Novel Synthesis of α-Acetylstyrylphosphonates

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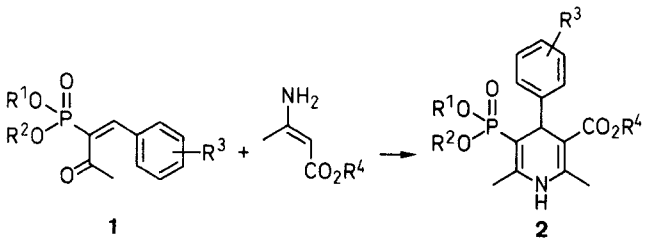
α-Acetylstyrylphosphonates were conveniently synthesized from 2-oxopropylphosphonates and substituted (dimorpholinomethyl)-benzenes (aminals). 4-Benzylidenemorpholinium carboxylates, generated from aminals by the action of α-halo acids, reacted with the phosphonates to give the products by elimination of the amine. The yields were influenced by the nature of substituents and their position in the phenyl ring and could be improved by adjustment of the acidities of the reacted acids. α-Acetylstyrylphosphonates containing various substituents on every position (at the 2-, 3-, or 4-position) in the phenyl ring were obtained generally in excellent yields using monochloroacetic acid.

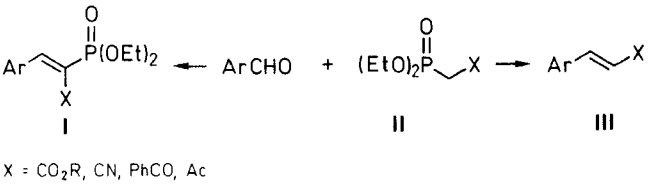
Owing to the discovery of new pharmacological applications[1-4] of 1,4-dihydropyridines **2**, effective synthesis of α-acetylstyrylphosphonates **1**, precursors of **2**,[5] has been needed (Scheme 1). However, the most commonly used Knoevenagel-type reaction of an acetonylphosphonate with an aromatic aldehyde gives the desired α-acetylstyrylphosphonate in low yield as the Wittig–Horner type alkylidenation of a carbonyl group takes place predominantly. In order to suppress the elimination of phosphonate from intermediary **6** and to obtain the desired phosphonate selectively, substitution of the hydroxy group of **5** with another leaving group seemed promising. As a dialkylamino group would be suitable, an aminal of the corresponding aldehyde was substituted for an aldehyde. This paper describes in detail the acid-mediated reaction of acetonylphosphonates **3** with aminal **12**.[6] Widely applicable and highly selective synthesis of **1** was performed by using a suitable α-halo acid, namely monochloroacetic acid (MCA). A mechanistic discussion is also added.



Compound	R^1	R^2	R^3	R^4
NZ-105			3-NO_2	

Scheme 1

1-(Functionally)substituted 2-arylvinylphosphonates **I** involving a class of α-acetylstyrylphosphonates **1** have been commonly synthesized by base or acid–base catalyzed reactions of aromatic aldehydes with phosphonates **II**, which have been intensively investigated for about one decade since 1960,[7,8] as in Scheme 2. However, these studies demonstrated that the reactions proceed in two processes to give the desired products **I** and Wittig–Horner type carbonyl alkylidenation products **III**, and electron-withdrawing substituents (X) in the aromatic aldehydes disfavor formation of **I**.



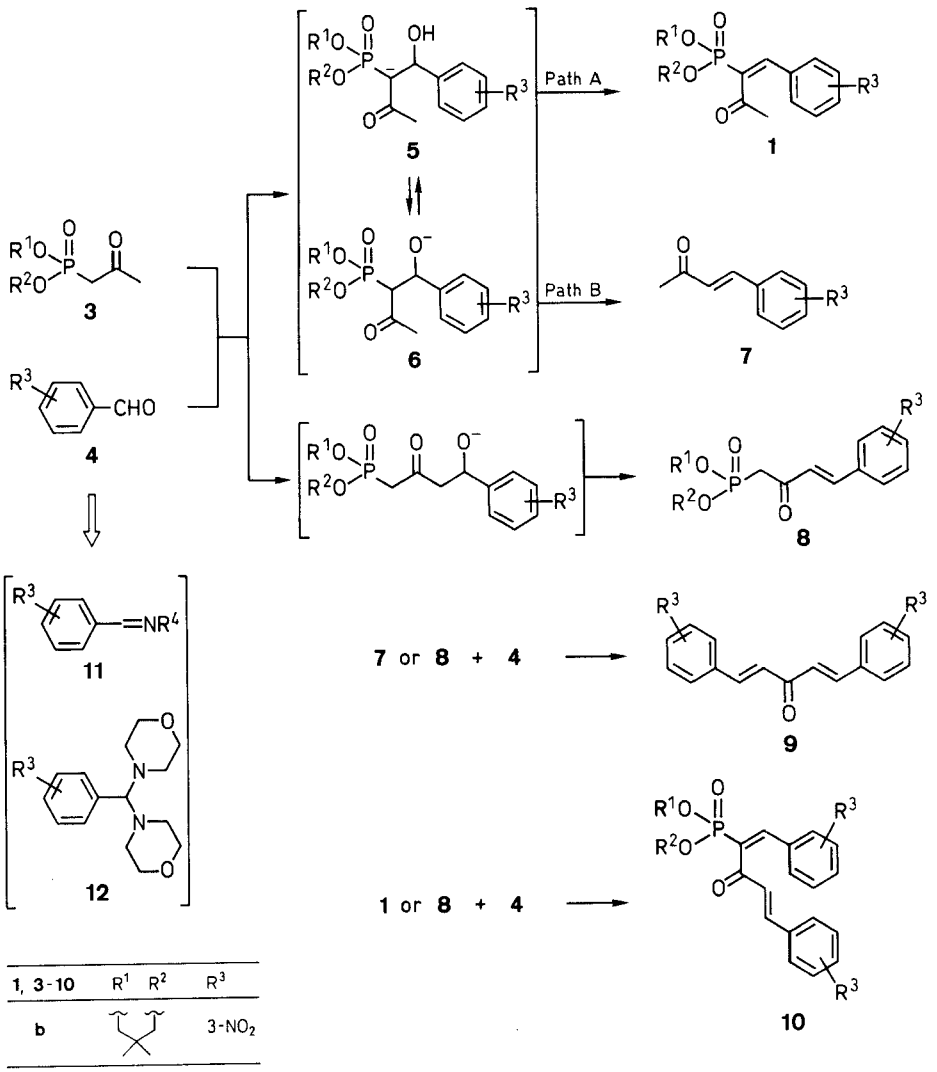
X = CO_2R, CN, PhCO, Ac

Scheme 2

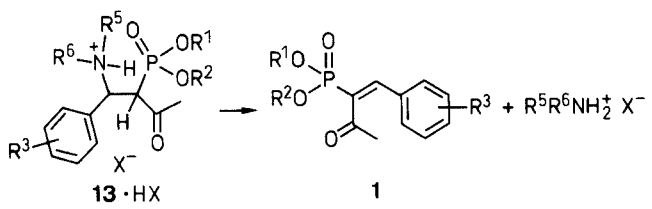
A synthesis of **1** has been reported by Pudovik et al.,[7] who obtained diethyl α-acetylstyrylphosphonate (**1**, R^1 = R^2 = Et, R^3 = H) in 65% yield by the condensation of diethyl acetonylphosphonate (**3**, R^1 = R^2 = Et) with benzaldehyde (**4**, R^3 = H) under the catalytic action of piperidine, but further synthetic investigations have not been reported until now. We prepared the 3-nitro-substituted derivative **1b** by this classical Knoevenagel-type reaction. The reaction of 2,2-dimethyl-1,3-propanediyl 2-oxopropylphosphonate (**3b**) with 3-nitrobenzaldehyde (**4b**) in the presence of more than one quivalent of piperidine quantitatively yielded the Wittig–Horner type reaction product **7b**. The reaction using piperidine/acetic acid as a catalyst proceeded by several competitive processes to give a complex mixture of the products: the desired phosphonate **1b** (about 30% yield), **7b** (about 10% yield), straight-condensation product **8b** and secondary product **9b** (about 20% yield), and **10b** (about 20% yield) (Scheme 3). Thus, it was necessary not only to overcome the general problem which remained in the synthesis of **I** (suppression of the Wittig–Horner type alkylidenation of the carbonyl group) but also to suppress the formation of the straight-condensation products in this study.

We first focussed on avoiding the formation of **6** which would undergo elimination of the phosphonate, and tried to replace the hydroxy group of **5** with a dialkylamino group. We expected to realize the selective synthesis of **1** by eliminating the amine from intermediates **13** · HX as in Scheme 4. Wittig–Horner type alkylidenation of the carbonyl group should be suppressed by the protonation of the amino group in **13** · HX, since this could inhibit the interaction between the phosphorus and the amino moieties. As intermediates **13** should be formed by reacting **3** with **12**, we tried the reaction in the presence of acid. The products **1** containing a wide variety of substituents located in 2, 3, or 4-position in the phenyl ring, were generally obtained in excellent yields almost without variation due to electronic and steric factors. The results are herein summarized.

Aminals **12** were prepared from the corresponding aldehydes **4** through the reaction with morpholine under azeotropical removal of water (83–98% yield) or dehydration with boric anhydride (64–92% yield).[9] The α-acetylstyrylphosphonates **1** were prepared by treating one equivalent of **3** with one equivalent of **12** in toluene



Scheme 3



Scheme 4

using two equivalents of α-halo acids at 60 °C for 0.5 hours or at room temperature for 2.5–4 hours under standard conditions. Trifluoroacetic acid (TFA) and MCA were used as the α-halo acids. The use of acetic acid and methanesulfonic acid was also examined in relation to the mechanistic discussion. The use of TFA afforded **1** in 51–93 % yield along with **8**. Although the yields were affected by the nature of the substituents and their position in the phenyl ring, Wittig–Horner type alkylidenation was entirely insignificant; the difference in the yields of **1** was approximately associated with the difference in both formation of **8** and recovery of **4**. Electron-withdrawing substituents (NO_2, CN and CF_3) favor selective formation of the desired products (87–93 % yield; Table 1, entries 4, 6, 8, and 10) but only the 2-nitro substituent was markedly disfavored (57 % yield; Table 1, entries 1 and 2). Also, the 2- and 4-methoxy substituents led to decreased yields (51–56 %; Table 1, entries 24, 28 and 29). These results were not improved even when the reactions were prolonged (Table 1, entry 30).

Since compounds **1** were considered to be produced via formation of iminium salts as described below, MCA was examined according to the idea that the use of a weaker acid would enhance a base-catalyzed condensation. The reaction in the presence of MCA in place of TFA proceeded exclusively as desired under the same conditions, to afford **1** as the sole products (85–94 % yield for cyclic phosphonates; Table 1, entries 3, 5, 7, 9, 11, 15, 17, 20, 23, 25, 27 and 31, and 83–84 % yield for acyclic; Table 1, entries 32 and 34). The extent of the formation of byproducts which could be isolated by chromatography was entirely insignificant in any case. The differences in the yields of **1** were small and almost totally associated with the difference in the recovery of **4**. These results demonstrated that the synthetic approach described above provides a versatile synthesis of **1**. Furthermore, **1**

Table 1. Synthesis of α-Acetylstyrylphosphonates **1**

Entry	Aminal	(R^3)	Acid[a]	Conditions	Product	Yield (%)	ratio E/Z[d]	By-product	Yield (%)	Aldehyde	Recovery (%)
1	**12a**	2-NO_2	TFA	60°C, 0.5 h	**1a**[b]	57	40 : 60	**8a**	13	**4a**	19
2	**12a**	2-NO_2	TFA	r.t., 2.5 h	**1a**	57	30 : 70	**8a**	15	**4a**	–
3	**12a**	2-NO_2	MCA	r.t., 3.0 h	**1a**	85	75 : 25	**8a**	trace	**4a**	11
4	**12b**	3-NO_2	TFA	60°C, 0.5 h	**1b**[b]	90	95 : 5	**8b**	< 2	**4b**	–
5	**12b**	3-NO_2	MCA	r.t., 2.5 h	**1b**	93	95 : 5	**8b**	< 2	**4b**	–
6	**12c**	4-NO_2	TFA	60°C, 0.5 h	**1c**	87	95 : 5	**8c**	< 2	**4c**	–
7	**12c**	4-NO_2	MCA	r.t., 3.0 h	**1c**	91	95 : 5	**8c**	trace	**4c**	5
8	**12d**	4-CN	TFA	60°C, 0.5 h	**1d**	93	95 : 5	**8d**	< 2	**4d**	–
9	**12d**	4-CN	MCA	r.t., 3.0 h	**1d**	92	85 : 15	**8d**	trace	**4d**	6
10	**12e**	2-CF_3	TFA	r.t., 3.0 h	**1e**[c]	91	20 : 80	**8e**	5	**4e**	1
11	**12e**	2-CF_3	MCA	r.t., 3.0 h	**1e**	94	80 : 20	**8e**	trace	**4e**	1
12	**12f**	2,3-Cl_2	TFA	r.t., 1.0 h	**1f**[c]	84	55 : 45[f]	**8f**	trace	**4f**	11
13	**12f**	2,3-Cl_2	TFA	r.t., 5.0 h	**1f**	89	60 : 40	**8f**	trace	**4f**	5
14	**12f**	2,3-Cl_2	TFA	r.t., 20 h	**1f**	91	70 : 30	**8f**	trace	**4f**	5
15	**12f**	2,3-Cl_2	MCA	r.t., 3.0 h	**1f**	90	75 : 25	**8f**	trace	**4f**	7
16	**12g**	4-Cl	TFA	60°C, 0.5 h	**1g**	85	85 : 15	**8g**	5	**4g**	5
17	**12g**	4-Cl	MCA	r.t., 3.0 h	**1g**	93	80 : 20	**8g**	trace	**4g**	6
18	**12h**	H	TFA	60°C, 0.5 h	**1h**	80	80 : 20	**8h**	8	**4h**	3
19	**12h**	H	TFA	r.t., 4.0 h	**1h**	79	80 : 20	**8h**	8	**4h**	–
20	**12h**	H	MCA	r.t., 3.0 h	**1h**	94	85 : 15	**8h**	trace	**4h**	3
21	**12i**	4-Me	TFA	60°C, 0.5 h	**1i**	71	90 : 10	**8i**	12	**4i**	3
22	**12i**	4-Me	TFA	r.t., 4.0 h	**1i**	75	80 : 20	**8i**	10	**4i**	–
23	**12i**	4-Me	MCA	r.t., 3.0 h	**1i**	89	85 : 15	**8i**	trace	**4i**	3
24	**12j**	2-OMe	TFA	60°C, 0.5 h	**1j**	56	85 : 15	**8j**	19	**4j**	17
25	**12j**	2-OMe	MCA	r.t., 3.0 h	**1j**	90	85 : 15	**8j**	trace	**4j**	8
26	**12k**	3-OMe	TFA	r.t., 4.0 h	**1k**	76	85 : 15	**8k**	6	**4k**	–
27	**12k**	3-OMe	MCA	r.t., 3.0 h	**1k**	90	85 : 15	**8k**	trace	**4k**	7
28	**12l**	4-OMe	TFA	60°C, 0.5 h	**1l**	51	85 : 15	**8l**	18	**4l**	21
29	**12l**	4-OMe	TFA	r.t., 3.0 h	**1l**	52	70 : 30	**8l**	14	**4l**	29
30	**12l**	4-OMe	TFA	r.t., 9.0 h	**1l**	46	85 : 15	**8l**	14	**4l**	23
31	**12l**	4-OMe	MCA	r.t., 3.0 h	**1l**	88	85 : 15	**8l**	trace	**4l**	8
32	**12b**	3-NO_2	MCA	r.t., 5.0 h	**1m**[e]	84	85 : 15	**8m**	trace	**4m**	14
33	**12c**	4-NO_2	TFA	r.t., 3.0 h	**1n**[e]	82	95 : 5	**8n**	–	**4n**	–
34	**12c**	4-NO_2	MCA	r.t., 3.0 h	**1n**	83	100 : 0	**8n**	trace	**4n**	14

[a] TFA/CF_3CO_2H, MCA/$ClCH_2CO_2H$.
[b] Refs. 3, 11.
[c] Ref. 11.
[d] Determined by integration of singlets for the acetyl group in the ^1H NMR spectrum of **1** before recrystallization.
[e] Diethyl ester obtained from the reaction using diethyl 2-oxopropylphosphonate (**3a**) in place of **3b**.
[f] E/Z-Ratio of crude product was 45 : 55.

can be prepared with a one-pot handling from **4** via **12** by means of toluene azeotropy. The morpholinium chloroacetate, formed from eliminated morpholine, is readily removed by washing with water, and if necessary, **4** by treatment with aqueous sodium hydrogen sulfite; therefore, **1** can be isolated with simple operations at high recovery. For instance, **1b**, the key intermediate of the potent antihypertensive agent NZ-105, was obtained in 87% overall yield through a two-step, single-flask reaction followed by separation by only crystallization without a chromatographic procedure.

On the other hand, an improved synthesis of **1** (R^3 = 2- and 3-electron-withdrawing groups), to which a Knoevenagel-type condensation using the imine **11** in the presence of acetic anhydride (two equivalents)[10] was applied, was independently reported[11] after our initial presentation. This imine method, which was carried out under rather severe conditions (benzene reflux, 4 hours), seems effective in some cases, but also suggests that yields of **1** are affected by the substitution pattern in the phenyl ring as well as in the phosphonate moiety. Namely, the yields of 3-substituted (NO_2) cyclic phosphonates are good (88 and 91% yield) but of 2-substituted (NO_2, CF_3 and Cl) and an acyclic phosphonate (3-NO_2) moderate (58–68 and 51% yield). In addition to this disadvantage, the imine method also suffers from complexity in the isolation of **1** because the neutral amide is formed accompanied by condensation.

The reaction products were obtained as a mixture of *E* and *Z* isomers. Although *E*/*Z*-ratios were high in almost all the examples, those of the products containing an electron-withdrawing group in position 2 (NO_2, CF_3 and Cl) were inverted with the use of TFA (Table 1, entries 1, 2, 10, 12, 13 and 14).

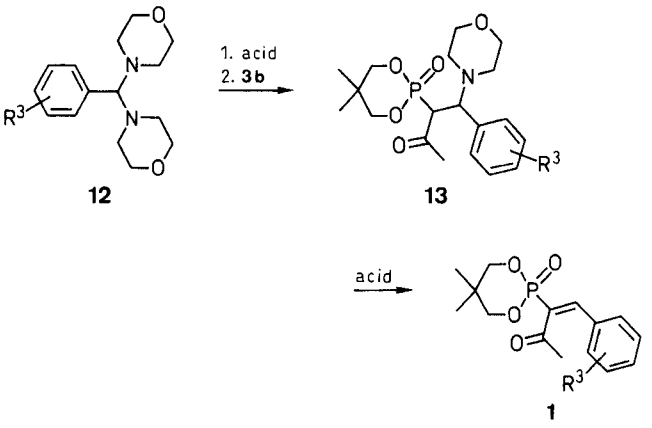
The use of acetic acid gave unsatisfactory results; **1b** was obtained in only 28% yield along with **7b** (21%) (Table 3, entry 3). The 4-methoxy-substituted compound was isolated as the intermediary condensation product **13l**, a major product (65% yield, Table 3, entry 4). Treatment of

Table 2. Properties of α-Acetylstyrylphosphonates **1**

Compound	mp[a] (°C) (solvent)	Ratio E/Z[a]	^{1}H NMR[b] δ_{COCH_3} E	Z	Molecular Formula[c]
1a	142–151 (toluene)[d]	30 : 70 (30 : 70)	2.27	2.57	$C_{15}H_{18}NO_6P$ (339.3)
1b	150–153 (toluene)[e]	95 : 5 (95 : 5)	2.32	2.58	$C_{15}H_{18}NO_6P$ (339.3)
1c	142–145 (toluene)	95 : 5 (95 : 5)	2.28	2.56	$C_{15}H_{18}NO_6P$ (339.3)
1d	102–107 (toluene)	35 : 65 (95 : 5)	2.27	2.56	$C_{16}H_{18}NO_4P$ (319.3)
1e	74–93 (toluene/hexane)[f]	90 : 10 (80 : 20)	2.14	2.57	$C_{16}H_{18}F_3O_4P$ (362.3)
1f	119–121 (toluene/hexane)[g]	100 : 0 (75 : 25)	2.20	2.57	$C_{15}H_{17}Cl_2O_4P$ (363.2)
1g	97–105 (toluene)	95 : 5 (85 : 15)	2.27	2.48	$C_{15}H_{18}ClO_4P$ (328.7)
1h	83–87 (toluene/hexane)	100 : 0 (80 : 20)	2.25	2.55	$C_{15}H_{19}O_4P$ (294.3)
1i	137–140 (toluene/hexane)	100 : 0 (80 : 20)	2.30	2.58	$C_{16}H_{21}O_4P$ (308.3)
1j	87–112 (toluene/hexane)	90 : 10 (85 : 15)	2.22	2.55	$C_{16}H_{21}O_5P$ (324.3)
1k	95–96 (toluene/hexane)	100 : 0 (85 : 15)	2.25	2.54	$C_{16}H_{21}O_5P$ (324.3)
1l	83–139 (toluene/hexane)	85 : 15 (85 : 15)	2.28	2.52	$C_{16}H_{21}O_5P$ (324.3)
1m	yellowish oil	(85 : 15)	2.30	2.51	$C_{14}H_{18}NO_6P$ (327.3)
1n	70–72 (toluene/hexane)	100 : 0 (100 : 0)	2.31	2.56	$C_{14}H_{18}NO_6P$ (327.3)

[a] In brackets ratio before recrystallization.
[b] In $CDCl_3$/TMS.
[c] Satisfactory microanalyses obtained: **1a–d, n**: C ± 0.39, H ± 0.38, N ± 0.38, **1e–l**: C ± 0.31, H ± 0.33; exception: **1m**.
[d] Lit.[11] mp 142–145 °C (E/Z = 41 : 59).
[e] Lit.[11] mp 136–140 °C (E/Z = 84 : 16).
[f] Lit.[11] mp 75–78 °C (E/Z = 62 : 38).
[g] Lit.[11] mp 113–119 °C (E/Z = 100 : 0).

Table 3. Acetic Acid Mediated Reaction of Aminals **12** with **3b**



Entry	Substrate	Acid	Conditions	Yield (%) of **1**[a]	Yield (%) of **13**
1	**12b**	none	r.t., 5 h	trace[b]	–
2	**12b**	none	80 °C, 2 h	trace[c]	–
3	**12b**	AcOH	r.t., 3 d	28[d]	–
4	**12l**	AcOH	r.t., 22 h	–	65[e]
5	**12b**	$MeSO_3H$	50 °C, 5 h	trace[f]	–

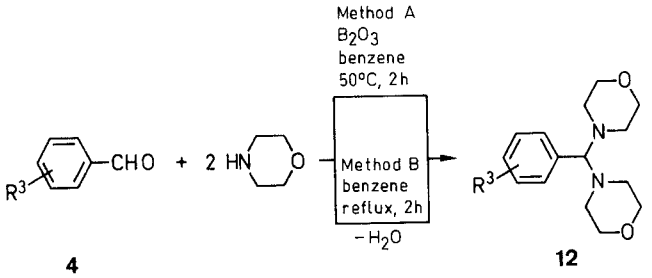
[a] Yields were determined by TLC except those of entries **3** and **4**.
[b] The reaction did not take place.
[c] Formation of **7b** was observed.
[d] Byproduct **7b** (21%) and 3-nitrobenzaldehyde (**4b**, 40%) were also isolated.
[e] Isolated yield by crystallization.
[f] 3-Nitrobenzaldehyde (**4b**) was quantitatively recovered.

13l with one equivalent of TFA or MCA afforded **1l** almost quantitatively.

The Knoevenagel reaction has resulted in a wide variety of intermediates in the alkylidenation process.[12] In these previous studies, a route via the aminal has been proposed. The results in this paper, however, suggest that a new reactive species different from aminal participates in the reaction; the reaction of **12b** with **3b** in the absence of the acid proceeded markedly slowly to give **7b** rather than the desired product **1b** (Table 3, entries 1 and 2). As the α-halo acid has great importance in the activation of the reaction, the reactive species is considered to be formed by treatment of the aminal with the α-halo acid.

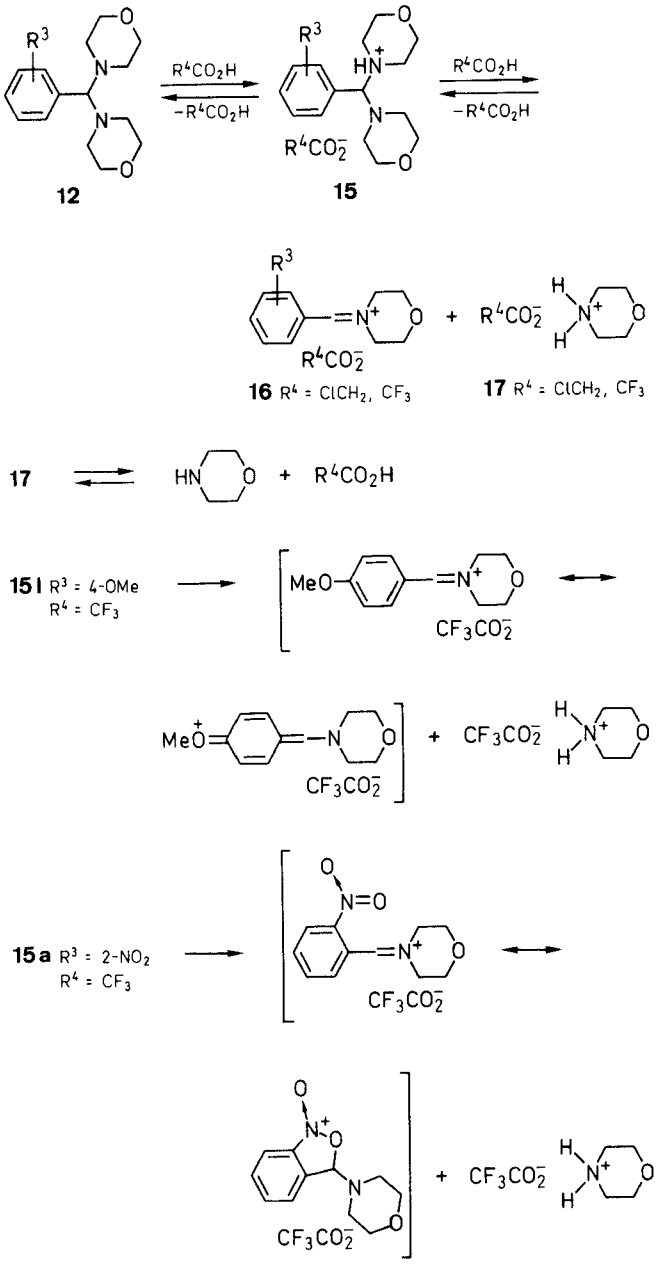
Some attempts have been made using ^{13}C NMR spectroscopy to determine the reactive species. The ^{13}C NMR spectrum of a mixture of 3-(dimorpholinomethyl)-1-nitrobenzene (**12b**) and TFA in a 1 : 2 molar ratio showed four broad signals (δ = 43, 56, 64 and 66) due to morpholine carbons at 20 °C and two signals [δ = 43–65 (broad) and 65] at 60 °C. Two (δ = 43 and 64) of the former signals agreed in the chemical shift with that of the ^{13}C NMR spectrum of a mixture of morpholine and TFA in a 1 : 1 molar ratio. These spectroscopic data indicate that morpholinium trifluoroacetate **17** ($R^4 = CF_3$) and another component containing the morpholine moiety in the structure are in an equilibrium state; there would be a rapid and reversible formation of iminium salt **16b**,[13] where the exchange of morpholine would take place via the protonated aminal **15b** as in Scheme 5. The formation of **16b** is supported by the fact that a signal due to the methine carbon of **12b** at δ = 88 was shifted to δ = 172 by addition of TFA. The ^{13}C NMR spectrum of a mixture of **12l** (R^3 = 4-OMe) and TFA in a 1 : 2 molar ratio showed two temperature-independent signals (δ = 43 and 65) and four dependent signals [δ = 53, 60, 67 and 68 (broad)]. The former agreed with that of the ^{13}C NMR spectrum of **17** in the chemical shift. These spectroscopic data suggest that **17** is not responsible for the equilibrium, and that **16l** exists in equilibrium with another component. Treatment of **12a** ($R^3 = 2\text{-}NO_2$) with TFA also provided a similar spectral pattern (**17** independent of the equilibrium and **16a** in equilibrium with another component). On the other hand, when **12l** or **12a** was treated with MCA in place of TFA, a significant change in the spectrum, which supports the existence of an equilibrium between the iminium salt and morpholine as in **16b**, was observed. A mixture of **12l** and acetic acid gave two broad signals (δ = 48 and 66) due to morpholine carbons; this pattern suggests that the exchange of morpholine is rapid, to such

Table 4. Synthesis of Aminals **12**



Entry	R^3	Product	Method	Yield (%)	mp (°C) (solvent)	Lit. mp (°C)
1	2-NO_2	**12a**	A	92	125–129 (i-Pr_2O)	130.5–131.5[9]
2	3-NO_2	**12b**	B	98	140–142 (i-Pr_2O)	140–142[9]
3	4-NO_2	**12c**[a]	B	97	180–182 (benzene)	195[9]
4	4-CN	**12d**[a]	B	92	179–183 (benzene)	
5	2-CF_3	**12e**[a]	B	83	140–144 (i-Pr_2O)	
6	2,3-Cl_2	**12f**[a]	B	91	90–92 (i-Pr_2O)	
7	4-Cl	**12g**	A	90	133–137 (i-Pr_2O)	137[9]
8	H	**12h**	B	90	102–103 (i-Pr_2O)	105[9]
9	4-Me	**12i**	B	88	91–94 (i-Pr_2O)	96[9]
10	2-OMe	**12j**[a]	B	86	70–74 (i-Pr_2O)	
11	3-OMe	**12k**[a]	B	88	77–81 (i-Pr_2O)	
12	4-OMe	**12l**[a]	B	94	108–115 (i-Pr_2O)	120[9]

[a] Satisfactory microanalyses obtained: C ±0.18, H ±0.16, N ±0.29.

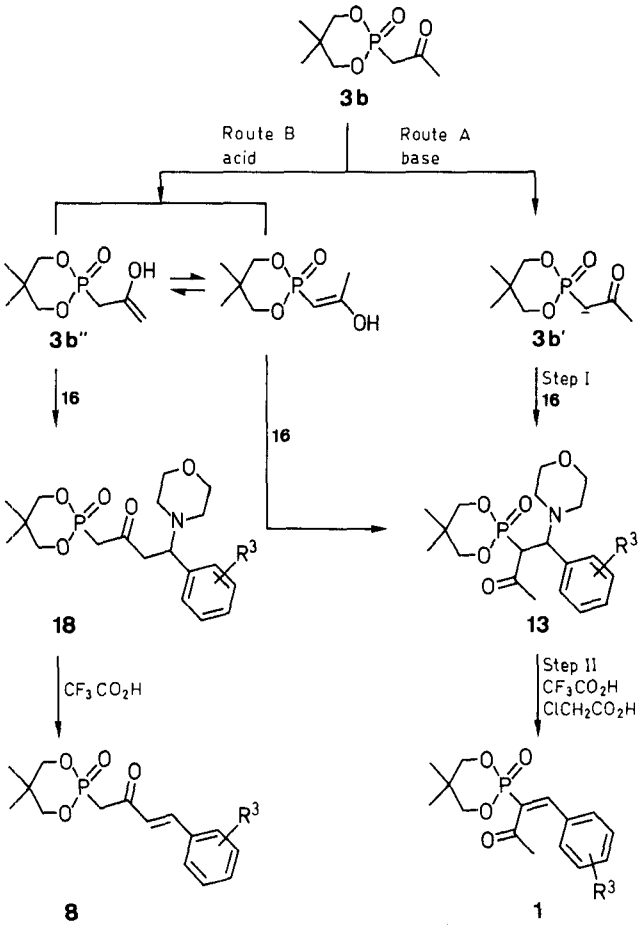


Scheme 5

an extent that signals due to iminium salts and morpholinium acetate are not individually observed. This existence of the equilibrium means addition of an eliminated amine (morpholine) to the iminium salts and suggests the existence of the free amine which is in equilibrium with the acids reacted; the free amine would become a catalyst in the subsequent reaction.

The synthetic and ^{13}C NMR analytical results suggest that the iminium salts **16**, which should be accessible through elimination of morpholine from **12** by the action of the acids, would readily undergo a base-induced condensation (step I) followed by an acid-induced alkylidenation (step II), as in route A in Scheme 6. Decreasing the acidity of the acid would favor the generation of nucleophiles **3′** from **3** to promote the base-induced condensation. While the formation of **1** from **13** is regulated by both the elimination of the amine via the effective protonation of the amino group in **13** and a Michael-type addition of the eliminated amine to **1** (reverse reaction); the low acidity of the acid should enhance the rate of the existence of the free amine and disfavor the formation of **1**. The significant decrease of the yields of **1a**, **1j** and **1l** with the use of TFA, which is consistent with the lack of morpholine exchange in the iminium salt formation in the ^{13}C NMR spectral observations, could be explained as follows. The decreased reactivity toward nucleophilic attack would be due to the intramolecular interaction in **16a** and the resonance effect in **16j** and **16l** as in Scheme 5. While straight-condensation products **8** would be produced predominantly via acid-induced terminal-unsaturated enols **3″**; the high acidity of TFA (pKa = 0.3) should favor this contribution (route B in Scheme 6). Results using acetic acid (pKa = 4.8) demonstrate that the acidity is too low to generate the effective protonation of the amino group in **13** in an equilibrium to which acetic acid and **13** participate or suppress the addition of free morpholine to **1** (step II). On the contrary, a strong acid such as

methanesulfonic acid, would make condensation impossible (step I). Success in the use of MCA (pKa = 2.9) would be due to the acidity suitable for the reaction to proceed exclusively in route A over all steps: the iminium salt formation, the nucleophile **3'** generation followed by the base-induced condensation and the protonation of the amino group in **13** followed by the alkylidenation in Schemes 5 and 6.



Scheme 6

We have found a new method for the effective synthesis of **1** by reaction of phosphonates **3** with **12** in the presence of α-halo acids; in particular, compounds **1** containing a wide variety of substituents were obtained generally in excellent yields with the use of MCA. This aminal method is significantly advantageous to large-scale preparation of **1** because of the exclusive formation of **1** and simple operations over the entire processes involving purification. The reaction proceeds under mild conditions through the formation of 4-benzylidenemorpholinium carboxylates **16** as reactive intermediates. This assumption was supported by ^{13}C NMR spectroscopic observations. Reactions using such iminium salts should generally provide efficient syntheses of (1-functionally)substituted 2-arylvinylphosphonates **I**. Compounds **I** are used for preparing highly substituted phosphonates which cannot be produced easily by the Arbuzov reaction.[14]

Melting points were determined on a YANACO micro melting point apparatus and are uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded on a JEOL PMX60SI (60 MHz), JEOL FX90Q (90 MHz) or JMN-GSX500 (500 MHz) instrument with TMS as an internal standard. TLC or silica gel column chromatography was carried out on Merck 60F-245 precoated silica gel plates (0.25 mm) or Merck Kieselgel 60 (70–230 mesh ASTM), respectively.

(Dimorpholinomethyl)benzene (12h);[9] Typical Procedures:

Method A: A suspension of benzaldehyde (**4h**; 5.31 g, 50.0 mmol), morpholine (10.5 g, 121 mmol) and B_2O_3 (5.80 g, 83.3 mmol) in benzene (30 mL) was stirred at 50 °C for 2 h. The solvent was removed under reduced pressure, and the residue was recrystallized from *i*-Pr_2O (40 mL) to give 11.02 g (84%) of **12h** as colorless crystals; mp 102–103 °C (Lit.[9] mp 105 °C).

Method B: A refluxing mixture of **4h** (5.31 g, 50.0 mmol) and morpholine (9.15 g, 105 mmol) in benzene (50.0 g) was stirred for 2 h with azeotropical removal of H_2O. The solvent was removed under reduced pressure, and the residue was recrystallized from *i*-Pr_2O (40 mL) to give 10.66 g (81%) of **12h** as colorless crystals, mp 102–103 °C. Mother liquor and washings were concentrated and recrystallization of the residue gave additional **12h** (1.19 g, 9%), mp 101–103 °C.

^1H NMR (60 MHz, $CDCl_3$): δ = 2.20–2.70 (m, 8 H), 3.40–3.90 (m, 9 H), 6.80–7.50 (m, 5 H).

All other aminals **12** were obtained by either Method A or Method B (Table 4).

2-(Dimorpholinomethyl)-1-nitrobenzene (**12a**):

^1H NMR (60 MHz, $CDCl_3$): δ = 2.10–2.60 (m, 8 H), 3.40–3.90 (m, 8 H), 4.48 (s, 1 H), 7.00–8.00 (m, 4 H).

3-(Dimorpholinomethyl)-1-nitrobenzene (**12b**):

^1H NMR (60 MHz, $CDCl_3$): δ = 2.20–2.70 (m, 8 H), 3.40–4.00 (m, 9 H), 7.30–8.30 (m, 4 H).

4-(Dimorpholinomethyl)-1-nitrobenzene (**12c**):

^1H NMR (60 MHz, $CDCl_3$): δ = 2.20–2.70 (m, 8 H), 3.40–4.00 (m, 9 H), 7.10–8.30 (m, 4 H).

4-Cyano-1-(dimorpholinomethyl)benzene (**12d**):

^1H NMR (60 MHz, $CDCl_3$): δ = 2.10–2.60 (m, 8 H), 3.40–3.90 (m, 9 H), 7.00–7.90 (m, 4 H).

2-(Dimorpholinomethyl)-1-(trifluoromethyl)benzene (**12e**):

^1H NMR (60 MHz, $CDCl_3$): δ = 1.90–2.70 (m, 8 H), 3.40–3.90 (m, 8 H), 4.19–4.40 (m, 1 H), 7.00–7.90 (m, 4 H).

1,2-Dichloro-3-(dimorpholinomethyl)benzene (**12f**):

^1H NMR (60 MHz, $CDCl_3$): δ = 2.10–2.70 (m, 8 H), 3.30–3.90 (m, 8 H), 4.50 (s, 1 H), 6.90–7.60 (m, 3 H).

1-Chloro-4-(dimorpholinomethyl)benzene (**12g**):

^1H NMR (60 MHz, $CDCl_3$): δ = 2.10–2.60 (m, 8 H), 3.30–3.80 (m, 9 H), 6.90–7.50 (m, 4 H).

1-(Dimorpholinomethyl)-4-methylbenzene (**12i**):

^1H NMR (60 MHz, $CDCl_3$): δ = 2.10–2.60 [m, 11 H, 2.30 (s, CH_3)], 3.40–3.90 (m, 9 H), 6.80–7.30 (m, 4 H).

2-(Dimorpholinomethyl)-1-methoxybenzene (**12j**):

^1H NMR (60 MHz, $CDCl_3$): δ = 2.10–2.70 (m, 8 H), 3.40–4.00 [m, 12 H, 3.73 (s, CH_3O)], 6.60–7.50 (m, 4 H).

3-(Dimorpholinomethyl)-1-methoxybenzene (**12k**):

^1H NMR (60 MHz, $CDCl_3$): δ = 2.10–2.70 (m, 8 H), 3.40–4.00 [m, 12 H, 3.76 (s, CH_3O)], 6.50–7.60 (m, 4 H).

4-(Dimorpholinomethyl)-1-methoxybenzene (**12l**):

^1H NMR (60 MHz, $CDCl_3$): δ = 2.10–2.70 (m, 8 H), 3.30–3.90 [m, 12 H, 3.75 (s, CH_3O)], 6.60–7.30 (m, 4 H).

α-Acetylstyrylphosphonates 1; General Procedure:

A mixture of aminal **12** (10 mmol), halo acid (20 mmol) and 2-oxopropylphosphonate **3** (10 mmol) in toluene (16 mL) was stirred under the conditions shown in Table 1. The mixture was cooled in an ice bath and then diluted with H_2O. The organic layer was dried

(Na_2SO_4) and concentrated in vacuo. Compound **1** was isolated as a mixture of *E* and *Z* isomers by silica gel column chromatography. If precipitates were observed after addition of H_2O to the mixture, the mixture was filtered. The solid was washed with H_2O, then with toluene, and dried in vacuo to give the desired product. The organic layer of the filtrate and toluene washings were combined and subjected to the chromatographic procedure described above to give the residual product.

2,2-Dimethyl-1,3-propanediyl α-Acetyl-3-nitrostyrylphosphonate (1b):[3,11]

Method A (using MCA): To a solution of 2,2-dimethyl-1,3-propanediyl 2-oxopropylphosphonate (**3b**; 2.06 g, 10.0 mmol) and MCA (1.84 g, 19.5 mmol) in toluene (12 g) was added **12b** (2.98 g, 9.70 mmol). The mixture was stirred at 12–18 °C for 2.5 h. After addition of H_2O (20 mL), the mixture was cooled in an ice bath and filtered. The cake was washed with H_2O (10 mL), then with cold toluene (3 mL) and dried in vacuo to give 3.02 g (89%) of **1b** (*E*/*Z* = 95:5) as yellow crystals. The organic layer of the filtrate and the toluene washings were combined, dried (Na_2SO_4) and concentrated in vacuo. The residue was subjected to a silica gel column chromatography using EtOAc as eluent to give additional **1b** (0.15 g, 4%). An analytical sample of **1b** was obtained by recrystallization from toluene: mp 150–153 °C [a mixture of *E* and *Z* isomers (95:5)].

^{1}H NMR (60 MHz, $CDCl_3$): δ = 0.83 (s, equatorial-CH_3, *Z*-isomer) and 1.06 (s, equatorial-CH_3, *E*-isomer) [total 3 H, equatorial-CH_3], 1.16 (s, axial-CH_3, *E*-isomer) and 1.21 (s, axial-CH_3, *Z*-isomer) [total 3 H,axial-CH_3], 2.32 [s, C(O)CH_3, *E*-isomer] and 2.58 (s, C(O)CH_3, *Z*-isomer] [total 3 H, C(O)CH_3), peak ratio of *E*/*Z* = 95:5, 3.50–4.47 [m, 4 H, (OCH_2) × 2], 7.05–8.40 (m, 5 H, ArH and PC=CH).

MS: *m*/*z* (%) = 339 (M^+, 19), 40 (100).

Method B (using TFA): A mixture of **12b** (3.07 g, 10.0 mmol) and TFA (2.28 g, 20.0 mmol) in toluene (16 mL) was stirred at 60 °C for 15 min. To this solution was added **3b** (2.06 g, 10.0 mmol). The mixture was stirred at 60 °C for 30 min, cooled in an ice bath, diluted with H_2O (20 mL), and then filtered. The solid was washed with H_2O (4 mL), then with cold toluene (3 mL), and dried in vacuo to give 2.79 g (82%) of the **1b** as yellow crystals. The organic layer of the filtrate and the toluene washings were combined, dried (Na_2SO_4) and concentrated in vacuo. The residue was subjected to silica gel column chromatography using EtOAc as eluent to give additional **1b** (0.26 g, 8%).

Method C (using AcOH): The reaction using AcOH, in place of an α-halo acid, was carried out at r.t. for 3 d. From the mixture were obtained 0.94 g (28%) of **1b**, 0.63 g (42%) of 3-nitrobenzaldehyde **(4b)** and 0.31 g (21%) of **7b**.

4-(3-Nitrophenyl)-3-buten-2-one **(7b)**:

^{1}H NMR (90 MHz, $CDCl_3$): δ = 2.40 [s, 3 H, C(O)CH_3], 6.80 [d, *J* = 15 Hz, 1 H, C(O)CH=], 7.20–8.50 (m, 5 H, ArH and =CHAr).

Method D (using $MeSO_3H$): 3-Nitrobenzaldehyde **(4b)** was quantitatively recovered when the reaction with $MeSO_3H$ was carried out at 50 °C for 5 h.

2,2-Dimethyl-1,3-propanediyl α-Acetyl-2-nitrostyrylphosphonate (1a):[3,11]

Following Method B described for **1b**, **12a** (3.07 g, 10.0 mmol) was converted to **1a**. Then, after cooling to r.t., was added H_2O (70 mL) and $CHCl_3$ (100 mL). The organic layer was dried (Na_2SO_4) and concentrated in vacuo. The residue was subjected to a silica gel column chromatography using EtOAc as eluent to give 1.92 g (57%) of **1a** (*E*/*Z* = 40:60), 0.29 g (19%) of 2-nitrobenzaldehyde **(4a)** and 0.43 g (13%) of **8a**. An analytical sample of **1a** was obtained by recrystallization from toluene: mp 142–151 °C [a mixture of *E*- and *Z*-isomers (30:70)].

^{1}H NMR (60 MHz, $CDCl_3$): δ = 0.81 (s, equatorial-CH_3, *Z*-isomer) and 1.01 (s, equatorial-CH_3, *E*-isomer) [total 3 H, equatorial-CH_3], 1.17 (s, axial-CH_3, *Z*-isomer) and 1.29 (s, axial-CH_3, *E*-isomer) [total 3 H, axial-CH_3], 2.27 [s, C(O)CH_3, *E*-isomer] and 2.57 (s, C(O)CH_3, *Z*-isomer] [total 3 H, C(O)CH_3], peak ratio of *E*/*Z* = 30:70), 3.26–4.34 [m, 4 H, (OCH_2) × 2], 6.92–8.68 (m, 5 H, ArH and PC=CH).

2,2-Dimethyl-1,3-propanediyl 4-(2-Nitrophenyl)-2-oxo-3-butenylphosphonate **(8a)**:

^{1}H NMR (60 MHz, $CDCl_3$): δ = 1.03 (s, 3 H, equatorial-CH_3), 1.12 (s, 3 H, axial-CH_3), 3.48 [d, *J* = 22 Hz, 2 H, P(O)CH_2], 3.80–4.50 [m, 4 H, (OCH_2) × 2], 6.80 [d, *J* = 16 Hz, 1 H, C(O)CH=], 7.30–8.20 (m, 4 H, ArH), 8.04 (d, *J* = 16 Hz, 1 H, =CHAr).

When the reaction was carried out at 20 °C, **1a** (57%) and **8a** (15%) were obtained.

2,2-Dimethyl-1,3-propanediyl α-Acetyl-4-methoxystyrylphosphonate (1l):

Following Method B, as described for **1b**, **12l** (2.92 g, 10.0 mmol) was converted to **1l**. Then, after cooling to r.t., was added H_2O (50 mL) and toluene (50 mL). The toluene layer was dried (Na_2SO_4) and concentrated in vacuo. The residue was subjected to silica gel column chromatography using EtOAc as eluent to give 1.66 g (51%) **1l** (*E*/*Z* = 85:15), 0.28 g (21%) of 4-methoxybenzaldehyde **(4l)** and 0.59 g (18%) of **8l**. An analytical sample of **1l** was obtained by recrystallization from toluene/hexane, mp 83–139 °C [a mixture of *E*- and *Z*-isomers (85:15).

^{1}H NMR (60 MHz, $CDCl_3$): δ = 0.73 (s, equatorial-CH_3, *Z*-isomer),1.07 (s, equatorial and axial-CH_3, *E*-isomer) and 1.22 (s, axial-CH_3, *Z*-isomer) [total 6 H, $(CH_3)_2$], 2.28 [s, C(O)CH_3, *E*-isomer] and 2.52 [s, C(O)CH_3, *Z*-isomer] [total 3 H, C(O)CH_3, peak ratio of *E*/*Z* = 85:15], 3.35–4.43 [m, 7 H, (OCH_2) × 2 and OCH_3], 6.57–8.22 (m, 5 H, ArH and PC=CH).

MS: *m*/*z* (%) = 324 (M^+, 30), 281 (100).

2,2-Dimethyl-1,3-propanediyl 4-(4-Methoxyphenyl)-2-oxo-3-butenylphosphonate **(8l)**:

^{1}H NMR (60 MHz, $CDCl_3$): δ = 1.00 (s, 3 H, equatorial-CH_3), 1.10 (s, 3 H, axial-CH_3), 3.42 [d, *J* = 22 Hz, 2 H, P(O)CH_2], 3.81 (s, 3 H, OCH_3), 3.80–4.50 [m, 4 H, (OCH_2) × 2], 6.74 [d, *J* = 17 Hz, 1 H, C(O)CH=], 6.70–7.70 (m, 4 H, ArH), 7.64 (d, *J* = 17 Hz, 1 H, =CHAr).

Method E (using AcOH, followed by treatment with TFA): A mixture of **12l** (8.77 g, 30.0 mmol) and AcOH (3.60 g, 60.0 mmol) in toluene (60.0 g) was stirred at r.t. for 30 min. To this solution was added **3b** (6.19 g, 30.0 mmol). The mixture was stirred at r.t. for 22 h, cooled in an ice bath and then diluted with H_2O (90 mL). After 1 h, the mixture was filtered, the solid washed with H_2O (50 mL) then with cold toluene (40 mL), and dried in vacuo to give 7.98 g (65%) of **13l** as colorless crystals. Analytical sample mp 150–152 °C.

2,2-Dimethyl-1,3-propanediyl 1-Acetyl-2-(4-methoxyphenyl)-2-morpholinoethylphosphonate **(13l)**:

^{1}H NMR(60 MHz, $CDCl_3$): δ = 0.85 (s, 3 H, equatorial-CH_3), 1.05 (s, 3 H, axial-CH_3), 1.97–2.7 [m, 4 H, (NCH_2) × 2], 2.45 [s, 3 H, C(O)CH_3], 3.24–4.78 [m, 10 H, CH_2OCH_2, CHCH and {P(O)OCH_2} × 2], 3.79 (s, 3 H, CH_3O), 6.70–7.45 (m, 4 H, ArH).

A mixture of **13l** (206 mg, 0.501 mmol) and TFA (65 mg, 0.57 mmol) in toluene (1.0 g) was stirred at r.t. for 30 min. To this solution was added $CHCl_3$ (50 mL) and then H_2O (40 mL). The $CHCl_3$ layer was separated, dried (Na_2SO_4), and concentrated in vacuo to give 0.17 g (100%) of **1l** as a colorless solid, *E*/*Z* = 30:70.

2,2-Dimethyl-1,3-propanediyl α-Acetyl-4-methylstyrylphosphonate (1i):

A mixture of **12i** (2.76 g, 10.0 mmol) and TFA (2.28 g, 20.0 mmol) in toluene (16 mL) was stirred at r.t. for 30 min. To this solution was added **3b** (2.06 g, 10.0 mmol). The mixture was stirred at r.t. for 4 h and then diluted with toluene (50 mL) and with H_2O (50 mL). The toluene layer was separated, dried (Na_2SO_4), and concentrated in vacuo. The residue was subjected to silica gel column chromatography using benzene/EtOAc (1:1 → EtOAc only) as eluent to give 2.30 g (75%) of **1i** (*E*/*Z* = 80:20), 0.03 g (3%) of 4-methylbenzaldehyde **(4i)** and 0.30 g (16%) of **8i**. An analytical sample of **1i** was

obtained by recrystallization from toluene/hexane, mp 137–140 °C (*E*-isomer only).

^{1}H NMR (90 MHz, $CDCl_3$): δ = 1.08 (s, 3 H, equatorial-CH_3), 1.10 (s, 3 H, axial-CH_3), 2.30 [s, 3 H, C(O)CH_3], 2.37 (s, 3 H, ArCH_3), 3.80–4.40 [m, 4 H, (OCH_2) × 2], 7.00–7.40 (m, 4 H, ArH), 7.68 (d, J = 26 Hz, 1 H, =CHAr).

MS: m/z (%) = 308 (M^+, 22), 40 (100).

Z-isomer of **1i** was also isolated from the *E*/*Z*-mixture of **1i** by silica gel column chromatography using benzene/EtOAc (1:2, v/v) [R_f = 0.36 (*E*), 0.44 (*Z*) in TLC].

^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.73 (s, 3 H, equatorial-CH_3), 1.23 (s, 3 H, axial-CH_3), 2.38 (s, 3 H, ArCH_3), 2.58 [s, 3 H, C(O)CH_3], 3.20–4.40 [m, 4 H, (OCH_2) × 2], 6.90–7.70 (m, 4 H, ArH), 8.01 (d, J = 44 Hz, 1 H, =CHAr).

2,2-Dimethyl-1,3-propanediyl 4-(4-Methylphenyl)-2-oxo-3-butenylphosphonate (**8i**):

^{1}H NMR (60 MHz, $CDCl_3$): δ = 1.01 (s, 3 H, equatorial-CH_3), 1.09 (s, 3 H, axial-CH_3), 2.34 (s, 3 H, ArCH_3), 3.40 [d, J = 22 Hz, 2 H, P(O)CH_2], 3.70–4.40 [m, 4 H, (OCH_2) × 2], 6.74 [d, J = 16 Hz, 1 H, C(O)CH=], 6.90–7.50 (m, 4 H, ArH), 7.57 (d, J = 16 Hz, 1 H, =CHAr).

^{1}H NMR data of α-acetylstyrylphosphonates **1c–h,j,k,m,n** obtained by either the General Procedure or one of the methods described (for further analytical data see Table 2):

2,2-Dimethyl-1,3-propanediyl α-Acetyl-4-nitrostyrylphosphonate (**1c**):

^{1}H NMR (60 MHz, $CDCl_3$): δ = 0.81 (s, equatorial-CH_3, *Z*-isomer) and 1.06 (s, equatorial-CH_3, *E*-isomer) [total 3 H, equatorial-CH_3], 1.15 (s, 3 H, axial-CH_3, *E*- and *Z*-isomers), 2.28 [s, C(O)CH_3, *E*-isomer] and 2.56 [s, C(O)CH_3, *Z*-isomer] [total 3 H, C(O)CH_3], peak ratio of *E*/*Z* = 95:5, 3.49–4.46 [m, 4 H, (OCH_2) × 2], 7.10–8.31 (m, 5 H, ArH and PC=CH).

2,2-Dimethyl-1,3-propanediyl α-Acetyl-4-cyanostyrylphosphonate (**1d**):

^{1}H NMR (60 MHz, $CDCl_3$): δ = 0.77 (s, equatorial-CH_3, *Z*-isomer) and 1.04 (s, equatorial-CH_3, *E*-isomer) [total 3 H, equatorial-CH_3], 1.14 (s, axial-CH_3, *E*-isomer) and 1.20 (s, axial-CH_3, *Z*-isomer) [total 3 H, axial-CH_3], 2.27 [s, C(O)CH_3, *E*-isomer] and 2.56 [s, C(O)CH_3, *Z*-isomer] [total 3 H, C(O)CH_3], peak ratio of *E*/*Z* = 35:65, 3.45–4.47 [m, 4 H, (OCH_2) × 2], 7.14–8.22 (m, 5 H, ArH and PC=CH).

2,2-Dimethyl-1,3-propanediyl α-Acetyl-2-(trifluoromethyl)styrylphosphonate (**1e**):

^{1}H NMR (60 MHz, $CDCl_3$): δ = 0.75 (s, equatorial-CH_3, *Z*-isomer) and 1.03 (s, equatorial-CH_3, *E*-isomer) [total 3 H, equatorial-CH_3], 1.21 (s, 3 H, axial-CH_3, *E*- and *Z*-isomers), 2.14 [s, C(O)CH_3, *E*-isomer] and 2.57 [s, C(O)CH_3, *Z*-isomer] [total 3 H, C(O)CH_3], peak ratio of *E*/*Z* = 90:10, 3.45–4.47 [m, 4 H, (OCH_2) × 2], 7.08–8.64 (m, 5 H, ArH and PC=CH).

2,2-Dimethyl-1,3-propanediyl α-Acetyl-2,3-dichlorostyrylphosphonate (**1f**):

^{1}H NMR (60 MHz, $CDCl_3$): δ = 0.80 (s, equatorial-CH_3, *Z*-isomer), 1.06 (s, axial-CH_3, *E*-isomer), 1.19 (s, equatorial-CH_3 of *E*-isomer and axial-CH_3 of *Z*-isomer) [total 6 H, $(CH_3)_2$], 2,20 [s, C(O)CH_3, *E*-isomer] and 2.57 [s, C(O)CH_3, *Z*-isomer] [total 3 H, C(O)CH_3], peak ratio of *E*/*Z* = 75:25, 3.50–4.50 [m, 4 H, (OCH_2) × 2], 7.00–8.50 (m, 4 H, ArH and PC=CH).

2,2-Dimethyl-1,3-propanediyl α-Acetyl-4-chlorostyrylphosphonate (**1g**):

^{1}H NMR (60 MHz, $CDCl_3$): δ = 0.74 (s, equatorial-CH_3, *Z*-isomer) and 1.05 (s, equatorial-CH_3, *E*-isomer) [total 3 H, equatorial-CH_3], 1.10 (s, axial-CH_3, *E*-isomer) and 1.20 (s, axial-CH_3, *Z*-isomer) [total 3 H, axial-CH_3], 2.27 [s, C(O)CH_3, *E*-isomer] and 2.48 [s, C(O)CH_3, *Z*-isomer] [total 3 H, C(O)CH_3], peak ratio of *E*/*Z* = 95:5, 3.40–4.50 [m, 4 H, (OCH_2) × 2], 7.00–8.30 (m, 5 H, ArH and PC=CH).

2,2-Dimethyl-1,3-propanediyl α-Acetylstyrylphosphonate (**1h**):

^{1}H NMR (60 MHz, $CDCl_3$): δ = 0.72 (s, equatorial-CH_3, *Z*-isomer) and 1.07 (s, equatorial-CH_3, *E*-isomer) [total 3 H, equatorial-CH_3], 1.11 (s, axial-CH_3, *E*-isomer) and 1.21 (s, axial-CH_3, *Z*-isomer) [total 3 H, axial-CH_3], 2.25 [s, C(O)CH_3, *E*-isomer] and 2.55 [s, C(O)CH_3, *Z*-isomer] [total 3 H, C(O)CH_3], peak ratio of *E*/*Z* = 80:20, 3.38–4.45 [m, 4 H, (OCH_2) × 2], 7.07–8.07 (m, 6 H, ArH and PC=CH).

2,2-Dimethyl-1,3-propanediyl α-Acetyl-2-methoxystyrylphosphonate (**1j**):

^{1}H NMR (60 MHz, $CDCl_3$): δ = 0.74 (s, equatorial-CH_3, *Z*-isomer) and 1.05 (s, equatorial-CH_3, *E*-isomer) [total 3 H, equatorial-CH_3], 1.13 (s, axial-CH_3, *E*-isomer) and 1.20 (s, axial-CH_3, *Z*-isomer) [total 3 H, axial-CH_3], 2.22 [s, C(O)CH_3, *E*-isomer] and 2.55 [s, C(O)CH_3, *Z*-isomer] [total 3 H, C(O)CH_3], peak ratio of *E*/*Z* = 90:10, 3.38–4.43 [m, 7 H, (OCH_2) × 2 and OCH_3], 6.62–8.60 (m, 5 H, ArH and PC=CH).

2,2-Dimethyl-1,3-propanediyl α-Acetyl-3-methoxystyrylphosphonate (**1k**):

^{1}H NMR (60 MHz, $CDCl_3$): δ = 0.73 (s, equatorial-CH_3, *Z*-isomer) and 1.08 (s, equatorial-CH_3, *E*-isomer) [total 3 H, equatorial-CH_3], 1.11 (s, axial-CH_3, *E*-isomer) and 1.21 (s, axial-CH_3, *Z*-isomer) [total 3 H, axial-CH_3], 2.25 [s, C(O)CH_3, *E*-isomer] and 2.54 [s, C(O)CH_3, *Z*-isomer] [total 3 H, C(O)CH_3], peak ratio of *E*/*Z* = 85:15, 3.42–4.47 [m, 7 H, (OCH_2) × 2 and OCH_3], 6.59–8.27 (m, 5 H, ArH and PC=CH).

Diethyl α-Acetyl-3-nitrostyrylphosphonate (**1m**):

^{1}H NMR (60 MHz, $CDCl_3$): δ = 1.17 [t, J = 7 Hz, (CH_3CH_2O) × 2, *Z*-isomer] and 1.36 [t, J = 7 Hz, (CH_3CH_2O) × 2, *E*-isomer] [total 6 H, (CH_3CH_2O) × 2], 2.30 [s, C(O)CH_3, *E*-isomer] and 2.51 [s, C(O)CH_3, *Z*-isomer] [total 3 H, C(O)CH_3], peak ratio of *E*/*Z* = 85:15, 3.71–4.50 [m, 4 H, (CH_3CH_2O) × 2], 7.10–8.48 (m, 5 H, ArH and PC=CH).

Diethyl α-Acetyl-4-nitrostyrylphosphonate (**1n**):

^{1}H NMR (60 MHz, $CDCl_3$): δ = 1.18 [t, J = 7 Hz, (CH_3CH_2O) × 2, *Z*-isomer] and 1.39 [t, J = 7 Hz, (CH_3CH_2O) × 2, *E*-isomer] [total 6 H, (CH_3CH_2O) × 2], 2.31 [s, C(O)CH_3, *E*-isomer] and 2.56 [s, C(O)CH_3, *Z*-isomer] [total 3 H, C(O)CH_3], peak ratio of *E*/*Z* = 95:5, 3.80–4.50 [m, 4 H, (CH_3CH_2O) × 2], 7.22–8.38 (m, 5 H, ArH and PC=CH).

Additional ^{1}H NMR data of byproducts **8**:

2,2-Dimethyl-1,3-propanediyl 2-Oxo-4-[2-(trifluoromethyl)phenyl]-3-butenylphosphonate (**8e**):

^{1}H NMR (60 MHz, $CDCl_3$): δ = 1.05 (s, 3 H, equatorial-CH_3), 1.14 (s, 3 H, axial-CH_3), 3.44 [d, J = 22 Hz, 2 H, P(O)CH_2], 3.70–4.50 [m, 4 H, (OCH_2) × 2], 6.84 [d, J = 16 Hz, 1 H, C(O)CH=], 7.20–8.21 (m, 5 H, ArH and =CHAr).

2,2-Dimethyl-1,3-propanediyl 4-(4-Chlorophenyl-2-oxo-3-butenylphosphonate (**8g**):

^{1}H NMR (60 MHz, $CDCl_3$): δ = 1.02 (s, 3 H, equatorial-CH_3), 1.12 (s, 3 H, axial-CH_3), 3.46 [d, J = 22 Hz, 2 H, P(O)CH_2], 3.75–4.46 [m, 4 H, (OCH_2) × 2], 6.86 [d, J = 16 Hz, 1 H, C(O)CH=], 7.15–7.89 (m, 4 H, ArH), 7.66 (d, J = 16 Hz, 1 H, =CHAr).

2,2-Dimethyl-1,3-propanediyl 2-Oxo-4-phenyl-3-butenylphosphonate (**8h**):

^{1}H NMR (60 MHz, $CDCl_3$): δ = 1.02 (s, 3 H, equatorial-CH_3), 1.09 (s, 3 H, axial-CH_3), 3.45 [d, J = 22 Hz, 2 H, P(O)CH_2], 3.70–4.45 [m, 4 H, (OCH_2) × 2], 6.86 [d, J = 17 Hz, 1 H, C(O)CH=], 7.12–7.95 (m, 5 H, ArH), 7.69 (d, J = 17 Hz, 1 H, =CHAr).

2,2-Dimethyl-1,3-propanediyl 4-(2-Methoxyphenyl)-2-oxo-3-butenylphosphonate (**8j**):

^{1}H NMR (60 MHz, $CDCl_3$): δ = 1.01 (s, 3 H, equatorial-CH_3), 1.10 (s, 3 H, axial-CH_3), 3.46 [d, J = 22 Hz, 2 H, P(O)CH_2], 3.80–4.40 [m, 4 H, (OCH_2) × 2], 3.86 (s, 3 H, CH_3O), 6.63–7.72 [m, 5 H, ArH and C(O)CH=], 8.01 (d, J = 16 Hz, 1 H, =CHAr).

2,2-Dimethyl-1,3-propanediyl 4-(3-Methoxyphenyl)-2-oxo-3-butenylphosphonate (**8k**):

^{1}H NMR (60 MHz, $CDCl_3$): δ = 0.99 (s, 3 H, equatorial-CH_3), 1.09 (s, 3 H, axial-CH_3), 3.45 [d, J = 22 Hz, 2 H, P(O)CH_2], 3.77 (s, 3 H, CH_3O), 3.85–4.30 [m, 4 H, $(OCH_2) \times 2$], 6.64–7.47 (m, 4 H, ArH), 6.83 [d, J = 16 Hz, 1 H, C(O)CH=], 7.63 (d, J = 16 Hz, 1 H, =CHAr).

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