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Reaction of 3-Bromobenzyl and 3-Bromoacetyl Coumarin with Phosphites. Synthesis of Some New Phosphonates and Phosphates in the Coumarin Series

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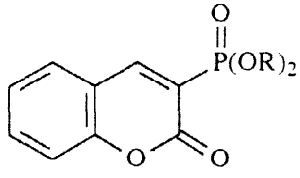
Abstract: The reaction of 3-(1-bromobenzyl)coumarin 3 with trialkyl phosphites afforded in good yields the corresponding dialkyl phosphonates 5, the Arbuzov reaction products. The interaction of trialkyl phosphites with 3-(ω-bromoacetyl)coumarin 4 gave the corresponding dialkyl vinylphosphates 8 as the only isolated products, whereas dialkyl phosphites reacted with 4 under phase transfer catalysis and gave vinylphosphates 8 or dialkyl 1,2-epoxy-ethylphosphonates 9. The β-oxo-phosphonates 7 were obtained from the reaction of hydrazono-derivative 10 with trialkyl phosphites and the subsequent hydrolysis of the dialkyl β-hydrazono-phosphonates 11 thus formed.

In the course of our work on coumarin derivatives[1-3] we have prepared a number of phosphorus compounds 1 and 2, for which, in a recent[4] study, plant growth regulating properties as well as relationships between chemical structure/biological activities were investigated.



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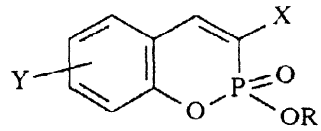

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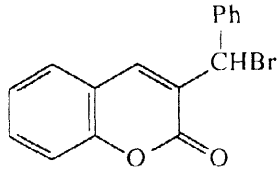
Y = H, 6-Br, 6-Cl, 7-$N(C_2H_5)_2$
X = $COOC_2H_5$, CN, COOH
R = CH_3, C_2H_5

In the context of this work and in order to search for other phosphorus-containing coumarin derivatives with potential biological activities, we decided to prepare some new phosphonocoumarins by reacting the easily prepared[5,6] and very reactive 3-(1-bromobenzyl)coumarin 3 and 3-(ω-bromoacetyl) coumarin 4 with phosphites.



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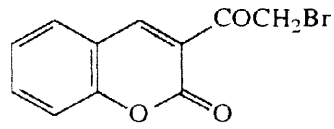

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Alkylphosphonates are normally prepared by the Arbuzov reaction[7-11] of trialkyl phosphites and the corresponding alkylhalides. In the case of α-oxo-alkylhalides however, the direct Arbuzov reaction leads mostly to mixtures of alkylphosphonates and enolphosphates[12,13] as a result of the competitive Perkow[14-15] reaction. In order to overcome this behaviour in the reaction of **4** with phosphites we tried both, the direct[7-11] and the modified two-stage[16] Arbuzov reaction as well as the Michaelis-Becker reaction.[17-19] In order to obtain better yields of the reaction products we also tried the above reactions under different experimental conditions.

RESULTS AND DISCUSSION

Reaction of 3-(1-bromobenzyl)coumarin 3 with trialkylphosphites. The reaction of compound **3** with trimethyl, triethyl or triphenylphosphite was realised either by refluxing **3** in an excess of the corresponding phosphite or by refluxing a solution of the reactants in an aromatic solvent. The results of these reactions are presented in Table 1.

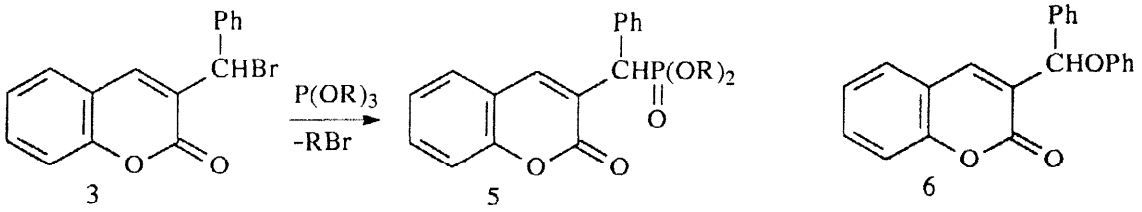


Table 1. Yields of the isolated phosphonates 5 obtained from the reaction of bromo derivative **3** with trialkyl phosphites under modified Arbuzov reaction conditions.

Product	R	Reaction conditions	Yield (%)[a]
5a	CH_3	trimethylphosphite used as solvent; reflux, 4 h	38
		toluene as solvent; 1:6;[b] reflux, 5 h	90
5b	C_2H_5	triethylphosphite used as solvent; reflux, 4 h	41
		toluene as solvent; 1:6;[b] reflux, 5 h	92
5c	C_6H_5	triphenylphosphite used as solvent; reflux, 4 h	-[c]
		xylene as solvent; 1:6;[b] distillation under reduced pressure, 5 h	22
		without solvent; 1:3;[b] distillation under reduced pressure, 0.5 h	65

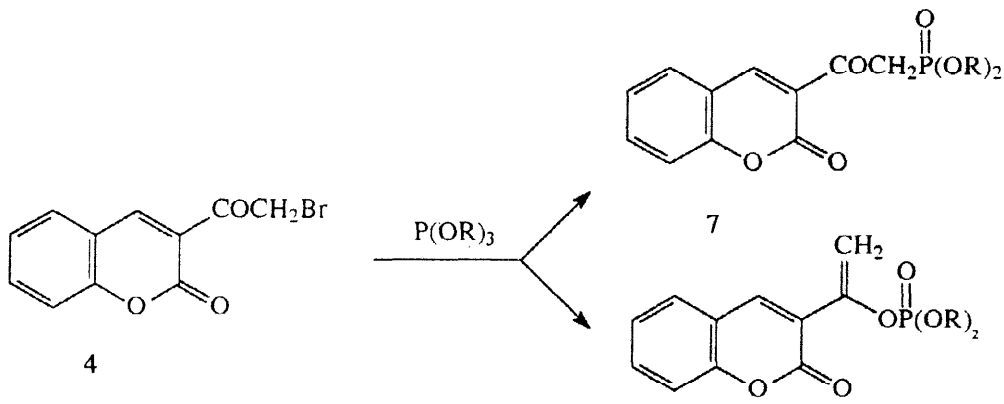
[a] Yield of the isolated product. [b] Molar ratio of the reagents : bromo derivative 3 : $P(OR)_3$.
[c] The phenyl ether **6** was isolated in 36% yield.

Trimethyl and triethyl phosphites gave the expected phosphonates **5a** and **5b** respectively in very good yield (90%) when the reaction was carried out in refluxing toluene. When the same reaction was carried out using trialkyl phosphite as a solvent the yield of the phosphonate was much more lower (40%). A differentiation was observed in the reaction of **3** with the less reactive triphenylphosphite where the corresponding phosphonate 5c was isolated in low yield (22%) when xylene was used as solvent, whereas by heating the reactants under reduced pressure the phosphonate 5c was isolated in 65% yield. It is noted that on refluxing bromoderivative **3** in triphenylphosphite for a longer time the only reaction product isolated was the phenylether **6**, probably from the interaction of **3** with phenol, which most probably resulted from

the decomposition of triphenyl phosphite under the reaction conditions (heating at higher temperatures for a longer time).

Compounds 5 show analytical and spectroscopic data in agreement with their structure. In the EI mass spectrum they show the molecular ion M^+ which constitutes the base peak of the spectrum. The most characteristic peaks in their ^1H nmr spectrum are those of 4-H of the coumarin ring and of the methinic proton (CHP) of the 3-benzylgroup, which appear as doublets at about δ 8.5 ($^4J_{HP}$ ~ 2.6 Hz) and δ 5.0 ($^2J_{HP}$ ~ 24.0 Hz) respectively. In ^{13}C nmr the C-2 (carbonyl carbon) and the C-4 of the coumarin ring give doublets at ~160 ppm ($^3J_{CP}$ = 4-6 Hz) and 141.5 ppm ($^3J_{CP}$ ~ 6 Hz) respectively, whereas the methinic carbon (CHP) appears at ~ 41 ppm with a $^1J_{CP}$ = 142-146 Hz.

Reaction of 3-(ω-bromoacetyl)coumarin 4 with trialkyl phosphites. As already mentioned, the reaction of α-halogenated ketones with trialkyl phosphites gives the corresponding β-oxo-phosphonates and vinylphosphates in different ratios depending on the nature of the halogen and the substituents of the ketone, the alkyl substituents of the phosphite as well as the reaction conditions.[12,13,20,21] It was therefore expected that the reaction of the bromoacetyl-coumarin 4 with trialkyl phosphites would proceed in two directions, leading to the formation of the corresponding β-oxo-phosphonates 7, the Arbuzov reaction products, and vinylphosphates 8, the Perkow reaction products.



4 7 8

a: R = Me; b: R = Et; c: R = Ph

The reaction of 4 with trimethyl and triethyl phosphite, however, gave as the only isolated product the vinylphosphates 8a,b (Tables 2 and 3) whereas with triphenyl phosphite gave only the β-oxo-phosphonate 7c (Table 4). In order to explore more the reaction and the possibility of isolating β-oxophosphonates 7, the bromo derivative 4 was reacted with trimethylphosphite under different experimental conditions, Table 2. In all cases however vinylphosphate 8a was the only isolated product in yields ranging from 58 to 95%.

From Table 2 it can be seen that the best yields (up to 95%) of the dimethyl vinylphosphate 8a were obtained by performing the reaction under the conditions of Methods B, C and H. It is noticed that in the case of Method H (carrying out the reaction under the action of ultrasound) product 7a was isolated by crystallisation only, contrary to all other cases where it was necessary for the reaction mixture to be chromatographed on a column.

The reaction of 4 with triethyl phosphite was carried out under the conditions of methods B, C and H and the yields (80-90 %) are given in Table 3. Diethyl vinylphosphate 8b, contrary to 8a, is unstable on standing at room temperature for a longer time or on heating.

Contrary to the behaviour of trimethyl and triethyl phosphite, the interaction of 4 with triphenyl phosphite, performed under the conditions of Methods B and C, followed the Arbuzov reaction, thus giving the expected β-oxo-phosphonate 7c in moderate yields (46-65%) (Table 4).

Table 2. Yields of dimethyl [1-(2-oxo-2H-1-benzopyran-3-yl)-vinyl]phosphate **8a** isolated from the reaction of **4** and trimethyl phosphite under different experimental conditions.

Method	Reaction conditions	Yield (%)
A	excess of $P(OMe)_3$ / reflux / 60 min	58
A1	excess of $P(OMe)_3$ / vacuum distillation / 30 min	61
A2	excess of $P(OMe)_3$ / -4 °C/20 h	65
B	dry toluene / (1:5)[a] / reflux / 15 min	95
B2	dry toluene/(1:2)[a] / distillation / 3.5 h	81
C	xylene /(1:5)[a] / distillation / 90 min	95
D	CH_2Cl_2 (1:2)[a] / rt. / 60 min	81
D1	CH_2Cl_2 /(1:2)[a] / -4 °C / 20 h	71
E	CH_3CN / (1:5)[a] / -4 °C / 20 h	65
G	dioxane / (1:4)[a] / dropwise / Δ / 30 min	61
F	CH_3COOH / (1:2)[a] / rt. / 5 min	84
H	CH_2Cl_2 / (1:2) / rt. /)))[b] / 20 min	95

[a] Ratio 2 : $P(OMe)_3$.
[b] Under ultrasound action.

Table 3. Yields of diethyl [1-(2-oxo-2H-1-benzopyran-3-yl)-vinyl]phosphate **8b** isolated from the reaction of **4** and triethyl phosphite under different experimental conditions.

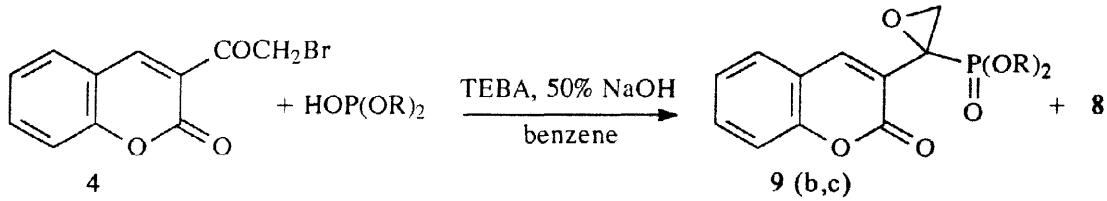
Method	Reaction conditions	Yield (%)
B	dry toluene / (1:6) / reflux / 10 min	80
C	dry xylene / (1:5) / distillation / 90 min	86
H	CH_2Cl_2 / (1:2) / rt. /)))[a] /20 min	90

[a] Under ultrasound action

Table 4. Yields of diphenyl of 2-(2-oxo-2*H*-1-benzopyran-3-yl)-2-oxo-ethylphosphonate **7c** isolated from the reaction of **4** and triphenyl phosphite.

Method	Reaction conditions	Yield (%)
B	dry toluene / (1:6) / reflux / 90 min	46
C	dry xylene / (1:5) / distillation / 90 min	65

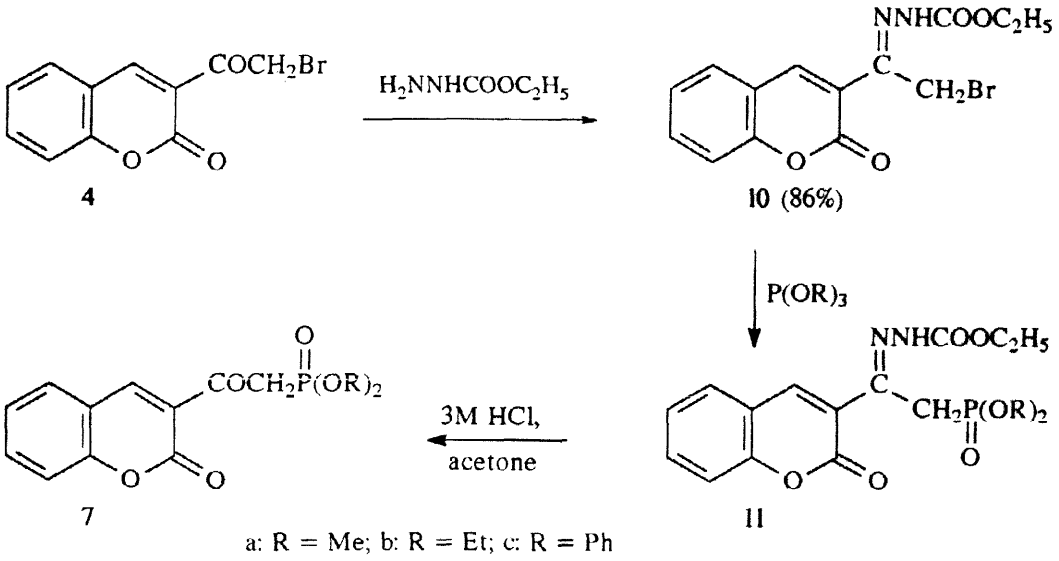
Reaction of 3-(ω-bromoacetyl)coumarin 4 with dialkyl phosphites. The reaction of the bromo derivative **4** and dimethyl, diethyl and di-*n*-butyl phosphite was performed under phase transfer catalysis[18,19] by using triethylbenzylammonium chloride (TEBA) as catalyst and under the action of 50% sodium hydroxide. The only products isolated from these reactions were the vinylphosphate **8a**, from the reaction with dimethyl phosphite, and the epoxyphosphonates **9b** and **9c**, from the reaction with diethyl and di-*n*-butyl phosphite respectively. Again the β-oxo-phosphonates **7** were not isolated from the above reactions. It is noted that the reaction of diethyl sodium phosphites with α-halogenated ketones (Michaelis-Becker reaction) gives β-oxo-phosphonates, vinylphosphates and epoxyphosphonates in yields and ratios strongly dependent on the reaction conditions and on the nature of the reactants.[12,22]



4 9 (b,c)

	R	Yield, %
8a	CH_3	24
9b	C_2H_5	70
9c	n-C_4H_9	34

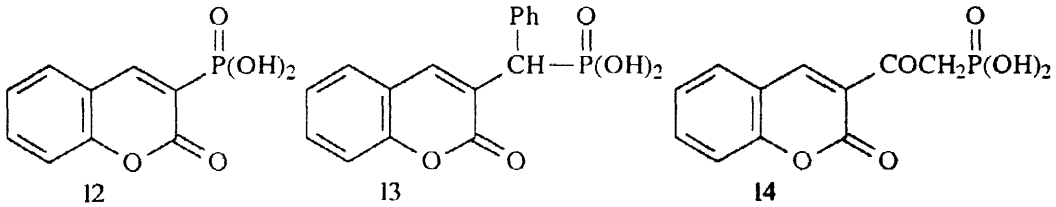
The results presented above clearly show that the reaction of the 3-(ω-bromoacetyl)coumarin **4** with phosphites, with the exception of triphenyl phosphite, leads exclusively to the formation of vinylphosphate **8** or, in the case of carrying out the reaction under phase transfer catalysis, to epoxyphosphonates **9**. These limitations prompted us to try other methods for the preparation of the alkyl β-oxo-phosphonates **7**. Numerous synthetic approaches are known in the literature,[16,23-25] among them the two step procedures using masked carbonyl compounds or methods where the carbonyl of the α-halogenated carbonyl compound is protected with an easily removed moiety. Following the second way, we chose an Arbuzov three-stage procedure, described earlier.[16] For protection of the carbonyl group in the starting bromoketone **4** we used the ethoxycarbonylhydrazono group, by reacting **4** with ethylcarbazate (ethyl hydrazinocarboxylate). The hydrazono derivative **10** reacted subsequently with trialkyl phosphites to give in very good yields the β-hydrazono-phosphonates **11**, which upon acid hydrolysis afforded in good yields the expected β-oxo-phosphonates **7**.



7	Yield, %	11	Yield, %
a	77	a	89
b	68	b	95
c	54[b]	c	[a]

[a] The product 11c was not isolated because of its decomposition during separation from the reaction mixture on the column; [b] On hydrolysis of the crude unpurified reaction product.

Additionally, acidic hydrolysis of the phosphonic esters **1b**, **5b** and **7b** by refluxing in conc. hydrochloric acid was carried out and the corresponding phosphonic acids **12**, **13** and **14** respectively were isolated.



The structures of all the new compounds were confirmed on the basis of their analytical and spectroscopic characteristics.

Thus all the new compounds give the molecular ion peak M^+ in their mass spectrum and in the ir spectrum they exhibit absorption bands for the C=O groups at 1700-1740 cm^{-1}. An ^1H nmr spectroscopy characteristic is the peak of 4-H of the coumarin ring, which appears as singlet at δ 8.0-8.5, and, in the case of epoxyphosphonates **9**, is split into a doublet ($^4J_{HP}$ = 2.5 Hz). The methylenic protons of the oxo-phosphonates 7 and of the hydrazono-derivatives 11 absorb at δ 4.0-4.3, coupled with the phosphorus atom with $^2J_{HP}$ = 22.5 Hz, in agreement with analogous β-oxophosphonate derivatives given in the literature.[16,21] The two vinylic protons of the enolphosphates 8 give peaks at δ 6.5 and δ 5.5 ppm showing a $^4J_{HP}$ of 2.7 and 2.2 Hz respectively[26] whereas the epoxy protons in the epoxy derivatives **9** appear at δ 3.5 and δ 3.1 ppm with $^3J_{HP}$ equal to 5.3 and 5.0 Hz respectively.

In the ^{13}C nmr spectra of the compounds studied all carbons give peaks at the expected shift values. From the various carbons it is worth mentioning the shifts of C-4 of the coumarin ring at δ 139-149 ppm

and the methylenic carbons of the phosphonates 7 and 11 at δ ~ 41 and ~27 ppm, showing a coupling with the phosphorus $^1J_{CP}$ ~128 and ~135 Hz respectively. The vinylic carbons of the enolphosphates 8 give peaks at δ 145 ($^2J_{CP}$ = 7.0 Hz) and at δ 105 ppm ($^3J_{CP}$ = 3.7 Hz) whereas the carbons of the oxirane ring in 9 appear at δ 52.0 (CH_2, $^2J_{CP}$ not observable) and δ 52.5 ppm with $^1J_{CP}$ = 208 Hz.

EXPERIMENTAL

Melting points were determined on a Kofler-hot-stage apparatus and are uncorrected. IR spectra were recorded with Specord 71 IR, Perkin-Elmer 297 or Perkin-Elmer PE 983 G spectrophotometers. ^{1}H-NMR and ^{13}C-NMR spectra, reported in δ units, were obtained with a Brucker AM 300 (at 300 and 75.4 MHz respectively) or a Brucker WM 250 (at 250 and 62.9 MHz respectively) instruments. All NMR spectra were obtained by using TMS as internal standard in $CDCl_3$ or DMSO-d_6 solutions. E.I. mass spectra were obtained at 70 eV with a VG TS-250 spectrometer. Elemental analyses of C, H and P were carried out in the Laboratory of Elemental Analysis at the Department of Organic Chemistry of the University of Sofia. Column chromatography was carried out on silica gel (Merck 60; 0.063-0.2 mm), using *n*-hexane /EtOAc mixtures with increasing polarity as eluant. Sonications were effected with Bransonic 321 (390W, 50 kHz).

Preparation of the Starting Materials. The starting 3-substituted 2-oxo-2*H*-1-benzopyrans **3** and **4** were prepared according to the literature procedures[3,5,6] and their spectroscopic characteristics (IR, ^{1}H-NMR and MS) were in agreement with their structures. Ethyl hydrazinocarboxylate was prepared by a procedure given in the literature.[26] Trialkyl phosphites and dialkyl phosphites were commercial reagents.

Reaction of the trialkyl phosphites with 3-(1-bromobenzyl)-2-oxo-2H-chromene (3). *General Procedure.* A solution of the bromo derivative 3 (2 mmol) and the corresponding trialkyl phosphite (12 mmol) in dry toluene (3 ml) was refluxed for 5 h. The solvent and the excess of the phosphite was removed under reduced pressure. The residue was chromatographed on silica gel column (eluted with *n*-hexane/EtOAc mixtures of increasing polarity). Some other experimental conditions were also tested. For results see Table 1.

Dimethyl 1-(2-oxo-2H-chromen-3-yl)benzylphosphonate (5a): From 3 and trimethyl phosphite: (yields and methods as in Table 1), prisms, m.p. 115-117 °C (*n*-hexane/ether). - IR ($CHCl_3$): ν = 1720, 1610, 1050, 1030 cm^{-1}. - ^{1}H-NMR (250 MHz): δ = 8.43 (d, $^4J_{HP}$ = 2.6 Hz; H-4, 1H), 7.45-760 (m, 3H), 7.24-7.38 (m, 6H), 4.93 (d, $^1J_{HP}$ = 24.0 Hz; CHP, 1H), 3.74 (d, $^3J_{HP}$ = 10.9 Hz; OCH_3, 3H), 3.52 (d, $^3J_{HP}$ = 10.7 Hz; OCH_3, 3H). - ^{13}C-NMR (62.9 MHz): δ = 160.80 (d, $^3J_{CP}$ = 6.0 Hz; C=O), 153.00 (C-8a), 141.17 (d, $^3J_{CP}$ = 5.9 Hz; C-4), 131.42 (C-7), 127.73 (C-5), 124.95 (C-3), 124.40 (C-6), 119.06 (C-4a), 116.29 (C-8), 53.94 (d, $^2J_{COP}$ = 6.5 Hz; OCH_3), 52.98 (d, $^2J_{COP}$ = 7.0 Hz; OCH_3), 40.93 (d, $^1J_{CP}$ = 141.7 Hz; CHP); Phenyl: 134.30 (d, $^2J_{CP}$ = 5.9 Hz; C-1), 129.43 (d, $^3J_{CP}$ = 7.6 Hz; C-2/C-6), 128.74 (C-3/C-5), 128.25 (C-4). - MS m/z (%): = 345 (28), 344 (M^+, 100), 313 (3), 312 (12), 236 (14), 235 (76), 218 (6), 207 (11), 205 (4), 191 (13), 179 (10), 178 (22), 165 (5), 152 (4) 109 (5) 77 (1).

$C_{18}H_{17}O_5P$	(344.31)	Calcd.	C	62.78	H	4.98	P 9.00
		Found:	C	62.77	H	4.97	P 8.95

Diethyl 1-(2-oxo-2H-chromen-3-yl)benzylphosphonate (5b): From 3 and triethyl phosphite: (yields and methods as in Table 1), prisms, m.p. 105-106 °C (*n*-hexane/ether). - IR ($CHCl_3$): ν = 1720, 1620, 1500, 1170, 1030, 970 cm^{-1}. - ^{1}H-NMR (80 MHz): δ = 8.46 (s; 1H), 7.46-7.68 (m; 4H), 7.20-7.44 (m; 5H), 4.9 (d, $^2J_{HP}$ = 24.0 Hz; CHP, 1H), 3.6-4.3 (m; CH_2, 4H), 1.24 (t, J = 7 Hz; CH_3, 3H), 1.05 (t, J = 7 Hz; CH_3, 3H). - ^{13}C-NMR (20 MHz): δ = 159.0 (d, $^3J_{CP}$ = 3.4 Hz; C=O), 153.1 (C-8a), 141.1 (d, $^3J_{CP}$ = 3.4 Hz; C-4), 131.5 (C-7), 127.7 (C-5), 125.4 (C-3), 124.5 (C-6), 119.2 (C-4a), 116.4 (C-8), 63.45 and 62.55 (two d, $^2J_{COP}$ = 5.8 Hz; CH_2), 42.6 (d, $^1J_{CP}$ = 142.3 Hz; CHP), 16.27 (CH_3); Phenyl: 134.5 (d, $^2J_{CP}$ = 6.0 Hz; C-1), 129.6 (d, $^3J_{CP}$ = 6.5 Hz, C-2/C-6), 128.75 (C-3/C-5), 128.4

(C-4). - MS m/z (%): =374 (23), 373 (97), 372 (M^+, 100), 344 (M-28, 4), 326 (3), 298 (5), 236 (19), 235 (86), 218 (8), 207 (24), 191 (15), 189 (6), 179 (14), 178 (37), 165 (6), 152 (7), 109 (2), 81 (3).

$C_{20}H_{21}O_5P$	(372.35)	Calcd.	C 64.51	H 5.68	P 8.32
		Found:	C 64.42	H 5.60	P 8.26

Diphenyl 1-(2-oxo-2H-chromen-3-yl)benzylphosphonate (5c): From 3 and triphenyl phosphite: (yields and methods as in Table 1), prisms, m.p. 112-114 °C (ether).- IR ($CHCl_3$): ν = 1720, 1620, 1600, 1270, 1025, 950 cm^{-1}. - ^{1}H-NMR (300 MHz): δ = 8.54 (d, $^4J_{HP}$ = 2.6 Hz; 4-H, 1H), 7.62-7.67 (m; 2H), 7.47-7.56 (m; 2H), 7.05-7.38 (m; 13H), 6.68-6.74 (m; 2H), 5.31 (d, $^2J_{HP}$ = 24.5 Hz; CHP, 1H). - ^{13}C-NMR (75.4 MHz): δ = 153.1 (C-8a), 141.71 (d, $^3J_{CP}$ = 6.2 Hz; C-4), 131.78 (C-7), 128.44 (C-5), 125.13 (C-3), 124.62 (C-6), 118.98 (d, $^4J_{CP}$ = 2.1 Hz; C-4a), 116.45 (C-8), 42.97 (d, $^1J_{CP}$ = 144.2 Hz; CHP); Phenyl: 133.53 (d, $^2J_{CP}$ = 5.3 Hz; C-1), 129.8 d, $^3J_{CP}$ = 6.0 Hz; C-2/C-6), 129.0 (d, $^4J_{CP}$ = 2.1 Hz; C-3/C-5), 128.17 (d, $^5J_{CP}$ = 2 Hz; C-4); PhO: 150.36, 150.37 (C-1), 129.51 (C-3/C-5), 125.33 (C-4), 120.73 (d, $^3J_{CP}$ = 5.2 Hz; C-2/C-6), 120.32 (d, $^3J_{CP}$ = 4.2 Hz; C-2/C-6). - MS m/z (%): = 468 (M^+, 6), 377 (90), 375 (85), 281 (7), 236 (68), 235 (88), 208 (13), 207 (73), 205 (55), 191 (74), 189 (77), 179 (79), 178 (100), 176 (48), 165 (63), 151 (28), 140 (52), 115 (20), 105 (16), 102 (14), 94 (34), 77 (87).

$C_{28}H_{21}O_5P$	(468.45)	Calcd.	C 71.79	H 4.52	P 6.68
		Found:	C 72.27	H 4.74	P 7.13

3-(1-Phenoxybenzyl)-2-oxo-2H-chromene (6): From 3 and triphenyl phosphite: (as in Table 1), yield: 0.24 g (36%), white solid, m.p. 274-276 °C (ethyl acetate). - IR (Nujol): ν= 1700, 1630 cm^{-1}. - ^{1}H-NMR (300 MHz): δ = 9.22 (s; 4-H, 1H), 7.50 (ddd, J = 8.5, 7.0 and 1.6 Hz; 1H), 7.39 (dd, J = 7.7 and 1.4 Hz; 1H), 7.17-7.34 (m; 8H), 7.09 (ddd, J = 2.0, 6.9 and 8.1 Hz; 1H), 6.88 (dd, J = 0.9 and 8.1 Hz; 1H), 6.76-6.82 (m; 2H), 5.90 (s; CHO, 1H). - ^{13}C-NMR (75.4 MHz): δ = 160.77 (C=O), 154.71 (C-8a), 140.82 (C-4), 131.75 (C-5), 128.75 (C-7), 124.23 (C-6), 119.11 (C-4a), 115.97 (C-8), 44.63 (CHO); Phenyl: 139.77 (C-1), 130.79 (C-2/C-6), 129.04 (C-3/C-5), 128.35 (C-4); PhO: 152.81 (C-1), 129.23 (C-3/C-5), 118.91 (C-4), 115.52 (C-2/C-6). - MS m/z (%): = 330 (12), 329 (75), 328 (M^+, 79), 327 (34), 310 (16), 300(19), 199 (15), 281 (22), 251 (20), 236 (13), 235 (30), 234 (38), 233 (50), 223 (25), 207 (35), 195 (11), 194 949),, 182 (32), 181 (100), 178 (45), 165 (79), 152 (51), 146 (10), 127 (12), 118 (25), 115 (17), 94 (47), 90 (17), 89(26), 77 (39).

$C_{22}H_{16}O_3$	(328.45)	Calcd.	C 80.47	H 4.91
		Found:	C 80.53	H 4.99

Reaction of 3-(ω-bromoacetyl)coumarin 4 with trialkyl phosphites. General Procedure. Depending on the reaction conditions (solvent, temperature) the following methods are distinguished:

Method A. A mixture of bromo derivative 4 (0.5 mmol) and the corresponding phosphite (3 ml) was refluxed for 1 h (until all the starting bromo derivative 4 was consumed, TLC monitoring). The solvent and the excess of the phosphite was removed under reduced pressure and the residue was chromatographed on a silica gel column with *n*-hexane/EtOAc (with increasing polarity) as eluant. (The last procedure was the same in all the following methods).

Method A1. The same as method A, but heating was under reduced pressure for 30 min.

Method A2. A mixture of bromo derivative 4 (0.5 mmol) and the corresponding phosphite (3 ml) was allowed to stand at -4 °C for 20 h.

Method B. A solution of bromo derivative 4 (0.5 mmol) and the corresponding phosphite (2.5 mmol) in dry toluene (3 ml) was refluxed until the starting bromo derivative 4 was consumed (TLC monitoring).

Method B1. A solution of bromo derivative 4 (0.5 mmol) and the corresponding phosphite (3 mmol) in dry toluene (40 ml) was slowly distilled until the bromoacetylcoumarin was consumed (TLC monitoring).

Method C. A solution of bromo derivative **4** (0.5 mmol) and the corresponding phosphite (3 mmol) in xylene (40 ml) was distilled slowly until the bromoacetylcoumarin was consumed (TLC monitoring).

Method D. A solution of bromo derivative **4** (0.5 mmol) and of the corresponding phosphite (2.5 mmol) in methylene chloride (4 ml) was allowed to stand at room temperature until the starting bromo derivative **4** was consumed (TLC monitoring).

Method D1. As in method D, but the solution was allowed to stand at -4 °C for 20 h.

Method E. A solution of bromo derivative **4** (0.5 mmol) and of the corresponding phosphite (2.5 mm) in acetonitrile (4 ml) was allowed to stand at -4 °C until the starting bromo derivative **4** was consumed (TLC monitoring).

Method G. To a boiling solution of the bromo derivative **4** (2 mmol) in dioxane (4 ml), a solution of the corresponding phosphite (8 mmol) in dioxane (4 ml) was added dropwise (20 min). The reaction mixture was refluxed for 30 min.

Method F. A solution of bromo derivative **4** (1 mmol) and the corresponding phosphite (2 mmol) in glacial acetic acid (1 ml) was allowed to stand at room temperature for 5 min. The reaction mixture was poured into ice water (50 ml) containing 4.4 g potassium carbonate. The precipitate was filtered, washed with water and crystallised from methylene chloride.

Method H. A solution of bromo derivative **4** (0.5 mmol) and the corresponding phosphite (1 mmol) in methylene chloride (3 ml) was irradiated with ultrasound until the starting bromo derivative **4** was consumed (TLC monitoring).

Dimethyl 1-(2-oxo-2H-chromen-3-yl)-vinylphosphate (**8a**): From **4** and trimethyl phosphite: (yields and methods as in Table 2), needles, m.p. 101-102 °C (ether). - IR ($CHCl_3$): ν = 1735, 1720, 1460, 1280 cm^{-1}. - ^{1}H-NMR (300 MHz): δ = 8.09 (s; 4-H, 1H), 7.54-7.59 (m; 2H), 7.29-7.35 (m; 2H), 6.40 (dd as t, J = 2.5 Hz; 1H) and 5.54 (dd as t, J = 2.3 Hz; 1H, $=CH_2$), 3.91 (d, $^3J_{HP}$ = 11.4 Hz; OCH_3, 6H). - ^{13}C-NMR (75.4 MHz): δ = 158.11 (C=O), 153.26 (C-8a), 145.71 (d, $^2J_{CP}$ = 7.3 Hz; =C-O-P), 139.05 (C-4), 132.46 (C-7), 128.73 (C-5), 124.73 (C-6), 120.27 (d, $^3J_{CP}$ = 6.7 Hz; C-3), 118.65 (C-4a), 116.34 (C-8), 105.87 (d, $^3J_{CP}$ = 3.7; $=CH_2$), 55.14 (d, $^2J_{CP}$ = 6.0 Hz; OCH_3). - MS m/z (%): = 298 (33), 297 (72) 296 (M^+, 89), 281 (63), 266 (59), 253 (48), 202 (56), 188 (42), 187 (71), 185 (58), 184 (75), 173 (66), 172 (55), 171 (77), 170 (100), 159 (71), 146 (51), 145 (55), 144 (66), 142 (99), 131 (76), 127 (77), 116 (44), 115 (88), 103 (58), 102 (51), 101 (51), 93 (66), 77 (75).

$C_{13}H_{13}O_6P$	(296.22)	Calcd.	C 52.71	H 4.42	P 10.46
		Found:	C 52.71	H 4.42	P 10.28

Diethyl 1-(2-oxo-2H-chromen-3-yl)-vinylphosphate (**8b**): From **4** and triethyl phosphite: (yields and methods as in Table 3), light-yellow oil. - IR ($CHCl_3$): ν = 1740, 1690, 1620, 1570, 1400, 1270 cm^{-1}. - ^{1}H-NMR (300 MHz): δ = 8.11 (s; 4-H, 1H), 7.49-7.59 (m; 2H), 7.28-7.36 (m; 2H), 6.40 (dd as t, J = 2.4 Hz; 1H) and 5.54 (dd as t, J = 2.2 Hz; 1H, $=CH_2$), 4.23-4.31 (m; CH_2O, 4H), 1.38 (td, J = 7.1 and 0.8 Hz; CH_3, 6H). - ^{13}C-NMR (75.4 MHz): δ =158.30 (C-2), 153.23 (C-8a), 145.73 (d, $^2J_{CP}$ = 7.3 Hz; =C-O-P), 139.05 (C-4), 132.38 (C-7), 128.71 (C-5), 124.70 (C-6), 120.38 (d, $^3J_{CP}$ = 6.8 Hz; C-3), 118.69 (C-4a), 116.34 (C-8), 105.82 (d, $^3J_{CP}$ = 3.7 Hz; $=CH_2$), 64.86 (d, $^2J_{CP}$ = 6.0 Hz; CH_2O), 16.16 (d, $^3J_{CP}$ = 6.7 Hz; CH_3).

$C_{15}H_{17}O_6P$	(324.27)	Calcd.	C 55.56	H 5.28	
		Found:	C 55.92	H 5.65	

Diphenyl 2-(2-oxo-2H-chromen-3-yl)-2-oxo-ethylphosphonate (**7c**): From **4** and triphenyl phosphite: (yields and methods as in Table 4), white crystals, m.p. 155-156 °C (*n*-hexane/ether). - IR ($CHCl_3$): ν =1745, 1705, 1630, 1570, 1280 cm^{-1}. - ^{1}H-NMR (300 MHz): δ = 8.53 (s; 4-H, 1H), 7.64-7.71 (m; 2H), 7.27- 7.39 (m; 6H), 7.13-7.23 (m; 6H), 4.34 (d, J_{HP} = 22.6 Hz; CH_2, 2H). - ^{13}C-NMR (75.4 MHz): δ = 188.1 (d, $^2J_{CP}$ = 7.1 Hz; C=O), 159.1 (C=O), 155.2 (C-8a), 148.87 (C-4), 135.1 (C-7), 130.7 (C-5), 125.26 (C-6), 123.31 (d, $^3J_{CP}$ = 2.6 Hz; C-3),

118.02 (C-4a), 116.49 (C-8) 40.63 (d, $^1J_{CP}$ = 132.1 Hz; CH_2); PhO: 149.85 (d, $^2J_{CP}$ = 8.8 Hz; C-1), 129.74 (d, $^4J_{CP}$ = 0.9 Hz; C-3/C-5), 125.41 (d, $^5J_{CP}$ = 1.1 Hz; C-4), 120.49 (d, $^3J_{CP}$ = 4.5 Hz; C-2/C-6). - MS m/z (%): =421 (0.4), 420 (M^+, 0.5), 419 (0.3), 393 (0.2), 392 (0.3), 329 (14), 328 (68), 327 (100), 310 (7), 309 (36), 285 (10), 234 (10), 233 (11), 187 (10), 181 (7), 173 (57), 172 (17), 171 (82), 145 (11), 143 (14), 115 (25), 102 (6), 101 (26), 95 (5), 94 (46), 93 (6), 89 (34), 77 (72), 75 (7).

$C_{23}H_{17}O_6P$	(420.36)	Calcd.	C 65.72	H 4.08	P 7.37
		Found:	C 65.56	H 4.14	P 7.57

Reaction of dialkylphosphites with 3-(ω-bromoacetyl)coumarin 4. General Procedure. To a solution of bromo derivative 4 (0.5 mmol), the corresponding dialkyl phosphite (1 mmol) and TEBA in benzene (4 ml) a solution of 50% NaOH (2 ml) was added dropwise. The mixture was stirred at 0 °C (ice water) for 10 min and then it was poured into ice water containing a few drops of conc. HCl. The resulting emulsion was extracted with methylene chloride (3 X 20 ml), the combined extracts were washed with a solution of 10% Na_2CO_3, then with water and dried (Na_2SO_4). After removing of the solvent the residue was chromatographed on silica gel column (eluant *n*-hexane/EtOAc mixtures with increasing polarity).

Dimethyl 1-(2-oxo-2H-chromen-3-yl)-vinylphosphate (8a): From 4 and dimethyl phosphite: yield: 0.14 g (24%), needles, m.p. 101-102 °C (ether). Spectroscopic and analytical data identical to those given above.

Diethyl 1-(2-oxo-2H-chromen-3-yl)-1,2-epoxy-ethylphosphonate (9b): From 4 and diethyl phosphite: yield: 0.36 g (75%), prisms, m.p. 90-91 °C (*n*-hexane/ether). - IR ($CHCl_3$): ν = 1735, 1640, 1620, 1050, 980 cm^{-1}. - ^{1}H-NMR (300 MHz): δ = 7.98 (d, $^3J_{HP}$ = 2.4 Hz; 1H, 4-H), 7.54-7.60 (m; 2H), 7.30-7.38 (m; 2H), 4.25 (two dq, J = 14.2 and 7.0 Hz; 4H, CH_2O), 3.56 (dd as t, J = 5.3 Hz; 1H, cPr-CH_AH_B), 3.06 (dd, J = 4.9 and 5.3 Hz; 1H, cPr-CH_AH_B), 1.36, 1.33 (two t, J = 6.9 Hz; 6H, CH_3). - ^{13}C-NMR (75.4 MHz): δ = 159.46 (d, $^3J_{CP}$ = 2.3 Hz; C=O), 153.83 ($^5J_{CP}$ = 0.9 Hz; C-8a), 143.91 (d, $^3J_{CP}$ = 4.0; C-4), 132.41 (C-7), 128.35 (d, $^5J_{CP}$ = 0.8 Hz; C-5), 124.72 (C-6), 123.50 (d, $^2J_{CP}$ = 13.4 Hz; C-3), 118.62 (d, $^4J_{CP}$ = 1.9 Hz; C-4a), 116.72 (C-8), 64.15 (d, $^2J_{CP}$ = 6.2 Hz; CH_2O), 63.56 (d, $^2J_{CP}$ = 6.6 Hz; CH_2O), 52.53 (d, $^1J_{CP}$ = 208.2 Hz; cPrC-2), 52.18 (cPrC-3), 16.43 and 16.34 (d, $^3J_{CP}$ = 6.2 Hz; CH_3); MS m/z (%): = 325 (36), 324 (M^+, 68), 296 (20), 295 (6), 294 (34), 280 (13), 279 (18), 268 (14), 267 (15), 266 (43), 265 (68), 252 (18), 251 (17), 250 (20), 222 (34), 189 (15), 188 (48), 187 (94), 175 (39), 174 (90), 173 (94), 172 (16), 171 (29), 170 (25), 160 (37), 159 (61), 147 (21), 146 (85), 145 (24), 132 (18), 131 (74), 122 (16), 121 (100) 118 (35), 116 (18), 115 (81), 109 (30), 102 (55), 101 (48), 93 (69), 91 (26), 89 (78), 81 (64), 77 (65), 75 (33), 65 (73).

$C_{15}H_{17}O_6P$	(324.27)	Calcd.	C 55.56	H 5.28	P 9.55
		Found:	C 55.36	H 5.14	P 9.97

Di-n-butyl 1-(2-oxo-2H-chromen-3-yl)-1,2-epoxy-ethylphosphonate (9c): From 4 and di-*n*-butyl phosphite: yield: 0.26 g (34%), prisms, m.p. 95-97 °C (*n*-hexane/ether). - IR ($CHCl_3$): ν = 1735, 1640, 1615, 1145, 1055, 990 cm^{-1}. - ^{1}H-NMR (300 MHz): δ = 7.97 (d, $^4J_{HP}$ = 2.4 Hz; 1H, 4-H), 7.52-7.60 (m; 2H), 7.29-7.37 (m; 2H), 4.17 (m; 4H, CH_2O), 3.55 (dd as t, J = 5.3 Hz; 1H, cPrCH_AH_B), 3.05 (dd, J = 4.9 and 5.3 Hz; 1H, cPrCH_AH_B), 1.61-1.74 (m; 4H), 1.32-1.45 (m; 4H), 0.92 (t, J = 7.3 Hz; 6H, CH_3). - ^{13}C-NMR (75.4 MHz): δ = 159.41 (C=O), 153.84 (d, $^5J_{CP}$ = 1.0 Hz; C-8a), 143.96 (d, $^3J_{CP}$ = 4.3 Hz; C-4), 132.41 (C-7), 128.31 (C-5), 124.72 (C-6), 123.50 (d, $^2J_{CP}$ = 13.6 Hz; C-3), 118.61 (d, $^4J_{CP}$ = 1.6 Hz; C-4a), 116.71 (C-8), 67.78 (d, $^2J_{CP}$ = 6.4 Hz; CH_2O), 67.18 (d, $^2J_{CP}$ = 6.7 Hz; CH_2O), 52.58 (d, $^1J_{CP}$ = 208.7 Hz; cPrC-2), 52.12 (cPrC-3), 32.50 (d, $^3J_{CP}$ = 5.9 Hz; CH_2), 32.46 (d, $^3J_{CP}$ = 5.9 Hz; CH_2), 18.64 (d, $^4J_{CP}$ = 1.1 Hz; CH_2), 13.59 (CH_3). - MS m/z (%): = 381 (5), 380 (M^+, 7), 350 (8), 325 (8), 324 (7), 294 (7), 293 (4), 270 (7), 267 (29), 268 (100), 252 (12), 251 (18), 250 (17), 240 (14), 239 (14), 238 (24), 237 (7), 223 (9), 222 (17), 189 (24), 188 (24), 187 (82), 175 (17), 174 (84), 173 (68), 172 (6), 171 (20), 160 (12), 159 (32), 147

(8), 146 (41), 145 (8), 131 (50), 118 (19), 116 (7), 115 (52), 103 (12), 102 (17), 90 (8), 89 (36), 83 (7), 77 (26), 75 (7), 65 (11), 63 (18).

$C_{19}H_{25}O_6P$	(380.38)	Calcd.	C 60.00	H 6.62
		Found:	C 59.64	H 6.27

***Bromomethyl 2-oxo-2H-chromen-3-yl ketone (2-ethoxycarbonyl)hydrazone* (10):** To a solution of ethylcarbazate (ethyl hydrazinocarboxylate) (30 mmol) in THF (100 ml) was added bromoketone **4** (30 mmol) and the reaction mixture was allowed to stand under stirring at room temperature for 3 h (TLC monitoring). The solvent was removed under reduced pressure and the residue was recrystallized from ethyl acetate to give **10**, 9.10 g (86%), needles, m.p. 186-186.5 °C (ethyl acetate). - IR ($CHCl_3$): ν = 3240, 1740, 1720, 1615 cm^{-1}. - ^{1}H-NMR (300 MHz): δ = 8.47 (s; 1H, NH), 8.17 (s; 1H, 4-H), 7.55-7.62 (m; 2H), 7.29-7.38 (m; 2H), 4.47 (s; 2H, CH_2), 4.36 (q, J = 7.1 Hz; 2H, CH_2), 1.38 (t, J = 7.1 Hz; 3H, CH_3). - ^{13}C-NMR (75.4 MHz): δ = 160.14 (C=O), 154.61 (NHC=O), 153.19 (C-8a), 143.94 (C-4), 143.77 (C=N), 132.73 (C-7), 128.98 (C-5), 124.94 (C-6), 123.43 (C-3), 118.98 (C-4a), 116.60 (C-8), 62.73 (CH_2O), 20.00 (CH_2Br), 14.48 (CH_3). - MS m/z (%): = 354/352 (M^+, 5), 275 (4), 274 (24), 273 (62), 245 (7), 244 (7), 228 (9), 227 (9), 202 (5), 201 (23), 200 (7), 199 (6), 187 (9), 186 (18), 185 (11), 173 (25), 172 (76), 171 (100), 155 (19), 145 (11), 144 (43), 143 (32), 142 (11), 128 (19), 127 (30), 116 (22), 115 (95), 91 (28), 89 (35), 82 (18), 81 (8), 77 (27), 75 (13), 65 (17), 63 (33).

$C_{14}H_{13}O_4N_2Br$	(353.17)	Calcd.	C 47.61	H 3.71	N 7.93
		Found:	C 47.49	H 3.96	N 7.55

Reaction of ethoxycarbonyl hydrazone 10 with trialkyl-phosphites. General Procedure. To a boiling solution of phosphite (2.5 mmol) in dry toluene (15 ml) a solution of ethoxycarbonylhydrazone **10** (2 mmol) in dry toluene (5 ml) was added dropwise. The reaction mixture was further refluxed for 30 min, the solvent was removed under reduced pressure and the residue was recrystallized from ethyl acetate to give the hydrazono phosphonate **11**.

***Dimethyl 2-(2-ethoxycarbonyl)hydrazono-2-(2-Oxo-2H-chromen-3-yl)ethylphosphonate* (11a):** From **10** and trimethyl phosphite: yield: 0.67 g (82%), white solid, m.p. 129-130 °C (*n*-hexane/CH_2Cl_2). - IR ($CHCl_3$): ν = 3200, 1720, 1610, 1090, 1045 cm^{-1}. - ^{1}H-NMR (250 MHz): δ = 10.0 (bs; NH), 8.23 (s; 1H, 4-H), 7.54-7.60 (m; 2H), 7.28-7.37 (m; 2H), 4.32 (q, J = 7.1 Hz; 2H, CH_2O), 3.76 (d, $^3J_{HP}$ = 11.3 Hz; 6H, OCH_3), 3.69 (d, $^2J_{HP}$ = 22.4 Hz; 2H, PCH_2), 1.35 (t, J = 7.1 Hz; 3H, CH_3). - ^{13}C-NMR (62.9 MHz): δ = 160.07 (C=O), 154.73 (C-8a), 154.08 (C=O), 143.53 (C-4), 141.70 (d, $^2J_{CP}$ = 11.2 Hz; C=N), 132.56 (C-7), 129.01 (C-5), 124.85 (C-6), 124.62 (C-3), 119.04 (C-4a), 116.48 (C-8), 62.12 (CH_2O), 53.40 (d, $^2J_{CP}$ = 6.5 Hz; CH_3OP), 26.44 (d, $^1J_{CP}$ = 135.7 Hz; CH_2P), 14.50 (CH_3). Ms m/z (%): = 383 (8), 382 (M^-, 50), 381 (73), 351 (3), 350 (20), 337 (11), 336 (9), 310 (11), 309 (70), 308 (6), 307 (6), 306 (23), 305 (12), 304 (21), 278 (27), 277 (36), 249 (30), 242 (8), 201 (9), 200 (24), 199 (27), 189 (7), 187 (13), 186 (16), 185 (32), 173 (20), 172 (62), 171 (100), 156 (12), 155 (21), 145 (10), 144 (48), 143 (24), 142 (20), 131 (10), 128 (14), 127 (26), 124 (19), 116 (18), 115 (96), 110 (28), 109 (53), 96 (64), 95 (24), 94 (80), 91 (32), 89 (28), 81 (16), 79 (58), 77 (36), 69 (23), 65 (16).

$C_{16}H_{19}O_7N_2P$	(382.31)	Calcd.	C 50.27	H 5.01	N 7.33
		Found:	C 50.47	H 5.17	N 7.13

***Diethyl 2-(2-ethoxycarbonyl)hydrazono-2-(2-oxo-2H-chromen-3-yl)ethylphosphonate* (11b):** From **10** and triethyl phosphite: yield: 0.79 g (95%), white solid, m.p. 153-154 °C (ethyl acetate). - IR ($CHCl_3$): ν = 3240, 1755, 1730, 1625, 1055, 1025, 980 cm^{-1}. - ^{1}H-NMR (250 MHz): δ = 10.0 (bs; NH), 8.19 (s; 1H, 4-H), 7.54-7.60 (m; 2H), 7.28-7.37 (m; 2H), 4.32 (q, J = 7.1 Hz; 2H, CH_2O), 4.06-4.18 (m; 4H), 3.66 (d, $^2J_{HP}$ = 22.4 Hz; 2H, PCH_2), 1.34 (t, J = 7.1 Hz; 3H, CH_3) 1.28 (t, J = 7.0 Hz; 3H, CH_3). - ^{13}C-NMR (62.9 MHz): δ = 160.03 (C=O), 154.71 (C-8a), 154.02 (C=O), 143.49 (C-4), 142.36 (d, $^2J_{CP}$ = 11.2 Hz; C=N), 132.48 (C-7), 128.87 (C-5), 124.82 (C-

6), 119.00 (C-4a), 116.43 (C-8), 63.00 (d, $^2J_{CP}$ = 6.7 Hz; CH_2OP), 62.03 (CH_2O), 27.86 (d, $^1J_{CP}$ = 135.4 Hz; CH_2P), 16.25 (d, $^3J_{CP}$ = 5.9 Hz; CH_3), 14.52 (CH_3). - MS m/z (%): = 411 (9), 410 (M^+, 62), 409 (100), 381 (6), 365 (10), 364 (16), 338 (5), 337 (27), 310 (9), 309 (37), 308 (11), 292 (16), 291 (13), 282 (7), 281 (54), 278 (8), 264 (15), 263 (25), 235 (21), 229 (10), 228 (21), 201 (14), 200 (43), 199 (41), 187 (13), 186 (16), 185 (10), 174 (9), 173 (56), 172 (52), 171 (83), 146 (7), 145 (11), 144 (41), 143 (21), 127 (20), 125 (14), 116 (17), 115 (90), 110 (13), 109 (22), 108 (13), 97 (13), 89 (21), 82 (23), 81 (31), 77 (18), 65 (34), 63 (14).

$C_{18}H_{23}O_7N_2P$	(410.36)	Calcd.	C 52.68	H 5.65	N 6.83
		Found:	C 53.08	H 5.65	N 6.76

Hydrolysis of the hydrazono-protecting group in 11. Preparation of the β-oxo-phosphonates 7. General Procedure. To a solution of hydrazone 11 (0.5 mmol) in acetone (3 ml) a solution of 3M HCl (3 ml) was added The reaction mixture was stirred at room temperature for 90 min (TLC monitoring). The resulting emulsion was extracted with methylene chloride (3 X 20 ml), and the combined extracts were washed with a 10% K_2CO_3 solution, then with water and dried (Na_2SO_4). The solvent was removed and the residue was recrystallized from *n*-hexane/ether to give the β-oxo-phosphonate 7.

Dimethyl 2-(2-oxo-2H-chromen-3-yl)-2-oxo-ethylphosphonate (7a): From acid hydrolysis of **11a**: yield: 0.12 g (77%), white crystals, m.p. 93-94 °C (ether). - IR ($CHCl_3$): ν = 1745, 1700, 1625, 1040, 990 cm^{-1}. - ^{1}H-NMR (250 MHz): δ = 8.55 (s; 1H, 4-H), 7.65-7.71 (m; 2H), 7.27-7.40 (m; 2H), 4.04 (d, $^2J_{HP}$ = 22.5 Hz; 2H, CH_2P), 3.80 (d, $^2J_{HP}$ = 11.3 Hz; 6H, CH_3). - ^{13}C-NMR (62.9 MHz): δ = 189.33 ($^2J_{CP}$ = 7.0 Hz; C=O), 159.32 (C=O), 155.41 (C-8a), 148.50 (C-4), 134.80 (C-7), 130.40 (C-5), 125.1 (C-4), 123.7 (C-3), 118.2 (C-4a), 116.8 (C-8), 53.05 (d, $^2J_{CP}$ = 6.0 Hz; CH_3OP), 40.02 (d, $^1J_{CP}$ = 128.4 Hz; CH_2). - MS m/z (%): = 297 (11), 296 (M^+, 61), 282 (4), 281 (23), 269 (7), 268 (51), 240 (11), 236 (8), 201 (21), 200 (25), 188 (19), 187 (12), 175 (8), 174 (40), 173 (100), 172 (10), 171 (21), 170 (7), 160 (23), 159 (67), 151 (61), 146 (11), 145 (26), 137 (12), 131 (23), 123 (7), 119 (28), 118 (21), 115 (19), 110 (8), 109 (76), 102 (9), 101 (33), 97 (14), 95 (15), 93 (14), 90 (13), 89 (59), 79 (23), 77 (19), 75 (10), 62 (13).

$C_{13}H_{13}O_6P$	(296.22)	Calcd.	C 52.71	H 4.42	
		Found:	C 52.97	H 4.70	

Diethyl 2-(2-oxo-2H-chromen-3-yl)-2-oxo-ethylphosphonate (7b): From acid hydrolysis of **11b**: yield: 0.11 g (68%), white crystals, m.p. 99-101 °C (ether). - IR ($CHCl_3$): ν = 1735, 1695, 1620, 1050, 1025, 975 cm^{-1}. - ^{1}H-NMR (300 MHz): δ = 8.51 (s; 1H, 4-H), 7.61-7.71 (m; 2H), 7.34-7.40 (m; 2H), 4.16 (dt as quintet, J = 7.1 Hz; 4H, CH_2OP), 4.02 (d, $^2J_{HP}$ = 22.6 Hz; 2H, CH_2P), 1.30 (t, J = 7.0 Hz; 6H, CH_3). - ^{13}C-NMR (75.4 MHz): δ = 189.7 ($^2J_{CP}$ = 6.9 Hz; C=O), 159.36 (C=O), 155.36 (C-8a), 148.10 (C-4), 134.71 (C-7), 130.39 (C-5), 125.14 (C-4), 124.20 (d, $^3J_{CP}$ = 1.5 Hz; C-3), 118.26 (C-4a), 116.77 (C-8), 62.53 (d, $^2J_{CP}$ = 6.2 Hz; CH_2OP), 41.01 (d, $^1J_{CP}$ = 127.1 Hz; CH_2), 16.33 (d, $^3J_{CP}$ = 6.4 Hz; CH_3). - MS m/z (%): = 325 (8), 324 (M^+, 36), 297 (10), 296 (39), 295 (16), 280 (18), 279 (17), 269 (8), 268 (13), 267 (15), 252 (9), 251 (24), 221 (8), 212 (10), 189 (21), 188 (70), 187 (21), 175 (8), 174 (47), 173 (100), 172 (96), 171 (45), 170 (19), 161 (10), 160 (66), 146 (10), 145 (25), 131 (20), 124 (37), 123 (45), 118 (24), 115 (22), 109 (39), 101 (32), 97 (13), 89 (59), 81 (42), 77 (18), 75 (17), 65 (11), 63 (29).

$C_{15}H_{17}O_6P$	(324.27)	Calcd.	C 55.56	H 5.28	P 9.55
		Found:	C 55.36	H 5.14	P 9.97

Diphenyl 2-(2-oxo-2H-chromen-3-yl)-2-oxo-ethylphosphonate (7c): From acid hydrolysis of the crude product 11c, isolated from the reaction of **10** and diphenyl phosphite: yield: 0.11 g (54%), white crystals, m.p. 155-156 °C (ether). Spectroscopic and analytical data identical to those given above.

Hydrolysis of alkyl phosphonates to phosphonic acids. General procedure. A suspension of the corresponding alkyl phosphonate (2 mmol) in conc. HCl (1.5 ml) was refluxed for 2 h. The reaction mixture

was concentrated to dryness under reduced pressure and the residue was recrystallized from ethyl acetate. The hydrolysis of diethyl phosphonate 7b was performed by refluxing in a 20% HCl solution.

2-Oxo-2H-chromene-3-phosphonic acid (12): From acid hydrolysis of diethyl phosphonate 1b: yield: 0.38 g (84%), needles, m.p. 234-235 °C (ethyl acetate). - IR (Nujol): ν = 3480-3400, 1720, 1610, 1025, 930 cm^{-1}. - ^{1}H-NMR (DMSO-d_6-$CDCl_3$, 300 MHz): δ = 8.43 (d, $^3J_{HP}$ = 16.4 Hz; 1H, 4-H), 7.59-7.75 (m; 2H), 7.28-7.35 (m; 2H). - ^{13}C-NMR (DMSO-d_6-$CDCl_3$, 75.4 MHz): δ = 158.75 (d, $^2J_{CP}$ = 3.4 Hz; C=O), 154.57 (C-8a), 150.11 (d, $^2J_{CP}$ = 6.3 Hz; C-4), 133.27 (C-7), 129.31 (C-5), 124.64 (C-6), 121.40 (d, $^1J_{CP}$ = 192.0 Hz; C-3), 11.14 (d, $^3J_{CP}$ = 13.5 Hz; C-4a), 116.22 (C-8). - MS m/z (%): = 227 (6), 226 M^+, 42), 198 (13), 183 (10), 182 (100), 180 (6), 152 (4), 151 (3), 146 (4), 145 (3), 136 (5), 134 (37), 133 (11), 119 (6), 118 (58), 106 (10), 105 (18), 90 (38), 89 (79), 88 (10), 81 (20), 78 (31), 77 (30), 65 (19), 64 (13), 63 (75), 62 (31), 51 (30), 50 (15), 47 (10).

$C_9H_7O_5P$	(226.13)	Calcd.	C 47.80	H 3.12	P 13.70
		Found:	C 48.00	H 3.36	P 13.87

(2-Oxo-2H-chromen-3-yl)benzylphosphonic acid (13): From acid hydrolysis of diethyl phosphonate 5b: yield: 0.46 g (73%), white solid, m.p. 154-156 °C (ethyl acetate). - IR (Nujol): ν = 3560, 2710, 1710, 1615, 1020, 965 cm^{-1}. ^{1}H-NMR (DMSO-d_6, 250 MHz): δ = 8.48 (d, $^3J_{HP}$ = 2.4 Hz; 1H, 4-H), 7.79 (dd, J = 1.5 and 7.8; 1H, 5-H), 760 (ddd, J = 1.5, 7.2 and 8.6 Hz; 1H, 7-H), 7.19-7.48 (m; 7H), 4.56 (d, $^2J_{HP}$ = 23.1 Hz; 1H, CHP). - MS m/z (%): = 317 (0.5), 316 (M^+, 2), 314 (10), 299 (7), 298 (31), 270 (4), 252 (5), 237 (17), 236 (100), 235 (50), 219 (7), 218 (5), 208 (7), 207 (28), 206 (7), 205 (16), 191 (12), 190 (6), 189 (15), 182 (14), 179 (19), 178 (52), 177 (14), 176 (16), 165 (11), 152 (19), 151 (14), 146 (4), 131 (8), 118 (16), 115 (8), 105 (8), 102 (8), 91 (11), 90 (11), 89 (25), 81 (11), 77 (23), 76 (9), 65 (11), 63 (19), 51 (18), 47 (5), 44 (26)

$C_{16}H_{13}O_5P$	(316.25)	Calcd.	C 60.77	H 4.14	P 9.80
		Found:	C 60.54	H 3.98	P 9.54

2-(2-Oxo-2H-chromen-3-yl)-2-oxo-ethylphosphonic acid (14): From acid hydrolysis of diethyl phosphonate 7b: yield: 0.38 g (71%), white solid, m.p. 171-173 °C (ethyl acetate). - IR (Nujol): ν = 3485, 1720, 1195, 1020 cm^{-1}. - ^{1}H-NMR (DMSO-d_6, 250 MHz): δ = 8.59 (s; 1H, 4-H), 7.96 (d, J = 7.5 Hz; 1H, 5-H), 7.75 (dd as t, J = 7.6 Hz; 1H, 7-H), 7.39-7.48 (m; 2H), 3.69 (d, $^2J_{HP}$ = 22.5 Hz; 2H, CH_2P).

$C_{11}H_9O_6P$	(268.25)	Calcd.	C 49.25	H 3.35
		Found:	C 49.04	H 3.15

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