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A new and efficient method for conjugate addition of trialkylphosphites to 3-acylsubstituted coumarins

Rositca D. Nikolova,[a] Anka G. Bojilova[a] and Nestor A. Rodios[b,*]

[a]*Department of Organic Chemistry, University of Sofia, J. Bourchier Avenue 1, Sofia 1126, Bulgaria*
[b]*Laboratory of Organic Chemistry, Department of Chemistry, Aristotle University of Thessaloniki, GR-54006 Thessaloniki, Greece*

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Abstract—A new and efficient conjugate addition of trialkylphosphites to 3-ω-bromoacetylcoumarin **1** catalysed by *p*-toluenesulfonic acid (TsOH) has been studied. Under the same conditions, an enolphosphate gave the corresponding esters of 3-acetyl-4-phosphono-2-oxochromans in high yields. The use of TsOH in the reaction of 3-acetyl-, 3-benzoyl-, and 3-ethoxycarbonyl coumarins led mainly to 1,4-addition products—the corresponding 3-acyl-4-dialkylphosphono-2-oxochromans—in very good yields.

1. Introduction

In a previous paper[1] we described the reaction of 3-(ω-bromoacetyl)coumarin **1** with trialkylphosphites, from which, depending on the reaction conditions and the phosphite used, the corresponding enolphosphates **2**, for R=CH_3 or C_2H_5, or the 2-oxophosphonate **3**, for R=Ph were the only isolated products. On the other hand, the interaction of the bromoderivative **1** with diethyl and dibutylphosphite under phase transfer conditions gave the corresponding epoxyphosphonates **4** as the main products.

The preparation of dialkyl 2-oxophosphonates **3** (CH_3 or C_2H_5) were realized[1] only when the carbonyl group in the starting ketone **1** was protected by the ethoxycarbonylhydrazono group, followed by Arbuzov reaction.

The experimental findings, concerning the mechanisms of the above transformations, taking into account theoretical considerations and the experimental data available for Perkow, Arbuzov and Michaelis-Becker reactions,[2–16] could be explained as follows:

1. The transformation of bromoderivative **1** to 2-oxophosphonates **3** proceeds as an Arbuzov reaction. According to the proposed mechanism for this reaction[4–9] the most simple and more likely pathway for this transformation involves the S_N2 displacement of the bromine by the phosphite. It should be emphasized that this transformation (**1**→**3**) goes only with the less reactive[2,9,16] triphenylphosphite whereas with trialkylphosphites no such products were isolated. This different behavior of triphenyl- and trialkylphosphites in the reaction with the bromoketone **1** could be explained via the formation of the more stable triphenyl phosphonium salt[7] and its thermal decomposition to the phosphonate **3**.
2. It also seems clear that the formation of epoxyphosphonates **4** proceeds under the Michaelis-Becker reaction conditions.[10–12] The first step is the nucleophilic addition of the deprotonated dialkylphosphite anion to the C=O group of **1**, followed by elimination of the bromine and cyclization to the epoxyphosphonates **4**. In fact, the transformation of **1** into epoxy derivative **4** proceed as another variation of the classic Darzen's reaction[17] and it looks normal that it proceeds with a stronger nucleophile as is the dialkylphosphite anion (Scheme 1).
3. The transformation of the bromoacetyl coumarin **1** into the enolphosphates **2**, realized under various conditions, typical for the Arbuzov/Perkow reaction, took place only with trialkyl phosphites. Surprisingly, when the reaction was performed in acetic acid, it was completed within 5 min giving the enolphosphate **2** in 84% yield.

It has been reported[3,15,16] that the reaction of α-haloketones with trialkylphosphites in the presence of acetic acid favors the formation of enolphosphates and a similar action has been observed[14] when this reaction was performed in the presence of phosphoric acid. The dramatic acceleration observed[1] in our case in the reaction of **1** with

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* Corresponding author. Tel.: +30-2310-99-78-03; fax: +30-2310-99-76-79; e-mail: rodios@chem.auth.gr

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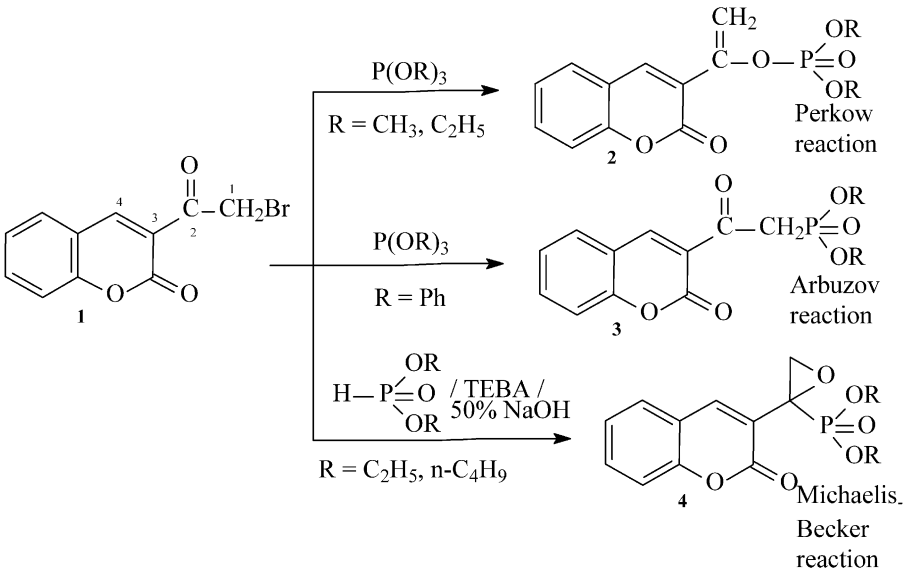


Scheme 1.

trialkylphosphites, prompted us to investigate what would be the result of this reaction in the case of carrying it out in the presence of a stronger acid such as *p*-toluenesulfonic acid (TsOH).

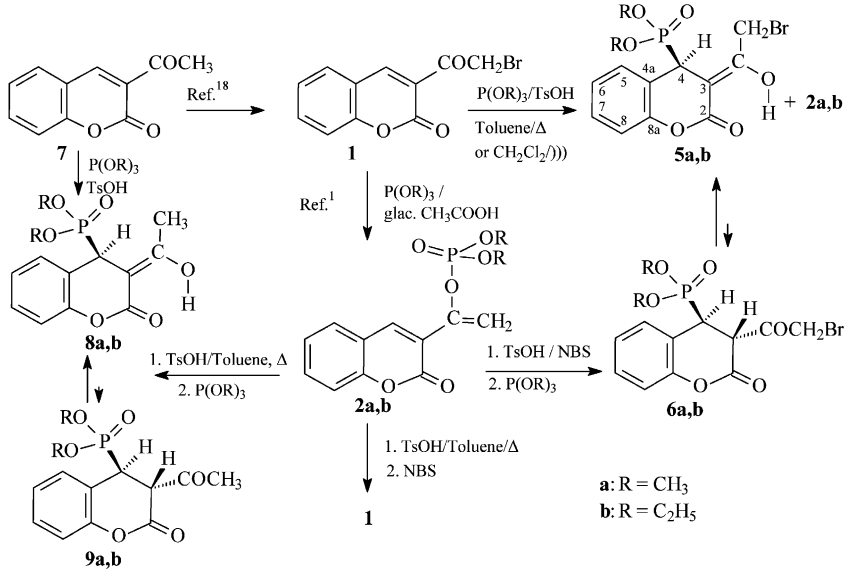
2. Results and discussion

The results of the reaction of **1** with trimethyl and triethylphosphites and in the presence of TsOH, performed

Table 1. Interaction of 3-bromoacetylcoumarin **1** with trialkylphosphites $P(OR)_3$ in the presence of TsOH[a]

Method	Reaction condition	Time [min]	Yields, %			
			2[b]		**5**[b]	
	Ratio **1**:$P(OR)_3$:TsOH		**a**	**b**	**a**	**b**
A	1:2:1/Δ/toluene	150		54		30
A_1	1:5:1/Δ/toluene	90	33		55	
B	1:5:0.1/CH_2Cl_2/)))[c]	20	86	94	8	Trace
C	1:5:1/CH_2Cl_2/)))	20	17	5	76	90
C_1	1:5:2/CH_2Cl_2/)))	20	10	3	82	93

[a] TsOH=*p*-toluenesulfonic acid.
[b] **a**: R=CH_3, **b**: R=C_2H_5.
[c]))): Reaction carried out under ultrasound irradiation.



Scheme 2.

in refluxing toluene (Methods A, A_1) or in methylene chloride under ultrasound irradiation (Methods B, C and C_1) and in different bromoketone **1**:trialkylphosphite:toluenesulfonic acid ratios are presented in Table 1.

The course of the reaction of **1** with $P(OR)_3$ in the presence of TsOH was completely different to that with acetic acid,[1] giving, in addition to the expected enolphosphates **2a**,**b**, new 1,4-addition products **5a**,**b** (Table 1, Scheme 2). Thus in refluxing toluene (Methods A, A_1), the reaction of **1** with $P(OR)_3$ gave the enolphosphates **2a** and **2b** in 33, 54% and the 1,4-adducts **5a** and **5b** in 30, 55% yields, respectively.

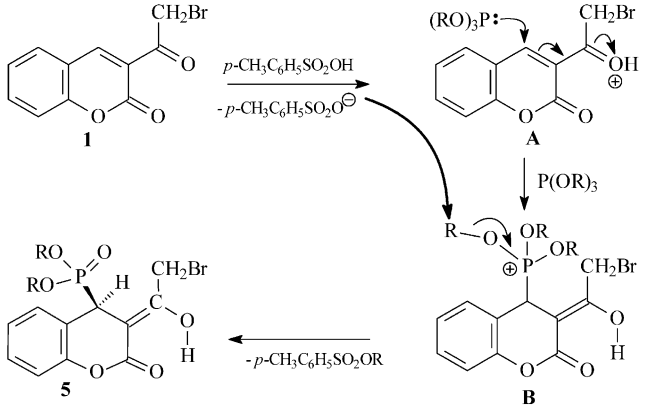
The results, concerning yields and the **2**:**5** ratios were significantly different when the reaction took place in methylene chloride and under the action of ultrasound irradiation (Methods B, C, C_1). The reaction was completed within 20 min and the yields of the isolated products **2** and **5** depended on the amount of TsOH used to perform the reaction. When TsOH was used in catalytic amounts (Table 1, Method B) the enolphosphates **2a**, **2b** were the main products, with yields of 86 and 94%, respectively. By increasing the bromocoumarin **1**:TsOH ratio to 1:1 (Table 1, Method C) the 1,4-addition products **5a**, **5b** were the main ones, with yields of 76 and 90%, respectively, whereas the corresponding enolphosphates **2a**, **2b** were isolated in yields of 17 and 5%, respectively. A further increase of the **1**:TsOH ratio to 1:2 did not substantially change the yields of the reaction products (Table 1, Method C_1).

The formation of the 1,4-adducts **5** from the reaction of bromoacetylcoumarin **1** and trialkylphosphites in the presence of TsOH could be explained by initial protonation of the C=O group. The protonated ketone **A** acting as an activated conjugate system reacts easily with trialkylphosphites to form the intermediate 1,4-adduct **B**. The transformation of the latter to the products **5** goes most probably with the participation of the TsOH anion (Scheme 3). The formation of the corresponding esters of *p*-toluenesulfonic acid was proved by their isolation from the reaction mixtures in yields of 70–75% and by comparing their R_f-values and IR spectra with authentic samples.

In the reaction mixture containing $P(OR)_3$ and TsOH, however, the possibility of trialkylphosphite to have been transformed into the corresponding dialkylphosphite[19] should be taken into account. In order therefore to prove the real reagent in the reaction of 1,4-addition of the phosphites to compound **1**, trialkylphosphite or dialkylphosphite, the reaction of **1** with dialkylphosphite under ultrasound irradiation in methylene chloride, without and in the presence of TsOH, was carried out. In both cases the starting coumarin **1** was isolated in quantitative yield.

When the reaction of **1** with dialkylphosphites was, however, carried out in refluxing toluene, a complicated reaction mixture (TLC) was obtained from which 3-acetylcoumarin **7** (at 2–5%), the corresponding enolphosphates **2** (at ~20%) and the products of 1,4-addition of dialkylphosphites to 3-acetylcoumarin (**8a**,**b**) were isolated (Table 2, Scheme 4).

The behavior of the enolphosphate **2a** in the reaction with trialkylphosphites in refluxing toluene and in the presence of TsOH was also studied. From this reaction (Methods A_2 and A_3, Table 3, Schemes 2 and 5) the 1,4-adducts **8a** and **8b** were isolated. When this reaction was performed in two stages, i.e. first the solution of **2a** and TsOH in toluene is refluxed for 5 min and after that addition of $P(OR)_3$ (Method A_3, Table 3), the transformation of **2a** to **8a** was almost quantitative (the enolic forms of the 3-acetyl-4-dialkylphosphono-2-oxochromans **8a** and **8b** were isolated in 87 and 93%, respectively, with no unreacted starting compound). These findings indicate that in the above reaction, the enolphosphate **2** is first hydrolyzed to 3-acetylcoumarin **7** by the strong acid TsOH[2] (and this was proved in a separate experiment, where hydrolysis of **2a** to **7** was completed within 15 min with 90% yield) and in a second step the 1,4 addition of trialkylphosphite is taking place (Scheme 5).

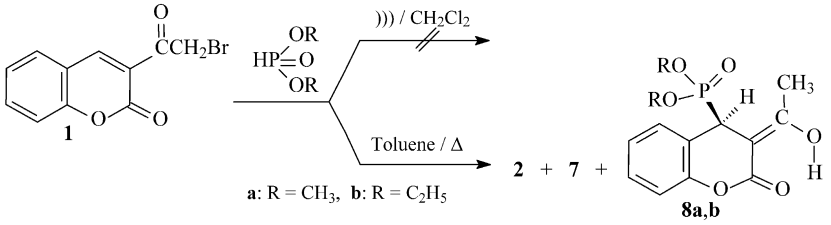


Scheme 3.

Table 2. Interaction[a] of 3-bromoacetylcoumarin **1** with dialkylphosphites $(RO)_2PH$

	R	2	7	8
a	CH_3	20	2	7
b	C_2H_5	6	5	17

[a] In refluxing toluene, 4 h.

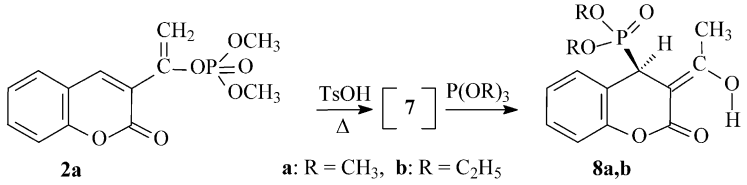


Scheme 4.

Table 3. Interaction of enolphosphates **2a** with trialkylphosphites

Method	Reaction conditions Ratio **2a**:$P(OR)_3$:TsOH	Time, h	Unreacted **2**	Yields, %	
				8a	**8b**
A_2	1:5:2.5/Δ/toluene	4	15/26[a]	43	39
A_3	1:2:2/Δ/toluene, 2-stage	0.5		87	93

[a] When the reaction was carried out in one stage.

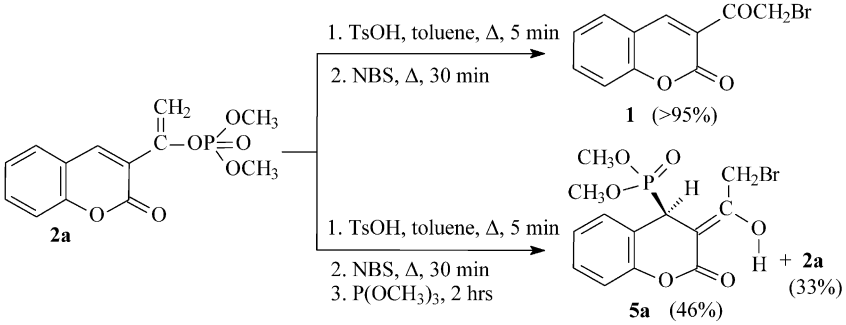


Scheme 5.

The possibility of the enolphosphate **2a** being transformed into 3-ω-bromoacetylcoumarin **1** was also studied. This was achieved in a one pot two-stage reaction by the action of TsOH for the hydrolysis of **2a** and then of NBS for the bromination of the hydrolysis product of 3-acetylcoumarin **7**. Compound **1** was obtained in almost quantitative yield. By repeating the same reaction and, in a third stage, by adding trimethylphosphite to the reaction mixture, compounds **2a** (33%) and **5a** (46%) were isolated (Scheme 6). Almost the same proportion (**2a**/**5a**) were obtained from reaction of **1** with $P(OCH_3)_3$, (Table 1, Method A_1).

Over the last few years the reaction of 3-acetylcoumarin **7** with dialkyl- and trialkylphosphites, from which the 1,4-addition products **8** were obtained in 40–80% yields on refluxing for 8–10 h, has been reported.[20–23] Since we have found that the use of TsOH favors the 1,4-addition of trialkylphosphites to 3-bromoacetylcoumarin **1** and substantially shortens the reaction time, we investigated the same reactions of trialkylphosphites with 3-acetylcoumarin **7** as well as with 3-benzoyl and 3-ethoxycarbonyl coumarins **10** and **11** respectively, in the presence of TsOH and under ultrasound irradiation. The results (Table 4) show that the corresponding 4-dialkylphosphono-2-oxocromans **8/9**, **12/13** and **14** (Scheme 7) were obtained in yields from 60 to 95% (Table 4, Method C).

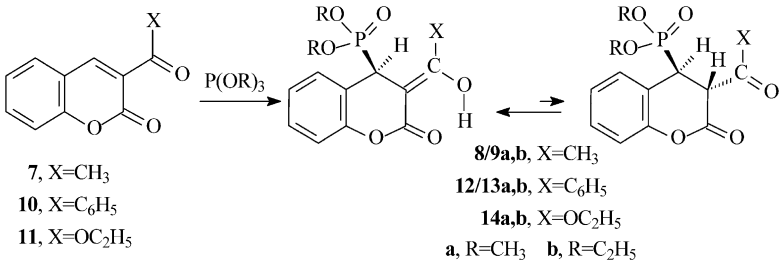
The structures of the isolated compounds were assigned mainly on the basis of their ^1H and ^{13}C NMR spectral data. Thus, compounds **5/6a**,**b** and **8/9a**,**b** appeared exclusively in the enol-tautomeric forms **5** and **8** respectively, and this is in agreement with the reported[21,23] structure of compound **8/9a**,**b**. Compounds **12/13b** and **14a**,**b** on the other hand appeared exclusively in the keto-tautomeric form **13** and **14** respectively, whereas compound **12/13a** appeared as a mixture of both tautomers **12a**⇆**13a**, with a **12**:**13** ratio of



Scheme 6.

Table 4. Reaction of trialkylphosphites with 3-acylsubstituted coumarins

Starting Compd.	Method	Reaction conditions (Ratio coumarin: $P(OR)_3$:TsOH)	Time[min]	Reaction product	Yield %	
					a	**b**
7	A_1	1:5:1/Δ/toluene	15	**8/9**	90	91
7	C	1:5:1/CH_2Cl_2/)))	30	**8/9**	95	95
7	D	1:5/CH_2Cl_2+ROH/))), without TsOH	30	**8/9**	86	94
7	E	1:5/CH_3COOH/))), without TsOH	15	**8/9**	87	93
10	C	1:5:1/CH_2Cl_2/)))	30	**12/13**	94	69
11	C	1:5:1/CH_2Cl_2/)))	30	**14**	58	88



Scheme 7.

9:1 (^{1}H NMR), which, on standing the sample in the NMR-tube ($CDCl_3$) for one week, changed to ~1:1.

The ^{1}H NMR spectra of the enol-forms **5a**,**b**, **8a**,**b** and **12a** showed an OH peak at $\delta \sim 13$ ppm, exchangeable with D_2O. The 4-H proton appeared as a doublet at $\delta = 4.19$–4.45 ppm with a $^2J_{HCP} \approx 22$ Hz, and the enolic methyl group of compounds **8a**,**b**, =C–CH_3, showed a doublet with a $^5J_{HP} \approx 3$ Hz (homoallylic), whereas the corresponding two methylenic protons of compounds **5a**,**b**, =C–CH_2Br appeared at ~4 and 4.5 ppm as dd ($^2J_{HCH} = 11.2$ Hz, $^5J_{HP} \approx 1$ Hz) and ddd ($^2J_{HCH} = 11.2$ Hz, $^5J_{HP} \approx {}^5J_{HH} \approx$ 1.5 Hz) respectively. Of interest is the observed coupling between the hydroxyl proton and one of the two methylenic protons of the CH_AHBr group, $^4J_{H,OH} = 1.5$–1.7 Hz. This indicates a fixed W disposition of these two protons, as a result of a restricted rotation of the CH_2Br group due to the bulky bromine atom, and of the OH group due to hydrogen bonding of the OH proton to the 2-oxochroman carbonyl oxygen. This hydrogen bonding has been also observed[23] in the crystal structure of compounds **7**/**8**. In their ^{13}C NMR spectra the enolic forms gave a peak for C-4 at ~37.5 ppm coupled with the phosphorus atom with $^1J_{CP} = 141$–144 Hz and a peak for C-3 at ~90 ppm, with a $^2J_{CP} = 8.9$ Hz. The enolic carbon =C–OH appeared as doublet, ($^3J_{CP} \approx 6$–7 Hz) at $\delta = 176$–179 ppm and the carbonyl carbon (C-2) gave a peak at $\delta \approx 169$ ppm. The absence of the keto-form peaks for the 3-H protons in the ^{1}H NMR spectra and for the saturated C-3 in the ^{13}C NMR spectra is characteristic of these tautomeric compounds.

The keto-forms on the other hand, **13a**,**b** and **14a**,**b**, showed a doublet for the 4-H proton at $\delta = 3.8$–3.9 ppm, coupled with the phosphorus atom with $^2J_{HCP} = 23$–24 Hz and a peak for 3-H proton at $\delta = 4.5$–5.2 ppm coupled with the phosphorus atom with $^3J_{HP} = 10.4$–14.5 Hz and with 4-H with a very small $^3J = 0.8$–1 Hz. The very small ^3J value between 4-H and 3-H suggests a dihedral angle of H–C4–C3–H of about 90°, which, as also revealed by inspection of stereomodels, indicates a *trans* disposition of the two protons. In their ^{13}C NMR spectra the most characteristic peaks are those of C-3 at $\delta = 47$–49 ppm and of C-4 at $\delta \sim 39$ ppm, coupled with the phosphorus atom with $^2J_{CP}$ of 2.3–3.5 Hz and $^1J_{CP} \approx 144$ Hz, respectively. The carbonyl carbon of the 3-benzoyl group in **13a**,**b** appeared at $\delta = 192$ ppm and that of the ethoxy-carbonyl group in **14a**,**b** at $\delta \approx 166$ ppm. In both cases these carbons were strongly coupled with phosphorous atom with a $^3J_{CP}$ value of ~17–22 Hz.

It is noted that a mixture of the two tautomers from the reaction of **7** with dialkylphosphites **8**/**9a**,**b**, i.e. **8**⇆**9**, has been also reported.[22] However, the NMR spectral data provided to support this suggestion are not as complete as they should be to support the proposed appearance of the two tautomers.

3. Conclusions

From the experimental data given above together with the results reported earlier,[1] it is concluded that the 3-bromoacetyl coumarin shows a special behavior in the reaction with phosphites:

1. It reacts with triphenylphosphite giving the 2-oxophosphonate **3** (R = Ph).
2. With trialkylphosphites compound **1** may react in two directions:
   i. To the formation of the enolphosphates **2** (maybe by the initial 1,2 addition of the trialkylphosphites to the conjugated system of the 3-bromoacethylcoumarin) and
   ii. To the formation mainly (about 90%) of the corresponding 3-(ω-bromoacetyl)-4-dialkyphosphono-2-oxochromans **5**/**6** by the 1,4-addition of the trialkylphosphites to the bromoacetylcoumarin **1**. This direction was realized only when the reaction was carried out in the presence of TsOH.

The use of TsOH in the reaction of 3-acyl-coumarines with trialkylphosphites leads mainly to 1,4-addition products, giving, in good yields and shorter reaction times, the corresponding 3-acyl-4-dialkylphosphono-2-oxochromans.

4. Experimental

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded with a Specord IR 71 or IR 75 spectrophotometers. ^{1}H NMR and ^{13}C NMR spectra, reported in δ units, were obtained with a Bruker WM 250 (at 250 and 62.9 MHz, respectively) or a Bruker AM 300 (at 300 and 75.4 MHz, respectively) instruments. All NMR spectra were obtained by using TMS as internal standard in $CDCl_3$. E.I. mass spectra were obtained at 70 eV a VG TS-250 spectrometer. Elemental analyses of C, H, P and N were carried out in the Laboratory of Elemental Analysis at the Department of Organic Chemistry, University of Sofia.

Column chromatography was carried out on silica gel (Merck or Fluka 0.063–0.2 mm) using as eluent

n-hexane/EtOAc mixtures with increasing polarity. Sonications were effected with Bransonic 321 (390 W, 50 kHz).

4.1. Preparation of the starting materials

The starting 3-substituted 2-oxo-2*H*-1-benzopyrans were prepared according to the literature procedures[1,18,24–26] and their spectroscopic characteristics (IR, ^{1}H NMR and MS) were in agreement with their structures. Trialkyl phosphites and dialkyl phosphites are commercially available (Fluka).

4.2. Interaction of 3-bromoacetylcoumarin 1 with trialkylphosphites. General procedure

Depending of the reaction conditions (ratio of the reagents, temperature, etc.) the following methods are distinguished:

Method A. A solution of 3-bromoacetylcoumarin **1** (0.27 g, 1 mmol), the corresponding phosphite (2 mmol) and *p*-toluenesulfonic acid (0.19 g, 1 mmol) was refluxed in dry toluene (3 mL) until the starting coumarin was consumed (TLC-monitoring). The solvent was removed under reduced pressure. To the residue methylene chloride (20 mL) was added, washed with water (40 mL), with 10% solution of potassium carbonate (20 mL), again with water (30 mL) and dried (Na_2SO_4). The precipitate obtained after the removal of the solvent was filtered and washed with ethyl acetate (10 mL).

Method A$_1$. The same as in Method A but the amount of the corresponding phosphite was 5 mmol.

Method B. A solution of 3-bromoacetylcoumarin **1** (0.27 g, 1 mmol), the corresponding phosphite (5 mmol) and *p*-toluenesulfonic acid (catalytic amount) in methylene chloride (3 mL) was irradiated with ultrasound at room temperature until the starting coumarin was consumed (TLC-monitoring). The reaction mixture was poured out into ice water (40 mL) and extracted with methylene chloride (3×30 mL). The organic layer was washed with water (30 mL) and dried (Na_2SO_4). After evaporation of the solvent the obtained crystals were isolated from ethyl acetate (5 mL). The filtrate was chromatographed on a silica gel column with *n*-hexane–ethyl acetate (with increasing polarity) as eluent.

Methods C and C$_1$. The same as in Method B, but the amount of the *p*-toluenesulfonic acid was 1 and 2 mmol, respectively.

4.2.1. Dimethyl 3-(2-bromo-1-hydroxyaethylidene)-2-oxochroman-4-ylphosphonate (5a). From **1** and trimethyl phosphite. Method B: 0.32 g, 86%, white crystals, mp= 151–153 °C (ethyl acetate); [Found: C, 41.21; H, 3.43. $C_{13}H_{14}O_6PBr$ requires C, 41.40; H, 3.74%]; IR (nujol): ν= 1720, 1630, 1590, 1190, 1080, 1055 cm^{-1}. ^{1}H NMR (300 MHz): δ=13.15 (s; OH, 1H), 7.31–7.38 (m; 5-, 7-H, 2H), 7.21 (m as t, J=7.5 Hz; 6-H, 1H), 7.11 (d, J=8.3 Hz; 8-H, 1H), 4.50 (ddd as dt, $^2J_{HH}$=11.2 Hz, $^4J_{H,OH}\sim$1.5 Hz, $^5J_{HP}\sim$1.3 Hz; CH_AHBr, 1H), 4.30 (d, J=21.9 Hz; 4-H, 1H), 3.99 (dd, $^2J_{HH}$=11.2 Hz, $^5J_{HP}$=1.0 Hz; CHH_BBr, 1H), 3.68 (d, $^3J_{HP}$=10.4 Hz; $POCH_3$, 3H), 3.66 (d, $^3J_{HP}$= 10.2 Hz; $POCH_3$, 3H). ^{13}C NMR (75.4 MHz): δ=173.8 (d, $^3J_{CP}$=6.8 Hz; =COH), 168.8 (d, $^3J_{CP}$=1.7 Hz; C-2), 150.9 (d, $^3J_{CP}$=5.6 Hz; C-8a), 129.6 (d, $^3J_{CP}$=2.9 Hz; C-5), 129.6 (d, $^5J_{CP}$=1.8 Hz; C-7), 125.1 (d, $^4J_{CP}$=3.4 Hz; C-6), 117.2 (d, $^4J_{CP}$=3.6 Hz; C-8), 116.5 (d, $^2J_{CP}$=8.5 Hz; C-4a), 91.0 (d, $^2J_{CP}$=9.9 Hz; C-3), 54.1 (d, $^2J_{COP}$= 7.7 Hz; $POCH_3$) 54.0 (d, $^2J_{COP}$=7.3 Hz; $POCH_3$), 37.3 (d, $^1J_{CP}$=142.7 Hz; C-4), 25.5 (CH_2Br).

4.2.2. Diethyl 3-(2-bromo-1-hydroxyaethylidene)-2-oxochroman-4-ylphosphonate (5b). From **1** and triethyl phosphite. Method B: 0.38 g, 94%, white crystals, mp= 147–149 °C (ethyl acetate); [Found: C, 44.61; H, 4.40. $C_{15}H_{18}O_6PBr$ requires C, 44.47; H, 4.48%]; IR (nujol): ν= 1730, 1635, 1500, 1190, 1090, 1050, 1020 cm^{-1}. ^{1}H NMR (300 MHz): δ=13.17 (s; OH, 1H), 7.32–7.40 (m; 5-, 7-H, 2H), 7.21 (m as t, J=7.5 Hz; 6-H, 1H), 7.12 (d, J=8.0 Hz; 8-H, 1H), 4.55 (ddd as dt, $^2J_{HH}$=11.1 Hz, $^4J_{H,OH}$=1.7 Hz, $^5J_{HP}$=1.2 Hz; CH_AHBr, 1H), 4.28 (d, $^2J_{HP}$=21.8 Hz; 4-H, 1H), 3.93–4.12 (m; CHH_BBr, $POCH_2$, 5H), 1.26 (t, J= 7.0 Hz; CH_3), 1.24 (t, J=7.0 Hz; CH_3). ^{13}C NMR (75.4 MHz): δ=173.6 (d, $^3J_{CP}$=7.1 Hz; =COH), 168.9 (d, $^3J_{CP}\sim$1.0 Hz; C-2), 150.2 (d, $^3J_{CP}$=5.4 Hz; C-8a), 129.7 (d, $^3J_{CP}$=4.4 Hz; C-5), 129.5 (d, $^5J_{CP}$=3.7 Hz; C-7), 125.0 (d, $^4J_{CP}$=3.5 Hz; C-6), 117.1 (d, $^4J_{CP}$=3.6 Hz; C-8), 116.8 (d, $^2J_{CP}$=8.7 Hz; C-4a), 91.2 (d, $^2J_{CP}$=9.9 Hz; C-3), 63.6 (d, $^3J_{CP}$=7.0 Hz; $POCH_2$), 63.5 (d, $^3J_{CP}$=7.4 Hz; $POCH_2$), 37.7 (d, $^1J_{CP}$=142.6 Hz; C-4), 25.6 (CH_2Br), 16.4 (d, $^3J_{CP}$=4.8 Hz; CH_3), 16.3 (d, $^3J_{CP}$=4.8 Hz; CH_3). MS *m*/*z* (%): 406/404 (M^+) (4), 325 (61), 283 (60), 268/266 (72), 188 (73), 173 (84), 146 (33), 118 (69), 77 (38), 29 (100).

4.3. Interaction of enolphosphate 2a and 3-acetylcoumarin 7 with trialkyl phosphites. General procedure

Depending of the reaction conditions the following methods are distinguished:

Method A$_2$. The ratio of the reagents **2a**:phosphites:TsOH 1:2:2.5 in refluxing toluene (3 mL). The reaction carried out and worked up as mentioned above for Method A.

Method A$_3$. To the refluxing solution of the starting coumarin (0.27 g, 1 mmol) in dry toluene (3 mL) was added 4-toluenesulphonic acid (0.38 g, 2 mmol). After 5 min to the reaction mixture the corresponding trialkyl phosphite (2 mmol) was added and refluxed until the starting coumarin was consumed (TLC-monitoring) for about 15 min. The solvent was removed under reduced pressure and the residue was chromatographed on a silica gel column with *n*-hexane–ethyl acetate (with increasing polarity) as an eluent.

Method D. A solution of the starting coumarin (0.27 g, 1 mmol) and the corresponding phosphite (5 mmol) in alcohol (methanol, resp. ethanol (2 mL)) and methylene chloride (1 mL) was irradiated with ultrasound at room temperature until the starting coumarin was consumed (TLC-monitoring). The solvent was distilled under reduced pressure. To the residue was added a small quantity of corresponding alcohol (1 mL) and water (drop wise) for crystallization at low temperature. The obtained crystals were filtrated.

Method E. A solution of the coumarin (0.27 g, 1 mmol) and the corresponding phosphite (5 mmol) in glacial acetic acid (2 mL) was irradiated with ultrasound at low temperature (ice-water-bath) until the starting coumarin was consumed (TLC-monitoring). The reaction mixture was decomposed on ice-water (50 mL). The obtained crystals were filtrated and washed with water to neutral pH.

4.3.1. Dimethyl 3-(1-hydroxyaethylidene)-2-oxochroman-4-ylphosphonate (8a). From **2a** or **7** and trimethyl phosphite. Method C: 0.28 g, 95%, white crystals, mp = 127–129 °C (ethyl acetate), (lit.[21,22] 129–130 °C).

4.3.2. Diethyl 3-(1-hydroxyaethylidene)-2-oxochroman-4-ylphosphonate (8b). From **2a** or **7** and triethyl phosphite. Method C: 0.31 g, 95%, white crystals, mp = 145–148 °C (ethyl acetate), (lit.[21,22] 147–148 °C).

4.3.3. Dimethyl 3-benzoyl-2-oxochroman-4-ylphosphonate (12/13a). From 3-benzoylcoumarin **10** and trimethyl phosphite. Method D: 0.34 g, 94%, white crystals, mp = 120–134 °C (methanol), (mixture of the two tautomers **12a** ⇆ **13a**, with a 9:1 ratio (^{1}H NMR), which on staying the sample in the NMR tube for about 1 week ($CDCl_3$) changed to ~1:1); [Found: C, 60.07; H, 4.90. $C_{18}H_{17}O_6P$ requires C, 60.00; H, 4.76%]; IR (CH_3Cl): ν = 1780, 1700, 1625, 1060, 1030 cm^{-1}. ^{1}H NMR (300 MHz), enol-form (**12a**): δ = 13.29 (s; OH, 1H), 7.58–7.65 (m; 2′-, 6′-H, 2H), 7.46–7.54 (m; 3′-, 5′-, 4′-H, 3H), 7.26–7.37 (m; 5-H, 7-H, 2H), 7.12–7.19 (m; 6-H, 8-H, 2H), 4.45 (d, $^2J_{HP}$ = 23.9 Hz; 4-H, 1H), 3.49 (d, $^3J_{HP}$ = 10.6 Hz; OCH_3, 3H), 3.41 (d, $^3J_{HP}$ = 10.6 Hz; OCH_3, 3H). Keto-form (**13a**): 7.96–7.99 (m, 2′-, 6′-H, 2H), 7.65 (dddd as tt, J = 7.4, 1.4 Hz; 4′-H, 1H), 7.48–7.55 (m; 3′-H, 5′-H, 2H), 7.34 (dddd as tt, J = 7.7, ~2.0 Hz; 7-H, 1H), 7.22 (ddd as dt, J = 8.2, ~2.1 Hz; 5-H, 1H), 7.11–7.17 (m; 6-, 8-H, 2H), 5.19 (dd, $^3J_{HP}$ = 13.7 Hz, $^3J_{HH}$ = 0.8 Hz; 3-H, 1H), 3.80 (bd, $^2J_{HP}$ = 23.4 Hz; 4-H, 1H), 3.81 (d, $^3J_{HP}$ = 10.8 Hz; OCH_3, 3H), 3.68 (d, $^3J_{HP}$ = 10.8 Hz; OCH_3, 3H). ^{13}C NMR (75.4 MHz), enol-form (**12a**): δ = 175.5 (d, $^3J_{CP}$ = 6.7 Hz; =COH), 169.1 (d, $^3J_{CP}$ ~ 1 Hz; C-2), 150.9 (d, $^3J_{CP}$ = 5.5 Hz; C-8a), 133.6 (d, $^4J_{CP}$ = 2.2 Hz; C-1′), 130.9 (C-4′), 129.9 (d, $^3J_{CP}$ = 4.5 Hz; C-5), 129.3 (d, $^5J_{CP}$ < 5 Hz; C-7), 128.8 (C-3′,-5′), 128.2 (C-2′, -6′), 125.0 (d, $^4J_{CP}$ = 3.3 Hz; C-6), 117.7 (d, $^2J_{CP}$ = 7.5 Hz; C-4a), 117.1 (d, $^4J_{CP}$ = 3.9 Hz; C-8), 89.7 (d, $^2J_{CP}$ = 9.9 Hz; C-3), 53.6 (d, $^2J_{COP}$ = 7.6 Hz; $POCH_3$), 53.3 (d, $^2J_{COP}$ = 7.4 Hz; $POCH_3$), 37.6 (d, $^1J_{CP}$ = 140.8 Hz; C-4). Keto-form (**13a**): 191.7 (d, $^3J_{CP}$ = 17.5 Hz; CO), 163.2 (d, $^3J_{CP}$ ~ 0.5 Hz; C-2), 151.2 (d, $^3J_{CP}$ = 6.5 Hz; C-8a), 134.5 (C-4′), 133.2 (C-1′), 129.4 (d, $^3J_{CP}$ = 2.9 Hz, C-5), 129.2 (C-2′,-6′), 129.2 (d, $^5J_{CP}$ < 5.2 Hz; C-7), 129.2 (C-3′,-5′), 125.0 (d, $^4J_{CP}$ = 3.3 Hz; C-6), 117.3 (d, $^4J_{CP}$ = 3.6 Hz; C-8), 114.5 (d, $^2J_{CP}$ = 7.8 Hz; C4a), 54.1 (d, $^2J_{COP}$ = 6.7 Hz; $POCH_3$), 53.8 (d, $^2J_{COP}$ = 7.6 Hz; $POCH_3$), 49.1 (d, $^2J_{CCP}$ = 3.4 Hz; C-3), 38.5 (d, $^1J_{CP}$ = 143.9 Hz; C-4). MS *m/z* (%): 361 (MH^+) (51), 360 (M^+) (20), 328 (18), 254 (48), 174 (81), 146 (52), 118 (49), 111 (79), 105 (50), 76 (100).

4.3.4. Diethyl 3-benzoyl-2-oxochroman-4-ylphosphonate (13b). From 3-benzoylcoumarin **10** and triethyl phosphite. Method D: 0.27 g, 69%, white solid, mp = 106–108 °C (ethanol); [Found: C, 61.77; H, 5.65. $C_{20}H_{21}O_6P$ requires C, 61.86; H, 5.45%]; IR (CH_3Cl): ν = 1780, 1700, 1620, 1500, 1170, 1055, 1030 cm^{-1}. ^{1}H NMR (300 MHz): δ = 7.98 (m; 2′, 6′-H, 2H), 7.64 (dddd as tt, J = 7.4, 1.3 Hz; 4′-H, 1H), 7.50 (dddd as tt, J = 7.4, 1.5 Hz; 3′, 5′-H, 2H), 7.32 (dddd as tt, J = 7.7, 2.0 Hz; 7-H, 1H), 7.21 (ddd as dt, J = 8.0, 2.0 Hz; 5-H, 1H), 7.08–7.14 (m, 6-, 8-H, 2H), 5.20 (dd, J = 14.0, 0.9 Hz; 3-H, 1H), 4.11–4.23 (m; $POCH_2$), 3.88 (dq, J = 8.2, 7.1 Hz; $POCH_2$), 3.73 (bd, $^2J_{HCP}$ = 23.3 Hz; 4-H, 1H), 1.36 (t, J = 7.1 Hz; CH_3, 3H), 1.24 (t, J = 7.0 Hz; CH_3, 3H). ^{13}C NMR (75.4 MHz): δ = 192.0 (d, $^3J_{CP}$ = 17.1 Hz; CO), 163.3 (d, $^3J_{CP}$ = 2.2 Hz; C-2), 151.3 (d, $^3J_{CP}$ = 5.7 Hz; C-8a), 134.4 (C-4′), 133.2 (C-1′), 130.0 (d, $^3J_{CP}$ = 4.4 Hz; C-5), 129.7 (d, $^5J_{CP}$ = 4.2 Hz; C-7), 129.2 (C-2′,-6′), 129.1 (C-3′, -5′), 124.8 (d, $^4J_{CP}$ = 3.2 Hz; C-6), 117.2 (d, $^4J_{CP}$ = 3.2 Hz; C-8), 114.7 (d, $^2J_{CP}$ = 7.7 Hz; C-4a), 63.8 (d, $^2J_{COP}$ = 7.5 Hz; $POCH_2$), 63.4 (d, $^2J_{COP}$ = 7.2 Hz; $POCH_2$), 49.2 (d, $^2J_{CP}$ = 3.5 Hz; C-3), 38.9 (d, $^1J_{CP}$ = 143.5 Hz; C-4), 16.3 (d, $^3J_{CP}$ = 6.2 Hz; CH_3), 16.2 (d, $^3J_{CP}$ = 5.5 Hz; CH_3). MS *m/z* (5): 389 (MH^+) (57), 388 (M^+) (21), 282 (74), 250 (58), 228 (92), 173 (41), 146 (52), 118 (43) 105 (100), 78 (92), 77 (79).

4.3.5. Ethyl 4-(dimethoxyphosphoryl)-2-oxo-3-chromanecarboxylate (14a). From ethyl 2-oxo-2*H*-1-benzopyran-3-carboxylate **11** and trimethyl phosphite. Method C: 0.19 g, 58%, colorless needles, mp = 94–95 °C (methanol); [Found: C, 50.84; H, 5.00. $C_{14}H_{17}O_7P$ requires C, 51.23; H, 5.22%]; IR (CH_3Cl): ν = 1795, 1755, 1620, 1160, 1030, 1045 cm^{-1}. ^{1}H NMR (300 MHz): δ = 7.30–7.37 (m; 5-, 7-H, 2H), 7.17 (ddd as dt, J = 7.5, 1.0 Hz; 6-H, 1H), 7.10 (d, J = 8.5 Hz; 8-H, 1H), 4.15 (dd, $^3J_{HH}$ = 1.3 Hz, $^3J_{HP}$ = 11.1 Hz; 3-H, 1H), 4.12 (dq, ^3J = 7.1 Hz, $^6J_{HP}$ = 2.6 Hz; OCH_2, 2H), 3.95 (bd, $^2J_{HP}$ = 22.6 Hz; 4-H, 1H), 3.75 (d, $^3J_{HP}$ = 10.8 Hz; $POCH_3$, 3H), 3.75 (d, $^3J_{HP}$ = 10.8 Hz; $POCH_3$, 3H), 1.11 (t, J = 7.1 Hz; CH_3, 3H). ^{13}C NMR (75.4 MHz): δ = 166.0 (d, $^3J_{CP}$ = 22.7 Hz; C=O), 162.2 (d, $^3J_{CP}$ = 2.2 Hz; C-2), 151.2 (d, $^3J_{CP}$ = 5.3 Hz; C-8a), 130.1 (d, $^3J_{CP}$ = 5.2 Hz; C-5), 129.9 (d, $^5J_{CP}$ = 3.4 Hz; C-7), 125.1 (d, $^4J_{CP}$ = 3.2 Hz; C-6), 117.3 (d, $^4J_{CP}$ = 3.2 Hz; C-8), 115.4 (d, $^2J_{CCP}$ = 7.5 Hz; C-4a), 63.0 (OCH_2), 53.9 (d, $^2JC_{COP}$ = 7.4 Hz; $POCH_3$), 53.7 (d, $^2J_{COP}$ = 7.4 Hz; $POCH_3$), 46.9 (d, $^2J_{CP}$ = 2.3 Hz; C-3), 38.7 (d, $^1J_{CP}$ = 144.5 Hz; C-4), 13.8 (CH_3). MS *m/z* (%): 328 (M^+) (22), 282 (7), 255 (100), 219 (24), 173 (87), 146 (11), 118 (13), 79 (6).

4.3.6. Ethyl 4-(diethoxyphosphoryl)-2-oxo-3-chromanecarboxylate (14b). From ethyl 2-oxo-2*H*-1-benzopyran-3-carboxylate **11** and triethyl phosphite. Method C: 0.32 g, 88%, light-yellow oil; [Found: C, 53.59; H, 5.96. $C_{16}H_{21}O_7P$ requires C, 53.93; H, 5.94%]; IR (CH_3Cl): ν = 1790, 1750, 1625, 1600, 1170, 1060sh, 1030 cm^{-1}. ^{1}H NMR (250 MHz) δ = 7.29–7.36 (m; 5-, 7-H, 2H), 7.16 (dd as t, J = 7.2 Hz; 6-H, 1H), 7.09 (d, J = 8.2 Hz; 8-H, 1H), 4.15 (d, J = 14.4 Hz; 3-H, 1H), 3.92–4.61 (m; CH_2O, 6H), 3.90 (d, $^2J_{HP}$ = 24.2 Hz; 4-H, 1H), 1.32 (t, J = 7.0 Hz; CH_3, 3H), 1.21 (t, J = 7.0 Hz; CH_3, 3H), 1.11 (t, J = 7.1 Hz; CH_3, 3H). ^{13}C NMR (62.59 MHz) δ = 166.1 (d, $^3J_{CP}$ = 21.5 Hz; CO), 162.3 (d, $^3J_{CP}$ = 2.0 Hz; C-2), 151.2 (d, $^3J_{CP}$ = 4.7 Hz; C-8a), 130.0 (d; $^3J_{CP}$ = 4.8 Hz; C-5), 129.7 (d, $^5J_{CP}$ = 3.7 Hz; C-7), 124.9 (d, $^4J_{CP}$ = 3.2 Hz; C-6), 117.1 (d, $^4J_{CP}$ = 3.2 Hz; C-8), 115.6 (d, $^2J_{CP}$ = 7.2 Hz; C-4a), 63.5 (d, $^2J_{COP}$ = 7.1 Hz; $POCH_2$), 63.2 (d, $^2J_{COP}$ = 7.1 Hz; $POCH_2$), 62.8 ($COOCH_2$), 46.9 (d, $^2J_{CP}$ = 2.7 Hz; C-3), 39.5 (d, $^1J_{CP}$ = 144.2 Hz; C-4), 16.2 (d, $^3J_{CP}$ = 5.7 Hz;

CH_3CH_2OP), 16.0 (d, $^3J_{CP}=5.6$ Hz; CH_3CH_2OP), 13.7 (CH_3). MS *m/z* (%): 356 (M^+ 1(1), 284 (11), 218 (6), 211 (8), 183 (18), 173 (18), 146 (25), 118 (16), 77 (9), 28 (100).

4.4. Interaction of 3-bromoacetylcoumarin 1 with dialkyl phosphites

A solution of 3-bromoacetylcoumarin **1** (0.27 g, 1 mmol) and the corresponding dialkyl phosphite (5 mmol) was refluxed in dry toluene (3 mL) for 4 h. The complicated reaction mixtures were worked up as usually (Method A) and after the column chromatography were isolated the compounds **2**, **7** and **8**—for the yields see Table 2.

Transformation of the enolphosphate **2a** into **7**. A solution of enolphosphate **2a** (0.29 g, 1 mmol) and 4-toluenesulfonic acid (0.95 g, 5 mmol) in dry toluene (3 mL) was refluxed until the starting compound was consumed (TLC-monitoring). The reaction mixture was worked up as above and the 3-acetyl coumarin **7** (0.17 g, 90%) was isolated from ethanol.

Transformation of the enolphosphate **2a** into **1**. To the refluxing solution of the starting coumarin **2a** (0.29 g, 1 mmol) in dry toluene (3 mL) 4-toluenesulfonic acid (0.19 g, 1 mmol) was added. After 5 min to the reaction mixture *N*-bromosuccinimide (0.18 g, 1 mmol) was added and refluxed until the starting coumarin was consumed (TLC-monitoring) for about 30 min. The solvent was removed under reduced pressure and the reaction mixture was worked up as pointed above and from ethyl acetate were isolated bromoacetylcoumarin **1** in quantitative yield.

Transformation of the enolphosphate **2a** into **5a**. To the refluxing solution of the starting coumarin **2a** (0.29 g, 1 mmol) in dry toluene (3 mL) 4-toluenesulfonic acid (0.19 g, 1 mmol) was added. After 5 min to the reaction mixture was added *N*-bromosuccinimide (0.18 g, 1 mmol) and after further 45 min the trimethylphosphite (0.25 g, 2 mmol) was added. The reaction mixture was refluxed until the starting coumarin was consumed (TLC-monitoring) for about 2 h. Standard workup and purification by column chromatography gave enolphosphate **2a** (0.09 g, 33%) and the product of 1,4-addition **5a** (0.17 g, 46%).

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