and G. Desimoni, *Tetrahedron*, 1971, **27**, 257.
18 S. S. Hall, G. F. Weber and A. Duggan, *J. Org. Chem.*, 1978, **43**, 667.
19 M. Maier and R. R. Schmidt, *Liebigs Ann. Chem.*, 1985, 2261.
20 K. Matsumoto and A. Sera, *Synthesis*, 1985, 999.
21 G. Jenner, *Tetrahedron*, 1997, **53**, 2669.
22 L. F. Tietze, M. Henrich, A. Niklaus and M. Buback, *Chem. Eur. J.*, 1999, **5**, 297.
23 J. M. Mellor and C. F. Webb, *J. Chem. Soc., Perkin Trans. 2*, 1974, 17.
24 D. L. Boger and K. D. Robarge, *J. Org. Chem.*, 1988, **53**, 3373.
25 G. Dujardin, M. Maudet and E. Brown, *Tetrahedron Lett.*, 1997, **38**, 1555.
26 J. Thorhauge, M. Johannsen and K. A. Jorgensen, *Angew. Chem., Int. Ed.*, 1998, **37**, 2404.
27 D. A. Evans, E. J. Olhava, J. S. Johnson and J. M. Janey, *Angew. Chem., Int. Ed.*, 1998, **37**, 3372.
28 B. B. Snider and Q. Zhang, *J. Org. Chem.*, 1991, **56**, 4908.
29 L. F. Tietze, C. Schneider and A. Grote, *Chem. Eur. J.*, 1996, **2**, 139.
30 L. F. Tietze and U. Beifuss, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 131.
31 L. F. Tietze, *J. Heterocycl. Chem.*, 1990, **27**, 47.

Paper 9/03972D