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Organic Chemistry

Arkivoc **2018**, part iii, 120-133

An efficient synthesis of 3-diethoxyphosphoryl-4-(1*H*-indol-3-yl)-3,4-dihydrocoumarins: a convenient approach to 3-methylene-4-(indol-3-yl)-3,4-dihydrocoumarins

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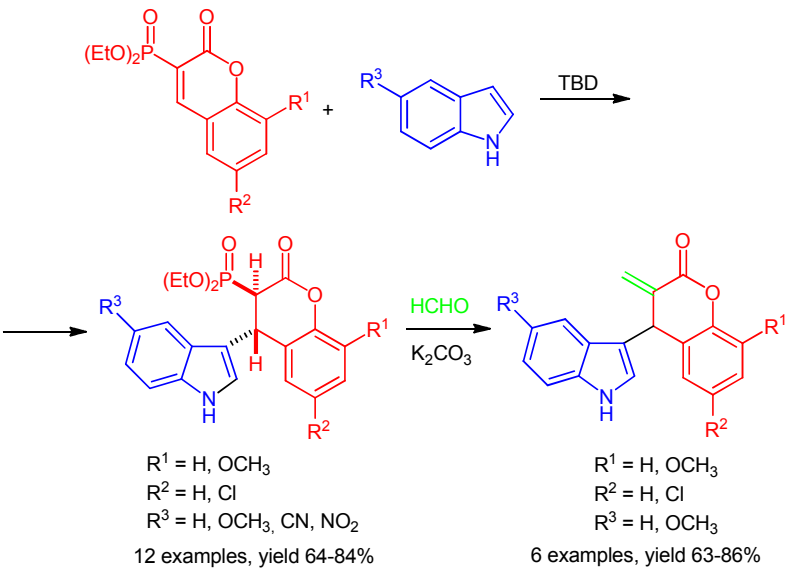
Received 12-01-2017 **Accepted** 12-29-2017 **Published on line** 01-28-2018

Abstract

TBD promoted conjugate addition of indoles to 3-diethoxyphosphorylcoumarins allows the synthesis 3-diethoxyphosphoryl-4-(indol-3-yl)-3,4-dihydrocoumarins. The adducts derived from unsubstituted or C-5 methoxy substituted indole could be converted into the corresponding 3-methylene-(indol-3-yl)-3,4-dihydrocoumarins by means of the HWE reaction with formaldehyde.



Keywords: Michael addition, HWE olefination, indoles, coumarins, 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD)

DOI: https://doi.org/10.24820/ark.5550190.p010.417

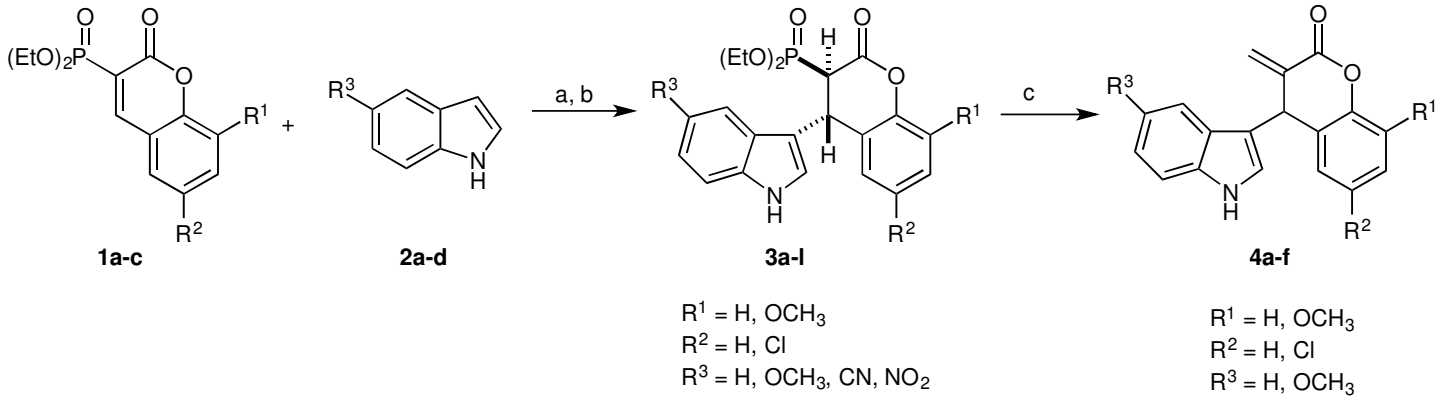
Introduction

Both indole and coumarin have been identified as privileged scaffolds in numerous biologically active molecules and natural products.[1-3] Therefore, the development of synthetic methodologies enabling the synthesis of compounds containing both of these heterocyclic structures is highly desirable. A promising strategy to address this task is conjugate Michael-type addition of indoles to coumarins. Among several reactions of indole, the reactions involving C-3 functionalization of indole with electron-deficient olefins have attracted and continue to attract interest from the synthetic community. While the reaction of indoles with highly electrophilic nitroolefins and enones to furnish β-(indol-3-yl) alkylated products has been widely investigated,[4-22] analogous reactions involving α,β-unsaturated esters to form 3-(indol-3-yl) alkanoates are rare. To date, two general strategies for the non-enantioselective synthesis of 3-(indol-3-yl) alkanoates have been reported. Ethyl 3-(indol-3-yl) alkanoates were obtained by one-pot, three-component Knoevenagel-Michael reaction of indoles, Meldrum's acid and various aldehydes followed by decarboxylative ethanolysis of the adducts obtained.[23-26] The other strategy is based on the conjugate addition of indoles to alkylidene-malonates.[6] Recently, urea palladecycles[27] and $Sc(OTf)_3$/sodium dodecyl sulfate[28] have been demonstrated to be efficient Lewis acid catalysts for Friedel–Crafts alkylation of indoles with alkylidene malonates. Meanwhile, the catalytic asymmetric reactions of indoles with alkylidenemalonates have been reported.[29-35] In sharp contrast, the conjugate addition of indoles to another class of doubly activated olefins, 3-EWG-coumarins, has rarely been reported. In fact, only two papers have been published, each containing a single entry, on the Lewis acid-catalysed conjugate addition of indoles to 3-ethoxycarbonylcoumarin.[27,28] Moreover, in 2006 Tang et al. reported $Mg(OTf)_2$-catalysed multicomponent tandem Michael additions of indoles with 3-nitrocoumarins and methyl vinyl ketone leading to facile synthesis 3,3-disubstituted-4-(indol-3-yl)-3,4-dihydro-coumarins.[36] Two efficient protocols for the synthesis of 3-unsubstituted-4-(indol-3-yl)-3,4-dihydrocoumarins have been reported. One of the methods utilises a one-pot three-component reaction of indoles, Meldrum's acid and salicylaldehyde.[37] The other relies on cascade Michael addition/decarboxylation reactions of coumarin-3-carboxylic acids with indoles.[38]

Results and Discussion

We have recently discovered that conjugate addition of enolizable ketones to 3-(diethoxyphosphoryl)coumarins is mediated by organic superbase 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD).[39,40] We envisioned that the use of the same approach would allow Michael addition of indole to 3-(diethoxyphosphoryl)coumarins. Herein, this challenge has been addressed and we present the efficient synthesis of 3-diethoxyphosphoryl-4-(indol-3-yl)-3,4-dihydrocoumarins by an unprecedented TBD-mediated reaction of indoles with 3-(diethoxyphosphoryl)coumarins. We also demonstrate that in some cases the resulting adducts can be transformed into corresponding α-methylene-δ-lactones. Our initial attempts were focused on the synthesis of compound **3a**. Preliminary experiments showed that TBD used in some excess is able to promote the smooth conjugate addition of indole **2a** to coumarin **1a**. The reaction of coumarin **1a** with 1.5 equivalents of indole **2a** in the presence of two equivalents of TBD in CH_2Cl_2 at room temperature for 24 hours gave the best results in terms of yield and purity of the product **3a**. After acidic quench, the crude product **3a** was isolated as a mixture of two diastereoisomers in a ratio 1.0 : 0.1 (as indicated by ^{31}P-NMR analysis) accompanied by unreacted coumarin (ca. 10%). Notably the crystalline product **3a** was isolated as a sole *trans*-adduct after column chromatography in 84% yield. This indicates that diastereoisomeric products

undergo rapid epimerization due to the presence of the acidic hydrogen at C-3. The protocol was successfully extended to a variety of coumarins and indoles (Scheme 1).



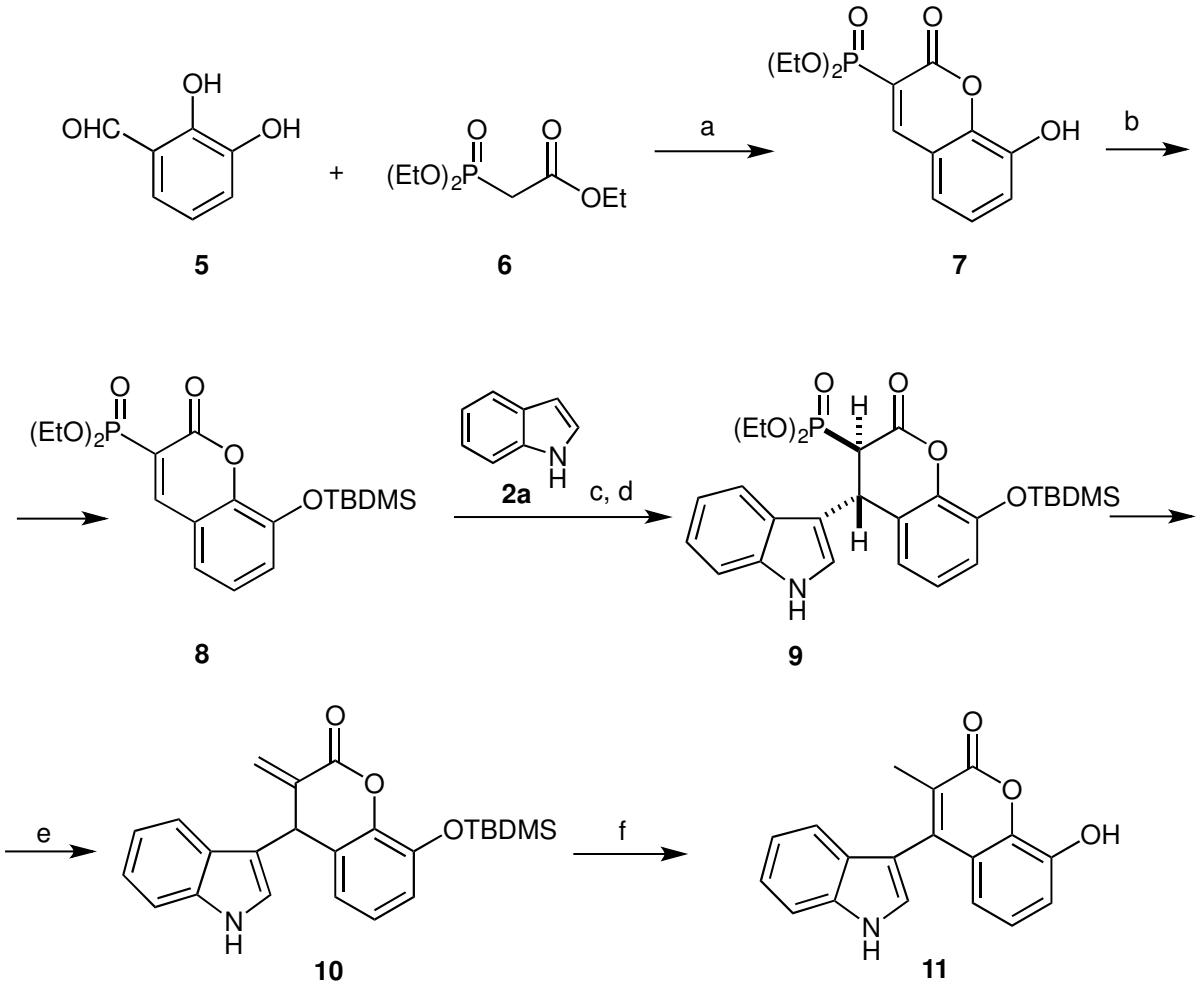
Scheme 1. *Reagents and conditions:* (a) TBD (2.0 equiv), CH_2Cl_2, r.t., 24 h; (b) 2M hydrochloric acid (excess), r.t.; (c) K_2CO_3 (3.0 equiv), THF, 0 °C, 15 min. then CH_2O (40% aq), r.t., 3 h.

As summarized in Table 1 all reactions proceeded smoothly to give corresponding dihydrocoumarins **3a-l** in high yields. Substituted coumarins **1b-c** and indoles **2b-d** participated in this process with high efficiency regardless of the presence of electron-withdrawing or electron-donating substituent on the aromatic ring. The crude products were formed as mixtures of *trans*- and *cis*-dihydrocoumarins. These mixtures were subjected to column chromatography to yield *trans*-adducts exclusively. The relative *trans* stereochemistry at the stereogenic centers C-3 and C-4 of 3-diethoxyphosphoryl-4-(indol-3-yl)-3,4-dihydrocoumarin **3a-l** was assigned on the basis of ^{13}C-NMR data. The observed values of the coupling constants $^3J_{PC(3)}$ = 17.6 - 18.6 Hz clearly proved the *trans* arrangement of the phosphoryl and indolyl group.[41,42] It is also worth noting that the formation of the corresponding N-adducts was not observed under these reaction conditions.

Table 1. Yields of the compounds produced via Scheme 1

Entry	R^1	R^2	R^3	Yield (%)	
				3	**4**
a	H	H	H	84	64
b	OCH_3	H	H	64	68
c	H	Cl	H	67	63
d	H	H	OCH_3	77	86
e	OCH_3	H	OCH_3	74	70
f	H	Cl	OCH_3	83	71
g	H	H	NO_2	78	-
h	OCH_3	H	NO_2	69	-
i	H	Cl	NO_2	73	-
j	H	H	CN	81	-
k	OCH_3	H	CN	76	-
l	H	Cl	CN	80	-

An examination of the HWE reaction of formaldehyde with phosphonolactones **3a-l** revealed that the outcome of the reaction is determined by the electronic nature of the substituent present in the homoaromatic indole ring. The Horner-Wadsworth-Emmons (HWE) reaction of unsubstituted **3a-c** and methoxy-substituted phosphonolactones **3d-f** with formaldehyde in the presence of aqueous K_2CO_3 afforded the corresponding 3-methylene-4-(indol-3-yl)-3,4-dihydrocoumarins **4a-c** and **4d-f**, respectively. On the other hand substrates **3g-l** and **3j-l** bearing an electron-withdrawing group at C-5 of the homoaromatic indole ring failed to give the desired methylenelactones **4g-l** and only the products of the retro-Michael reaction were observed.



Scheme 2. *Reagents and conditions:* (a) CH_3COOH/piperidine (cat.), toluene, reflux, 15 h.; (b) TBDMSCl (1.1 equiv), imidazole (2.0 equiv), CH_2Cl_2, r.t., 24 h.; (c) TBD (2.0 equiv), CH_2Cl_2, r.t., 24 h; (d) 2M hydrochloric acid (excess), r.t.; (e) K_2CO_3 (3.0 equiv), THF, 0 °C, 15 min. then CH_2O (40% aq), r.t., 3 h.; (f) TBAF (1.1 equiv),THF, r.t., 3 h.

Next, we extended the protocol of the Michael addition for 3-diethoxyphosphorylcoumarin **7** bearing an hydroxyl group in the aromatic ring (Scheme 2). Previously unknown 8-hydroxy-3-diethoxyphosphoryl-coumarin **7** was readily prepared by Knoevenagel condensation of 2,3-dihydroxybenzaldehyde **5** with triethyl phosphonacetate **6** according to a classical procedure.[43] We initially wanted to add indole to the unprotected coumarin **7**, however attempted addition failed to give desired product. At that point the phenolic hydroxyl group in coumarin **7** was protected by silylation with *t*-BuMe_2SiCl. The silyl ether **8,** stable both in basic and

acidic conditions, was transformed cleanly into the desired protected *trans* 4-(indol-3-yl)-3,4-dihydrocoumarin **9** in 53% yield. Finally, the HWE reaction of formaldehyde with **9** gave the corresponding protected 3-methylene-4-(indol-3-yl)-3,4-dihydrocoumarin **10**. Surprisingly, removal of the t-butyldimethylsilyl group by treatment with tetrabutylammonium fluoride in THF solution was accompanied by spontaneous *exo-endo* isomerization of the carbon-carbon double bond leading to 3-methyl-4-(indol-3-yl)coumarin **11**. Recently, palladium-catalyzed coupling reactions of 4-cumarinyl triflates with indoles leading to the similar 4-(indol-3-yl)coumarins have been reported.[44]

Conclusions

In summary, we have identified TBD as efficient promotor for Michael reaction of a variety of indoles with 3-diethoxyphosphorylcoumarins. The HWE reaction of formaldehyde with the adducts bearing electron-rich indoles allowed facile preparation of methylene-4-(indol-3-yl)-3,4-dihydrocoumarins.

Experimental Section

General. NMR spectra were recorded on a Bruker Avance II Plus spectrometer at 700.0 MHz (^{1}H), 283.3 MHz (^{31}P) and 176.0 MHz (^{13}C) respectively. Measurements were carried out in deuterochloroform (99.96% d, Aldrich) at 25°C. Chemical shifts were calibrated relative to residual solvent peak (^{1}H NMR δ_{CHCl3} = 7.26 ppm and ^{13}C NMR δ_{CDCl3} = 77.16 ppm) and 85% H_3PO_4 (^{31}P NMR). Chemical shifts are reported in ppm (δ), *J* values are given in Hz. IR spectra were measured on Bruker Alpha FT-IR ATR spectrometer. Elemental analyses were performed on Perkin-Elmer PE 2400 analyser. Mass Spectrometry was carried out using Bruker amaZon speed EDT instrument. Melting points were determined in open capillaries on Büchi SMP 30 aparatus and were uncorrected. Flash chromatography was carried out using silica gel 60 (230-400 mesh). Thin layer chromatography was carried out on commercially available pre-coated plates (Fluka Silica gel on TLC plates).

General procedure for the synthesis of 3-diethoxyphosphoryl-4-(1*H*-indol-3-yl)-3,4-dihydrocoumarins (3a-l). To a stirred solution of the coumarin **1a-c** (1.0 mmol) and indole **2a-d** (1.5 mmol) in CH_2Cl_2 (10 mL), 1,5,7-triazabicyclo[4.4. 0]dec-5-ene (0.278 g, 2.0 mmol) was added in one portion. Stirring was continued at rt for 24 h. The resulting mixture was acidified with 5% hydrochloric acid (10 mL) and separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated. The oily residue was subjected for column chromatography on silica gel using CH_2Cl_2/MeOH (20:1) as eluent (R_F ~ 0.60 - 0.65) to give pure phosphonates **3a-l**.

Diethyl ((3*R,4*S**)-4-(1*H*-indol-3-yl)-2-oxochroman-3-yl)phosphonate** (**3a**). Colorless crystals, mp 172-174 °C; Anal. calcd for $C_{21}H_{22}NO_5P$: C, 63.15; H, 5.55; N, 3.51; Found C, 63.2; H, 5.5; N, 3.5; IR(ATR): 3268, 2987, 1765, 1459, 1242, 1142, 1061, 1019, 1006, 964, 943, 738, 516, 428 cm^{-1}; δ_H (700 MHz, $CDCl_3$) 8.21 (bs, 1H, N*H*), 7.70 (d, $^{3}J_{HH}$ 7.9 Hz, 1H, *H*-C_{Ar}), 7.11-7.36 (m, 7H, *H*-C_{Ar}), 6.51 (dd, $^{3}J_{HH}$ 2.5 Hz, $^{4}J_{HH}$ 0.75 Hz, 1H, -C*H*-NH-), 5.11 (bd, $^{3}J_{PH}$ 12.8 Hz, 1H, -C*H*-C_{Ar}), 4.11-4.21 (m, 2H, -C*H*$_2$-), 3.88-3.92 and 3.60-3.67 (m, 2H, -C*H*$_2$-), 3.84 (dd, $^{2}J_{PH}$ 24.8 Hz, $^{3}J_{HH}$ 1.1 Hz, 1H, *H*-C-P), 1.33 (dt, $^{3}J_{HH}$ 7.1, $^{4}J_{PH}$ 0.5 Hz, 3H, C*H*$_3$-), 0.98 (dt, $^{3}J_{HH}$ 7.1 Hz, $^{4}J_{PH}$ 0.5 Hz, 3H, C*H*$_3$-); δ_C (176 MHz, $CDCl_3$) 163.8 (d, $^{2}J_{PC}$ 5.7 Hz, O-*C*(O)), 151.7 (*C*$_{Ar}$), 136.8 (*C*$_{Ar}$), 129.1 (*C*$_{Ar}$H), 129.0 (*C*$_{Ar}$H), 125.2 (*C*$_{Ar}$), 125.2 (*C*$_{Ar}$H), 123.3 (*C*$_{Ar}$), 122.9 (*C*$_{Ar}$H), 122.1 (*C*$_{Ar}$H), 120.3 (*C*$_{Ar}$H), 118.3 (*C*$_{Ar}$H), 116.9 (*C*$_{Ar}$H), 116.8 (d, $^{3}J_{PC}$ 18.0 Hz, -*C*$_{Ar}$-C$_{Ar}$H-N), 111.8 (*C*$_{Ar}$H), 63.5 (d, $^{2}J_{PC}$ 6.5 Hz, CH_3-*C*H_2-OP), 63.2 (d, $^{2}J_{PC}$ 6.5 Hz, CH_3-*C*H_2-OP), 47.5 (d, $^{1}J_{PC}$

123.5 Hz, -*C*H-P), 34.6 (d, $^3J_{PC}$ 3.0 Hz, -C_{Ar}-*C*H-C_{Ar}), 16.4 (d, $^3J_{PC}$ 6.2 Hz, *C*H_3-CH_2-OP), 16.1 (d, $^3J_{PC}$ 6.2 Hz, *C*H_3-CH_2-OP); δ_P (283.3 MHz, $CDCl_3$) 18.6ppm.

Diethyl ((3*R,4*S**)-4-(1*H*-indol-3-yl)-8-methoxy-2-oxochroman-3-yl)phosphonate** (**3b**). Colorless crystals, mp 160-162 °C; Anal. calcd for $C_{22}H_{24}NO_6P$: C, 61.54; H, 5.63; N, 3.26; Found C, 61.1; H, 5.6; N, 3.3; IR(ATR): 3272, 2977, 1756, 1487, 1241, 1226, 1219, 1146, 1092, 1047, 966, 949, 737, 425 cm^{-1}; δ_H (700 MHz, $CDCl_3$) 8.24 (bs, 1H, N*H*), 7.70 (bd, $^3J_{HH}$ 7.9 Hz, 1H, *H*-C_{Ar}), 6.88-7.36 (m, 6H, *H*-C_{Ar}), 6.56 (bd, $^3J_{HH}$ 2.5 Hz, 1H, -C*H*-NH-), 5.09 (bd, $^3J_{PH}$ 12.7 Hz, 1H, -C*H*-C_{Ar}), 4.11-4.20 (m, 2H, -CH_2-), 3.86-3.93 and 3.60-3.69 (m, 2H, -CH_2-), 3.90 (s, 3H, -OCH_3), 3.82 (dd, $^2J_{PH}$ 24.7 Hz, $^3J_{HH}$ 0.9 Hz, 1H, *H*-C-P), 1.33 (t, $^3J_{HH}$ 7.1 Hz, 3H, CH_3-), 0.99 (t, $^3J_{HH}$ 7.1 Hz, 3H, CH_3-); δ_C (176 MHz, $CDCl_3$) 163.2 (d, $^2J_{PC}$ 5.7 Hz, O-*C*(O)), 147.6 (*C*$_{Ar}$),141.1 (*C*$_{Ar}$), 136.8 (*C*$_{Ar}$), 125.3 (*C*$_{Ar}$), 125.1 (*C*$_{Ar}$H), 124.4 (*C*$_{Ar}$), 122.8 (*C*$_{Ar}$H), 122.2 (*C*$_{Ar}$H), 120.5 (*C*$_{Ar}$H), 120.2 (*C*$_{Ar}$H), 118.3 (*C*$_{Ar}$H), 116.4 (d, $^3J_{PC}$ 17.9 Hz, -*C*$_{Ar}$-C_{Ar}H-N), 111.8 (*C*$_{Ar}$H), 111.6 (*C*$_{Ar}$H), 63.5 (d, $^2J_{PC}$ 6.2 Hz, CH_3-*C*H_2-OP), 63.2 (d, $^2J_{PC}$ = 6.2 Hz, CH_3-*C*H_2-OP), 56.3 (-O*C*H_3), 47.3 (d, $^1J_{PC}$ 123.7 Hz, -*C*H-P), 34.8 (d, $^3J_{PC}$ 3.0 Hz, -C_{Ar}-*C*H-C_{Ar}), 16.3 (d, $^3J_{PC}$ 6.2 Hz, *C*H_3-CH_2-OP), 16.0 (d, $^3J_{PC}$ 6.2 Hz, *C*H_3-CH_2-OP); δ_P (283.3 MHz, $CDCl_3$) 19.4 ppm.

Diethyl ((3*R,4*S**)-6-chloro-4-(1*H*-indol-3-yl)-2-oxochroman-3-yl)phosphonate** (**3c**). Colorless crystals, mp 164-166 °C; Anal. calcd for $C_{21}H_{21}ClNO_5P$: C, 58.14; H, 4.88; N, 3.23; found C, 58.1; H, 4.9; N, 3.2; IR(ATR): 3263, 2982, 2930, 1769, 1749, 1485, 1231, 1218, 1145, 1010, 979, 748, 739, 502 cm^{-1}; δ_H (700 MHz, $CDCl_3$) 8.22 (bs, 1H, N*H*), 7.67 (bd, $^3J_{HH}$ 7.9 Hz, 1H, *H*-C_{Ar}), 7.17-7.37 (m, 6H, *H*-C_{Ar}), 6.54 (bd, $^3J_{HH}$ 2.4 Hz, 1H, -C*H*-NH-), 5.07 (bd, $^3J_{PH}$ 12.7 Hz, 1H, -C*H*-C_{Ar}), 4.13-4.22 (m, 2H, -CH_2-), 3.92-3.99 and 3.76-3.83 (m, 2H, -CH_2-), 3.81 (dd, $^2J_{PH}$ 24.7 Hz, $^3J_{HH}$ 1.1 Hz, 1H, *H*-C-P), 1.34 (t, $^3J_{HH}$ 7.0 Hz, 3H, CH_3-), 1.05 (t, $^3J_{HH}$ 7.0 Hz, 3H, CH_3-); δ_C (176 MHz, $CDCl_3$) 163.2 (d, $^2J_{PC}$ 5.7 Hz, O-*C*(O)), 150.3 (*C*$_{Ar}$),141.1 (*C*$_{Ar}$), 136.8 (*C*$_{Ar}$), 130.1 (*C*$_{Ar}$), 129.0 (*C*$_{Ar}$H), 128.9 (*C*$_{Ar}$H), 125.0 (d, $^2J_{PC}$ 7.6 Hz, (*C*$_{Ar}$), 123.1 (*C*$_{Ar}$H), 122.0 (*C*$_{Ar}$H), 120.5 (*C*$_{Ar}$H), 118.2 (*C*$_{Ar}$H), 118.2 (*C*$_{Ar}$H), 116.1 (d, $^3J_{PC}$ 17.8 Hz, -*C*$_{Ar}$-C_{Ar}H-N), 111.8 (*C*$_{Ar}$H), 63.7 (d, $^2J_{PC}$ 6.4 Hz, CH_3-*C*H_2-OP), 63.3 (d, $^2J_{PC}$ 6.4 Hz, CH_3-*C*H_2-OP), 47.2 (d, $^1J_{PC}$ 123.7 Hz, -*C*H-P), 34.6 (d, $^3J_{PC}$ 3.0 Hz, -C_{Ar}-*C*H-C_{Ar}), 16.3 (d, $^3J_{PC}$ 6.3 Hz, *C*H_3-CH_2-OP), 16.1 (d, $^3J_{PC}$ 6.3 Hz, *C*H_3-CH_2-OP); δ_P (283.3 MHz, $CDCl_3$) 19.1 ppm.

Diethyl ((3*R,4*S**)-4-(5-methoxy-1*H*-indol-3-yl)-2-oxochroman-3-yl)phosphonate** (**3d**). Colorless crystals, mp 158-160 °C; Anal. calcd for $C_{22}H_{24}NO_6P$: C, 61.54; H, 5.63; N, 3.26; Found C, 61.5; H, 5.6; N, 3.3; IR(ATR): 3304, 2992, 2905, 1769, 1489, 1217, 1144, 1048, 1021, 1009, 930, 761, 512 cm^{-1}; δ_H (700 MHz, $CDCl_3$) 7.98 (bs, 1H, N*H*), 7.10-7.38 (m, 6H, *H*-C_{Ar}), 6.89 (dd, $^3J_{HH}$ 8.7 Hz, $^4J_{HH}$ 2.3 Hz, 1H, *H*-C_{Ar}), 6.51 (bd, $^3J_{HH}$ 1.9 Hz, 1H, -C*H*-NH-), 5.06 (bd, $^3J_{PH}$ 12.8 Hz, 1H, -C*H*-C_{Ar}), 4.12-4.21 (m, 2H, -CH_2-), 3.85-3.92 and 3.60-3.67 (m, 2H, -CH_2-), 3.90 (s, 3H, -OCH_3), 3.82 (dd, $^2J_{PH}$ 24.8 Hz, $^3J_{HH}$ 1.0 Hz, 1H, *H*-C-P), 1.33 (t, $^3J_{HH}$ 7.0 Hz, 3H, CH_3-), 0.98 (t, $^3J_{HH}$ 7.0 Hz, 3H, CH_3-); δ_C (176 MHz, $CDCl_3$) 163.8 (d, $^2J_{PC}$ 5.2 Hz, O-*C*(O)), 154.7 (*C*$_{Ar}$), 151.7 (*C*$_{Ar}$), 131.9 (*C*$_{Ar}$), 129.1 (*C*$_{Ar}$H), 129.0 (*C*$_{Ar}$), 125.7 (*C*$_{Ar}$), 125.2 (*C*$_{Ar}$H), 123.3 (*C*$_{Ar}$), 122.7 (*C*$_{Ar}$H), 116.9 (*C*$_{Ar}$H), 116.7 (d, $^3J_{PC}$ 18.3 Hz, -*C*$_{Ar}$-C_{Ar}H-N), 113.2 (*C*$_{Ar}$H), 112.5 (*C*$_{Ar}$H), 100.2 (*C*$_{Ar}$H), 63.5 (d, $^2J_{PC}$ 6.2 Hz, CH_3-*C*H_2-OP), 63.2 (d, $^2J_{PC}$ 6.2 Hz, CH_3-*C*H_2-OP), 56.1 (-O*C*H_3), 47.4 (d, $^1J_{PC}$ 123.6 Hz, -*C*H-P), 34.6 (d, $^3J_{PC}$ 3.0 Hz, -C_{Ar}-*C*H-C_{Ar}), 16.4 (d, $^3J_{PC}$ 6.2 Hz, *C*H_3-CH_2-OP), 16.1 (d, $^3J_{PC}$ 6.2 Hz, *C*H_3-CH_2-OP); δ_P (283.3 MHz, $CDCl_3$) 19.6 ppm.

Diethyl ((3*R*,*4*S)-8-methoxy-4-(5-methoxy-1*H*-indol-3-yl)-2-oxochroman-3-yl)phosphonate** (**3e**). Colorless crystals, mp 146-149 °C; Anal. calcd for $C_{23}H_{26}NO_7P$: C, 60.13; H, 5.70; N, 3.05; Found C, 60.1; H, 5.7; N, 3.1; IR(ATR): 3256, 2982, 2936, 2903, 1755, 1484, 1210, 1147, 1091, 1046, 1009, 973, 794, 744, 525 cm^{-1}; δ_H (700 MHz, $CDCl_3$) 7.98 (bs, 1H, N*H*), 6.60-7.25 (m, 6H, *H*-C_{Ar}), 6.55 (bd, $^3J_{HH}$ 2.5 Hz, 1H, -C*H*-NH-), 5.04 (bd, $^3J_{PH}$ 12.7 Hz, 1H, -C*H*-C_{Ar}), 4.12-4.21 (m, 2H, -CH_2-), 3.86-3.92 and 3.62-3.69 (m, 2H, -CH_2-), 3.91 (s, 3H, -OCH_3), -), 3.88 (s, 3H, -OCH_3), 3.80 (dd, $^2J_{PH}$ 24.7 Hz, $^3J_{HH}$ 1.1 Hz, 1H, *H*-C-P), 1.33 (t, $^3J_{HH}$ 7.0 Hz, 3H, CH_3-), 1.00 (t, $^3J_{HH}$ 7.0 Hz, 3H, CH_3-); δ_C (176 MHz, $CDCl_3$) 163.2 (d, $^2J_{PC}$ 5.3 Hz, O-*C*(O)), 154.6 (*C*$_{Ar}$), 147.6 (*C*$_{Ar}$), 141.1 (*C*$_{Ar}$), 131.9 (*C*$_{Ar}$), 125.6 (*C*$_{Ar}$), 125.1 (*C*$_{Ar}$H), 124.4 (*C*$_{Ar}$), 122.8 (*C*$_{Ar}$H), 120.5 (*C*$_{Ar}$H), 116.1 (d, $^3J_{PC}$ 17.9 Hz, -*C*$_{Ar}$-C_{Ar}H-N), 113.0 (*C*$_{Ar}$H), 112.5(*C*$_{Ar}$H), 111.6 (*C*$_{Ar}$H), 100.1 (*C*$_{Ar}$H), 63.4 (d, $^2J_{PC}$ 6.8 Hz, CH_3-*C*H_2-OP), 63.2 (d, $^2J_{PC}$ 6.8 Hz, CH_3-*C*H_2-OP), 56.3

(-O*C*H$_3$), 56.1 (-O*C*H$_3$), 47.2 (d, $^1J_{PC}$ 123.4 Hz, -*C*H-P), 34.8 (d, $^3J_{PC}$ 2.6 Hz, -C$_{Ar}$-*C*H-C$_{Ar}$), 16.4 (d, $^3J_{PC}$ 6.2 Hz, *C*H$_3$-CH$_2$-OP), 16.0 (d, $^3J_{PC}$ 6.2 Hz, *C*H$_3$-CH$_2$-OP); δ_P (283.3 MHz, CDCl$_3$) 18.5 ppm.

Diethyl ((3*R,4*S**)-6-chloro-4-(5-methoxy-1*H*-indol-3-yl)-2-oxochroman-3-yl)phosphonate** (**3f**). Colorless crystals, mp 192-194 °C; Anal. calcd for $C_{22}H_{23}ClNO_6P$: C, 56.97; H, 5.00; N, 3.02; Found C, 57.0; H, 5.0; N, 3.0; IR(ATR): 3393, 2992, 2903, 1768, 1485, 1228, 1218, 1144, 1048, 1015, 979, 820, 800, 507 cm^{-1}; δ_H (700 MHz, CDCl$_3$) 7.98 (bs, 1H, N*H*), 6.86-7.40 (m, 6H, *H*-C$_{Ar}$), 6.53 (bd, $^3J_{HH}$ 2.5 Hz, 1H, -C*H*-NH-), 5.01 (bd, $^3J_{PH}$ 12.9 Hz, 1H, -C*H*-C$_{Ar}$), 4.13-4.22 (m, 2H, -C*H*$_2$-), 3.92-3.99 and 3.76-3.83 (m, 2H, -C*H*$_2$-), 3.88 (s, 3H, -OC*H*$_3$), 3.80 (dd, $^2J_{PH}$ 24.8 Hz, $^3J_{HH}$ 1.1 Hz, 1H, *H*-C-P), 1.34 (t, $^3J_{HH}$ 7.0 Hz, 3H, C*H*$_3$-), 1.1 (t, $^3J_{HH}$ 7.0 Hz, 3H, C*H*$_3$-); δ_C (176 MHz, CDCl$_3$) 163.2 (d, $^2J_{PC}$ 5.0 Hz, O-*C*(O)), 154.7 (*C*$_{Ar}$), 150.2 (*C*$_{Ar}$), 131.8 (*C*$_{Ar}$), 130.1 (*C*$_{Ar}$), 129.0 (*C*$_{Ar}$H), 128.9 (*C*$_{Ar}$H), 125.5 (*C*$_{Ar}$), 125.0 (*C*$_{Ar}$), 122.6 (*C*$_{Ar}$H), 118.2 (*C*$_{Ar}$H), 115.9 (d, $^3J_{PC}$ 17.6 Hz, -*C*$_{Ar}$-C$_{Ar}$H-N), 113.3 (*C*$_{Ar}$H), 112.6 (*C*$_{Ar}$H), 100.0 (*C*$_{Ar}$H), 63.7 (d, $^2J_{PC}$ 6.7 Hz, CH$_3$-*C*H$_2$-OP), 63.7 (d, $^2J_{PC}$ 6.7 Hz, CH$_3$-*C*H$_2$-OP), 56.1 (-O*C*H$_3$), 47.0 (d, $^1J_{PC}$ 123.8 Hz, -*C*H-P), 34.6 (d, $^3J_{PC}$ = 2.6 Hz, -C$_{Ar}$-*C*H-C$_{Ar}$), 16.4 (d, $^3J_{PC}$ 6.2 Hz, *C*H$_3$-CH$_2$-OP), 16.1 (d, $^3J_{PC}$ 6.2 Hz *C*H$_3$-CH$_2$-OP); δ_P (283.3 MHz, CDCl$_3$) 19.2 ppm.

Diethyl ((3*R,4*S**)-4-(5-nitro-1*H*-indol-3-yl)-2-oxochroman-3-yl)-phosphonate** (**3g**). Colorless crystals, mp 185-188 °C; Anal. calcd for $C_{21}H_{21}N_2O_7P$: C, 56.76; H, 4.76; N, 6.30; Found C, 56.8; H, 4.7; N, 6.3; IR(ATR): 3183, 2984, 2927, 2907, 1753, 1517, 1479, 1335, 1227, 1152, 1009, 973, 767, 740, 506 cm^{-1}; δ_H (700 MHz, CDCl$_3$) 9.01 (bs, 1H, N*H*), 8.62 (d, $^4J_{HH}$ 2.0 Hz, 1H, C-C*H*-CNO$_2$), 8.13 (dd, $^3J_{HH}$ 8.9 Hz, $^4J_{HH}$ 2.0 Hz, 1H, HC-C*H*-CNO$_2$), 7.40 (d, $^3J_{HH}$ 8.9 Hz, 1H, C*H*-CH-CNO$_2$), 7.11-7.38 (m, 4H, *H*-C$_{Ar}$), 6.71 (bd, $^3J_{HH}$ 2.3 Hz, 1H, -C*H*-NH-), 5.09 (bd, $^3J_{PH}$ 12.6 Hz, 1H, -C*H*-C$_{Ar}$), 4.10-4.21 (m, 2H, -C*H*$_2$-), 3.92-3.99 and 3.70-3.75 (m, 2H, -C*H*$_2$-), 3.78 (dd, $^2J_{PH}$ 24.8 Hz, $^3J_{HH}$ 1.1 Hz, 1H, *H*-C-P), 1.33 (t, $^3J_{HH}$ 7.1 Hz, 3H, C*H*$_3$-), 1.08 (t, $^3J_{HH}$ 7.1 Hz, 3H, C*H*$_3$-); δ_C (176 MHz, CDCl$_3$) 163.6 (d, $^2J_{PC}$ 5.1 Hz, O-*C*(O)), 151.6 (*C*$_{Ar}$), 142.2 (*C*$_{Ar}$), 139.8 (*C*$_{Ar}$), 129.5 (*C*$_{Ar}$H), 129.0 (*C*$_{Ar}$H), 125.5 (*C*$_{Ar}$H), 125.4 (*C*$_{Ar}$H), 124.7 (*C*$_{Ar}$), 122.5 (*C*$_{Ar}$), 119.1 (d, $^3J_{PC}$ 18.0 Hz, -*C*$_{Ar}$-C$_{Ar}$H-N), 118.5 (*C*$_{Ar}$H), 117.1 (*C*$_{Ar}$H), 115.5 (*C*$_{Ar}$H), 112.0 (*C*$_{Ar}$H), 63.7 (d, $^2J_{PC}$ 6.6 Hz, CH$_3$-*C*H$_2$-OP), 63.6 (d, $^2J_{PC}$ 6.6 Hz, CH$_3$-*C*H$_2$-OP), 48.8 (d, $^1J_{PC}$ 124.7 Hz, -*C*H-P), 34.5 (d, $^3J_{PC}$ 2.8 Hz, -C$_{Ar}$-*C*H-C$_{Ar}$), 16.4 (d, $^3J_{PC}$ 6.2 Hz, *C*H$_3$-CH$_2$-OP), 16.2 (d, $^3J_{PC}$ 6.2 Hz, *C*H$_3$-CH$_2$-OP); δ_P (283.3 MHz, CDCl$_3$) 18.7 ppm.

Diethyl ((3*R,4*S**)-8-methoxy-4-(5-nitro-1*H*-indol-3-yl)-2-oxochroman-3-yl)phosphonate** (**3h**). Colorless crystals, mp 195-197 °C; Anal. calcd for $C_{22}H_{23}N_2O_8P$: C, 55.70; H, 4.89; N, 5.91; Found C, 55.8; H, 4.9; N, 5.8; IR(ATR): 3438, 2975, 2932, 2907, 1757, 1518, 1486, 1323, 1284, 1245, 1219, 1169, 1043, 1004, 971, 783, 738, 505 cm^{-1}; δ_H (700 MHz, CDCl$_3$) 9.09 (bs, 1H, N*H*), 8.61 (d, $^4J_{HH}$ 2.1 Hz, 1H, C-C*H*-CNO$_2$), 8.11 (dd, $^3J_{HH}$ 9.0 Hz, $^4J_{HH}$ 2.1 Hz, 1H, HC-C*H*-CNO$_2$), 7.40 (d, $^3J_{HH}$ 9.0 Hz, 1H, C*H*-CH-CNO$_2$), 6.80-7.14 (m, 3H, *H*-C$_{Ar}$), 6.74 (bd, $^3J_{HH}$ 2.3 Hz, 1H, -C*H*-NH-), 5.07 (bd, $^3J_{PH}$ 12.3 Hz, 1H, -C*H*-C$_{Ar}$), 4.12-4.21 (m, 2H, -C*H*$_2$-), 3.90-4.00 and 3.71-3.78 (m, 2H, -C*H*$_2$-), 3.87 (s, 3H, -OC*H*$_3$), 3.77 (dd, $^2J_{PH}$ 24.8 Hz, $^3J_{HH}$ 1.1 Hz, 1H, *H*-C-P), 1.34 (t, $^3J_{HH}$ 7.0 Hz, 3H, C*H*$_3$-), 1.09 (t, $^3J_{HH}$ 7.0 Hz, 3H, C*H*$_3$-); δ_C (176 MHz, CDCl$_3$) 163.3 (d, $^2J_{PC}$ 4.9 Hz, O-*C*(O)), 147.7 (*C*$_{Ar}$), 142.1 (*C*$_{Ar}$), 140.9 (*C*$_{Ar}$), 139.8 (*C*$_{Ar}$), 125.5 (*C*$_{Ar}$H), 124.7 (*C*$_{Ar}$), 123.7 (*C*$_{Ar}$), 120.3 (*C*$_{Ar}$H), 118.5 (d, $^3J_{PC}$ 18.0 Hz, -*C*$_{Ar}$-C$_{Ar}$H-N), 118.4 (*C*$_{Ar}$H), 115.5 (*C*$_{Ar}$H), 112.0 (*C*$_{Ar}$H), 111.9 (*C*$_{Ar}$H), 125.5 125.4 (*C*$_{Ar}$H), 124.7 (*C*$_{Ar}$), 122.5 (*C*$_{Ar}$), 119.1 118.5 (*C*$_{Ar}$H), 117.1 (*C*$_{Ar}$H), 115.5 (*C*$_{Ar}$H), 112.0 (*C*$_{Ar}$H), 63.7 (d, $^2J_{PC}$ 6.6 Hz, CH$_3$-*C*H$_2$-OP), 63.6 (d, $^2J_{PC}$ 6.6 Hz, CH$_3$-*C*H$_2$-OP), 56.2 (-O*C*H$_3$), 47.6 (d, $^1J_{PC}$ 125.1 Hz, -*C*H-P), 34.6 (d, $^3J_{PC}$ 2.0 Hz, -C$_{Ar}$-*C*H-C$_{Ar}$), 16.3 (d, $^3J_{PC}$ 6.1 Hz, *C*H$_3$-CH$_2$-OP), 16.1 (d, $^3J_{PC}$ 6.1 Hz, *C*H$_3$-CH$_2$-OP); δ_P (283.3 MHz, CDCl$_3$) 18.7 ppm.

Diethyl ((3*R,4*S**)-6-chloro-4-(5-nitro-1*H*-indol-3-yl)-2-oxochroman-3-yl)phosphonate** (**3i**). Colorless crystals, mp 215-217 °C; Anal. calcd for $C_{21}H_{20}ClN_2O_7P$: C, 52.68; H, 4.21; N, 7.40; Found C, 52.8; H, 4.2; N, 7.4; IR(ATR): 3222, 2982, 1763, 1476, 1330, 1243, 1217, 1149, 1048, 1025, 739, 509 cm^{-1}; δ_H (700 MHz, acetone-d6) 10.90 (bs, 1H, N*H*), 8.67 (d, $^4J_{HH}$ 2.1 Hz, 1H, C-C*H*-CNO$_2$), 8.10 (dd, $^3J_{HH}$ 9.0 Hz, $^4J_{HH}$ 2.1 Hz, 1H, HC-C*H*-CNO$_2$), 7.65 (d, $^4J_{HH}$ 2.5 Hz, 1H, C-C*H*-CCl), 7.63 (d, $^3J_{HH}$ 9.0 Hz, 1H, *H*C-CH-CNO$_2$), 7.46 (dd, $^3J_{HH}$ 8.7 Hz, $^4J_{HH}$ 2.5 Hz, 1H, C*H*-CH-CCl), 7.21 (d, $^3J_{HH}$ 8.7 Hz, 1H, CH-C*H*-CCl), 7.05 (bs, 1H, -C*H*-NH-), 5.26 (bd, $^3J_{PH}$ 12.6 Hz, 1H, -C*H*-C$_{Ar}$), 4.13-4.20 (m, 2H, -C*H*$_2$-), 4.07-4.14 and 3.83-3.90 (m, 2H, -C*H*$_2$-), 3.88 (dd, $^2J_{PH}$ 24.9 Hz, $^3J_{HH}$ 1.3 Hz, 1H, *H*-C-P), 1.30 (t, $^3J_{HH}$

7.1 Hz, 3H, C*H*$_3$-), 1.01 (t, $^3J_{HH}$ 7.1 Hz, 3H, C*H*$_3$-); δ_C (176 MHz, acetone-d6) 163.2 (d, $^2J_{PC}$ 5.2 Hz, O-*C*(O)), 151.5 (*C*$_{Ar}$), 142.6 (*C*$_{Ar}$), 141.0 (*C*$_{Ar}$), 130.3 (*C*$_{Ar}$), 129.9 (*C*$_{Ar}$H), 129.7 (*C*$_{Ar}$H), 127.2 (*C*$_{Ar}$H), 126.2 (*C*$_{Ar}$), 125.4 (*C*$_{Ar}$), 119.3 (*C*$_{Ar}$H), 119.2 (d, $^3J_{PC}$ 18.0 Hz, -*C*$_{Ar}$-C$_{Ar}$H-N), 118.4 (*C*$_{Ar}$H), 116.2 (*C*$_{Ar}$H), 113.2 (*C*$_{Ar}$H), 64.0 (d, $^2J_{PC}$ 6.5 Hz, CH$_3$-*C*H$_2$-OP), 63.7 (d, $^2J_{PC}$ 6.5 Hz, CH$_3$-*C*H$_2$-OP), 48.2 (d, $^1J_{PC}$ 123.3 Hz, -*C*H-P), 35.0 (d, $^3J_{PC}$ 3.4 Hz, -C$_{Ar}$-*C*H-C$_{Ar}$), 16.5 (d, $^3J_{PC}$ 6.2 Hz, *C*H$_3$-CH$_2$-OP), 16.4 (d, $^3J_{PC}$ 6.2 Hz, *C*H$_3$-CH$_2$-OP); δ_P (283.3 MHz, acetone-d6) 17.1 ppm.

Diethyl ((3*R,4*S**)-4-(5-cyano-1*H*-indol-3-yl)-2-oxochroman-3-yl)phosphonate** (**3j**). Colorless crystals, mp 223-224 °C; Anal. calcd for $C_{22}H_{21}N_2O_5P$: C, 62.26; H, 4.99; N, 6.60; Found C, 62.3; H, 5.1; N, 6.6; IR(ATR): 3226, 2990, 2904, 2222, 1754, 1228, 1167, 1022, 1011, 806, 771, 505 cm^{-1}; δ_H (700 MHz, $CDCl_3$) 8.83 (bs, 1H, N*H*), 8.00-8.01 (m, 1H, C-C*H*-CCN), 7.45 (dd, $^3J_{HH}$ 8.5 Hz, $^4J_{HH}$ 1.5 Hz, 1H, HC-C*H*-CCN), 7.41 (dd, $^3J_{HH}$ 8.5 Hz, $^5J_{HH}$ 0.6 Hz, 1H, C*H*-CH-CCN), 7.10-7.36 (m, 4H, *H*-C$_{Ar}$), 6.71 (dd, $^3J_{HH}$ 2.6 Hz, $^4J_{HH}$ 0.9 Hz, 1H, -C*H*-NH-), 5.07 (bd, $^3J_{PH}$ 12.6 Hz, 1H, -C*H*-C$_{Ar}$), 4.10-4.22 (m, 2H, -C*H*$_2$-), 3.87-3.92 and 3.63-3.70 (m, 2H, -C*H*$_2$-), 3.73 (dd, $^2J_{PH}$ 24.8 Hz, $^3J_{HH}$ 1.1 Hz, 1H, *H*-C-P), 1.33 (t, $^3J_{HH}$ 7.1 Hz, 3H, C*H*$_3$-), 1.02 (t, $^3J_{HH}$ 7.1 Hz, 3H, C*H*$_3$-); δ_C (176 MHz, $CDCl_3$) 163.6 (d, $^2J_{PC}$ 5.1 Hz, O-*C*(O)), 151.6 (*C*$_{Ar}$), 138.5 (*C*$_{Ar}$), 129.4 (*C*$_{Ar}$H), 129.0 (*C*$_{Ar}$H), 125.8 (*C*$_{Ar}$H), 125.5 (*C*$_{Ar}$H), 125.1 (*C*$_{Ar}$), 124.5 (*C*$_{Ar}$H), 123.9 (*C*$_{Ar}$H), 122.5 (*C*$_{Ar}$), 120.5 (*C*$_{Ar}$), 117.6 (d, $^3J_{PC}$ 18.3 Hz, -*C*$_{Ar}$-C$_{Ar}$H-N), 117.1 (*C*$_{Ar}$H), 112.8 (*C*$_{Ar}$H), 103.5 (*C*$_{Ar}$), 63.7 (d, $^2J_{PC}$ 6.6 Hz, CH$_3$-*C*H$_2$-OP), 63.5 (d, $^2J_{PC}$ 6.6 Hz, CH$_3$-*C*H$_2$-OP), 48.6 (d, $^1J_{PC}$ 124.7 Hz, -*C*H-P), 34.4 (d, $^3J_{PC}$ 2.1 Hz, -C$_{Ar}$-*C*H-C$_{Ar}$), 16.4 (d, $^3J_{PC}$ 6.2 Hz, *C*H$_3$-CH$_2$-OP), 16.1 (d, $^3J_{PC}$ 6.2 Hz, *C*H$_3$-CH$_2$-OP); δ_P (283.3 MHz, $CDCl_3$) 18.9 ppm.

Diethyl ((3*R,4*S**)-4-(5-cyano-1*H*-indol-3-yl)-8-methoxy-2-oxochroman-3-yl)phosphonate** (**3k**). Colorless crystals, mp 205-207 °C; Anal. calcd for $C_{23}H_{23}N_2O_6P$: C, 60.79; H, 5.10; N, 6.16; Found C, 60.1; H, 5.1; N, 6.1; IR(ATR): 3237, 2991, 2942, 2903, 2842, 2223, 1753, 1424, 1222, 1175, 1149, 1013, 806, 769, 494 cm^{-1}; δ_H (700 MHz, $CDCl_3$) 8.87 (bs, 1H, N*H*), 7.99-8.01 (m, 1H, C-C*H*-CCN), 7.44 (dd, $^3J_{HH}$ 8.4 Hz, $^4J_{HH}$ 1.5 Hz, 1H, HC-C*H*-CCN), 7.41 (dd, $^3J_{HH}$ 8.4 Hz, $^5J_{HH}$ 0.7 Hz, 1H, C*H*-CH-CCN), 7.11 (dd, $^3J_{HH}$ $^3J'_{HH}$ = 8.0 Hz, -CH-C*H*-CH-), 6.91 (d, $^3J_{HH}$ 8.0, 2H, 2x-C*H*-CH), 6.69 (bd, $^3J_{HH}$ 2.6 Hz, $^5J_{HH}$ 0.8 Hz, 1H, -C*H*-NH-), 5.04 (bd, $^3J_{PH}$ 12.3 Hz, 1H, -C*H*-C$_{Ar}$), 4.12-4.21 (m, 2H, -C*H*$_2$-), 3.89-3.95 and 3.65-3.71 (m, 2H, -C*H*$_2$-), 3.88 (s, 3H, -OC*H*$_3$), 3.72 (dd, $^2J_{PH}$ 24.7 Hz, $^3J_{HH}$ 1.2 Hz, 1H, *H*-C-P), 1.34 (t, $^3J_{HH}$ 7.0 Hz, 3H, C*H*$_3$-), 1.03 (t, $^3J_{HH}$ 7.0 Hz, 3H, C*H*$_3$-); δ_C (176 MHz, $CDCl_3$) 163.2 (d, $^2J_{PC}$ 5.1 Hz, O-*C*(O)), 147.7 (*C*$_{Ar}$), 140.9 (*C*$_{Ar}$), 141.1 (*C*$_{Ar}$), 138.5 (*C*$_{Ar}$), 125.7 (*C*$_{Ar}$H), 125.4 (*C*$_{Ar}$H), 125.1 (*C*$_{Ar}$), 124.6 (*C*$_{Ar}$H), 123.8 (*C*$_{Ar}$H), 123.7 (*C*$_{Ar}$), 120.5 (*C*$_{Ar}$), 120.3 (*C*$_{Ar}$H), 117.1(d, $^3J_{PC}$ 18.6 Hz, -*C*$_{Ar}$-C$_{Ar}$H-N), 112.9 (*C*$_{Ar}$H), 111.9 (*C*$_{Ar}$H), 103.4 (*C*$_{Ar}$), 63.7 (d, $^2J_{PC}$ 6.6 Hz, CH$_3$-*C*H$_2$-OP), 63.5 (d, $^2J_{PC}$ 6.6 Hz, CH$_3$-*C*H$_2$-OP), 56.2 (-OC*H*$_3$), 47.5 (d, $^1J_{PC}$ 125.1 Hz, -*C*H-P), 34.5 (d, $^3J_{PC}$ 2.1 Hz, -C$_{Ar}$-*C*H-C$_{Ar}$), 16.4 (d, $^3J_{PC}$ 6.2 Hz, *C*H$_3$-CH$_2$-OP), 16.0 (d, $^3J_{PC}$ 6.2 Hz, *C*H$_3$-CH$_2$-OP); δ_P (283.3 MHz, $CDCl_3$) 17.7 ppm.

Diethyl ((3*R,4*S**)-6-chloro-4-(5-cyano-1*H*-indol-3-yl)-2-oxochroman-3-yl)phosphonate** (**3l**). Colorless crystals, mp 208-210 °C; Anal. calcd for $C_{22}H_{20}ClN_2O_5P$: C, 57.59; H, 4.39; N, 7.73; Found C, 57.7; H, 4.4; N, 7.7; IR(ATR): 3336, 2983, 2940, 2908, 2223, 1765, 1479, 1419, 1253, 1226, 1138, 1053, 1014, 975, 811, 651, 513, 492 cm^{-1}; δ_H (700 MHz, acetone-d6) 10.78 (bs, 1H, N*H*), 8.14 (bs, 1H, C-C*H*-CCN), 7.65 (d, $^4J_{HH}$ 2.5 Hz, 1H, -C-C*H*-CCl), 7.62 (d, $^3J_{HH}$ 8.4 Hz, 1H, CH-C*H*-CCN), 7.50 (dd, $^3J_{HH}$ 8.4 Hz, $^5J_{HH}$ 1.3 Hz 1H, C*H*-CH-CCN), 7.44 (dd, $^3J_{HH}$ 8.8 Hz, $^5J_{HH}$ 2.5 Hz 1H, -C-CH-C*H*-CCl), 7.20 (d, $^3J_{HH}$ 8.8 Hz, 1H, -C-C*H*-CH-CCl), 6.99 (bs, 1H, -C*H*-NH-), 5.18 (bd, $^3J_{PH}$ 12.6 Hz, 1H, -C*H*-C$_{Ar}$), 4.13-4.24 (m, 2H, -C*H*$_2$-), 3.94-4.03 and 3.80-3.86 (m, 2H, -C*H*$_2$-), 3.89 (dd, $^2J_{PH}$ 24.9 Hz, $^3J_{HH}$ 0.9 Hz, 1H, *H*-C-P), 1.29 (t, $^3J_{HH}$ 7.0 Hz, 3H, C*H*$_3$-), 1.07 (t, $^3J_{HH}$ 7.0 Hz, 3H, C*H*$_3$-); δ_C (176 MHz, acetone-d6) 163.4 (d, $^2J_{PC}$ 5.4 Hz, O-*C*(O)), 151.5 (*C*$_{Ar}$), 139.6 (*C*$_{Ar}$), 130.2 (*C*$_{Ar}$), 129.8 (-C-*C*$_{Ar}$H-CCl), 129.6 (CH-*C*$_{Ar}$H-CCN), 126.4 (*C*$_{Ar}$), 126.0 (*C*$_{Ar}$H), 125.8 (-*C*$_{Ar}$H-NH-), 124.7 (C-*C*$_{Ar}$H-CCN), 120.9 (*C*$_{Ar}$), 119.3 (-C-*C*$_{Ar}$H-CH-CCl), 117.6 (d, $^3J_{PC}$ 17.9 Hz, -*C*$_{Ar}$-C$_{Ar}$H-N), 114.1 (C-*C*$_{Ar}$H-CCl), 103.6 (*C*$_{Ar}$), 64.0 (d, $^2J_{PC}$ 6.4 Hz, CH$_3$-*C*H$_2$-OP), 63.7 (d, $^2J_{PC}$ 6.6 Hz, CH$_3$-*C*H$_2$-OP), 47.9 (d, $^1J_{PC}$ 123.5 Hz, -*C*H-P), 35.0 (d, $^3J_{PC}$ 3.2 Hz, -C$_{Ar}$-*C*H-C$_{Ar}$), 16.5 (d, $^3J_{PC}$ 6.1 Hz, *C*H$_3$-CH$_2$-OP), 16.3 (d, $^3J_{PC}$ 6.1 Hz, *C*H$_3$-CH$_2$-OP); δ_P (283.3 MHz, acetone-d6) 17.6 ppm.

General procedure for the synthesis 3-methylene-4-(indol-3-yl)-3,4-dihydrocoumarins (**4a-f**). A mixture of a 3-diethoxyphosphoryl-4-(1*H*-indol-3-yl)-3,4-dihydrocoumarin (**3a-f**) (0.5 mmol) and K_2CO_3 (0.207 g, 1.5 mmol) in THF (5 mL) was stirred at 0 °C for 15 min. Then, aq formaldehyde (40%, 0.20 mL) was added and resulting suspension was stirred at 20 °C for an additional 3 h. The mixture was then concentrated *in vacuo* and the solid residue was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over $MgSO_4$ and evaporated. The oily residue was subjected for column chromatography on silica gel using CH_2Cl_2/Me_2CO (10:1) as eluent (R_F ~ 0.8) to afford desired products (**4a-f**).

4-(1*H*-Indol-3-yl)-3-methylenechroman-2-one (**4a**). Colorless foam; Anal. calcd for $C_{18}H_{13}NO_2$: C, 78.53; H, 4.76; N, 5.09; Found C, 78.6; H, 4.7; N, 5.1; IR(ATR): 3333, 1724, 1454, 1278, 1235, 1219, 1153, 1141, 1105, 1094, 972, 756, 740, 668, 639, 597, 552, 430 cm^{-1}; δ_H (700 MHz, $CDCl_3$) 8.13 (bs, 1H, N*H*), 7.05-7.42 (m, 8H, *H*-C_{Ar}), 6.94 (bd, $^3J_{HH}$ 2.5 Hz, 1H, -C*H*-NH-), 6.41 (dd, $^2J_{HH}$ 1.7 Hz, $^4J_{HH}$ 0.9 Hz, 1H, =C*H*H), 5.72 (dd, $^2J_{HH}$ 1.7 Hz, $^4J_{HH}$ 0.9 Hz, 1H, =CH*H*), 5.25 (bs, 1H, -C*H*-C=CH_2); δ_C (176 MHz, $CDCl_3$) 163.9 (O-*C*(O)), 151.8 (*C*$_{Ar}$), 137.1 (*C*$_{Ar}$), 136.1 (=*C*$_{Ar}$<), 128.7 (*C*$_{Ar}$H), 128.6 (=*C*H_2), 128.4 (*C*$_{Ar}$H), 125.5 (*C*$_{Ar}$), 125.2 (*C*$_{Ar}$),, 124.9 (*C*$_{Ar}$H), 123.7 (*C*$_{Ar}$H), 122.7 (*C*$_{Ar}$H), 119.8 (*C*$_{Ar}$H), 117.2 (*C*$_{Ar}$H), 114.1 (-*C*$_{Ar}$-C_{Ar}H-N), 111.7 (*C*$_{Ar}$H), 40.3 (-C_{Ar}-*C*H-C_{Ar}).

4-(1*H*-Indol-3-yl)-8-methoxy-3-methylenechroman-2-one (**4b**). Colorless foam; Anal. calcd for $C_{19}H_{15}NO_3$: C, 74.74; H, 4.95; N, 4.59; Found C, 74.9; H, 5.0; N, 4.6; IR(ATR): 3403, 1738, 1481, 1456, 1285, 1271, 1186, 1123, 1089, 1062, 955, 769, 740 cm^{-1}; δ_H (700 MHz, $CDCl_3$) 8.19 (bs, 1H, N*H*), 7.04-7.40 (m, 4H, H_{ind}), 6.99 (t, $^3J_{HH}$ 8.0 Hz, 1H, -C*H*-CH-C-OMe), 6.93 (bd, $^3J_{HH}$ 2.4 Hz, 1H, -C*H*-NH-), 6.88 (dd, $^3J_{HH}$ 8.0 Hz, $^4J_{HH}$ 1.3 Hz, 1H, -C*H*-C-C-O), 6.68 (dd, $^3J_{HH}$ 8.0 Hz, $^4J_{HH}$ = 1.3 Hz, 1H, -C*H*-C-OMe), 6.39 (dd, $^2J_{HH}$ 1.7 Hz, $^4J_{HH}$ 0.9 Hz, 1H, =C*H*H), 5.72 (dd, $^2J_{HH}$ 1.7 Hz, $^4J_{HH}$ 0.9 Hz, 1H, =CH*H*), 5.23 (bs, 1H, -C*H*-C=CH_2), 3.92 (s, 3H, -OC*H*$_3$); δ_C (176 MHz, $CDCl_3$) 163.3 (O-*C*(O)), 147.9 (*C*$_{Ar}$), 140.2 (*C*$_{Ar}$), 137.1 (*C*$_{Ar}$), 136.0 (=*C*<), 128.4 (=*C*H_2), 126.4 (*C*$_{Ar}$), 125.5 (*C*$_{Ar}$), 124.7 (*C*$_{Ar}$H), 123.6 (*C*$_{Ar}$H), 122.6 (*C*$_{Ar}$H), 119.9 (*C*$_{Ar}$H), 119.8 (2x*C*$_{Ar}$H), 114.1 (*C*$_{Ar}$), 111.7 (*C*$_{Ar}$H), 111.4 (*C*$_{Ar}$H), 56.3 (-OC*H*$_3$), 40.5 (-C_{Ar}-*C*H-C_{Ar}).

6-Chloro-4-(1*H*-indol-3-yl)-3-methylenechroman-2-one (**4c**). Colorless foam; Anal. calcd for $C_{18}H_{12}ClNO_2$: C, 69.80; H, 3.90; N, 4.52; Found C, 70.0.; H, 3.9; N, 4.5; IR(ATR): 3402, 1736, 1477, 1457, 1409, 1296, 1232, 1178, 1133, 1105, 1086, 817, 740, 526, 425 cm^{-1}; δ_H (700 MHz, $CDCl_3$) 8.23 (bs, 1H, N*H*), 7.04-7.43 (m, 7H, H aromat.), 6.97 (bd, $^3J_{HH}$ 2.5 Hz, 1H, -C*H*-NH-), 6.44 (dd, $^2J_{HH}$ 1.8 Hz, $^4J_{HH}$ 0.7 Hz, 1H, =C*H*H), 5.72 (dd, $^2J_{HH}$ 1.8 Hz, $^4J_{HH}$ 0.7 Hz, 1H, =CH*H*), 5.21 (bs, 1H, -C*H*-C=CH_2); δ_C (176 MHz, $CDCl_3$) 163.2 (O-*C*(O)), 149.4 (*C*$_{Ar}$), 137.1 (*C*$_{Ar}$), 135.2 (=*C*<), 130.0 (*C*$_{Ar}$), 129.6 (*C*$_{Ar}$H),128.8 (=*C*H_2), 128.2 (*C*$_{Ar}$H), 127.0 (*C*$_{Ar}$), 125.2 (*C*$_{Ar}$), 123.7 (*C*$_{Ar}$H), 122.9 (*C*$_{Ar}$H), 120.2 (*C*$_{Ar}$H), 119.7 (*C*$_{Ar}$H), 118.6 (*C*$_{Ar}$H), 113.4 (*C*$_{Ar}$), 111.8 (*C*$_{Ar}$H), 40.2 (-C_{Ar}-*C*H-C_{Ar}).

4-(5-Methoxy-1*H*-indol-3-yl)-3-methylenechroman-2-one (**4d**). Colorless foam; Anal. calcd for $C_{19}H_{15}NO_3$: C, 74.74; H, 4.95; N, 4.59; Found C, 74.6; H, 5.0; N, 4.6; IR(ATR): 3304, 1731, 1483, 1452, 1251, 1230, 1169, 1141, 1099, 1061, 948, 801, 753, 657, 634, 615, 562 cm^{-1}; δ_H (700 MHz, $CDCl_3$) 8.03 (bs, 1H, N*H*), 7.27-7.30 (m, 2H, *H*-C_{Ar}), 7.15 (dd, $^3J_{HH}$ 8.1 Hz, $^5J_{HH}$ 1.3 Hz, 1H, -C*H*-CH-C-OMe), 7.04-7.11 (m, 2H, *H*-C_{Ar}), 6.93 (bd, $^3J_{HH}$ 2.4 Hz, 1H, -C*H*-NH-), 6.87 (dd, $^3J_{HH}$ 8.8 Hz, $^4J_{HH}$ = 2.5 Hz, 1H, -CH-C*H*-C-OMe), 6.73 (d, $^4J_{HH}$ 2.5 Hz, 1H, -C-C*H*-C-OMe), 6.41 (dd, $^2J_{HH}$ 1.7 Hz, $^4J_{HH}$ 0.9 Hz, 1H, =C*H*H), 5.71 (dd, $^2J_{HH}$ 1.7 Hz, $^4J_{HH}$ 0.9 Hz, 1H, =CH*H*), 5.21 (bs, 1H, -C*H*-C=CH_2), 3.74 (s, 3H, -C*H*$_3$); δ_C (176 MHz, $CDCl_3$) 164.0 (O-*C*(O)), 154.2 (*C*$_{Ar}$), 150.9 (*C*$_{Ar}$), 136.0 (=*C*<), 132.2 (*C*$_{Ar}$), 128.7 (*C*$_{Ar}$H), 128.5 (=*C*H_2), 128.4 (*C*$_{Ar}$H), 126.0 (*C*$_{Ar}$), 125.1 (*C*$_{Ar}$), 124.9 (*C*$_{Ar}$H), 124.5 (*C*$_{Ar}$H), 117.2 (*C*$_{Ar}$H), 113.6 (*C*$_{Ar}$), 112.6 (*C*$_{Ar}$H), 112.4 (*C*$_{Ar}$H), 102.0 (*C*$_{Ar}$H), 56.0 (-OC*H*$_3$), 40.3 (-C_{Ar}-*C*H-C_{Ar}).

8-Methoxy-4-(5-methoxy-1*H*-indol-3-yl)-3-methylenechroman-2-one (**4e**). Colorless foam; Anal. calcd for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18; Found C, 71.8; H, 5.1; N, 4.1; IR(ATR): 3442, 1738, 1484, 1444, 1285, 1189, 1132, 1093, 801, 795, 767, 604, 499 cm^{-1}; δ_H (700 MHz, $CDCl_3$) 8.03 (bs, 1H, N*H*), 7.28 (dd, $^3J_{HH}$ 8.8 Hz, $^5J_{HH}$ 0.5 Hz, 1H, -N-C-C*H*-CH-C-OMe), 7.00 (t, $^3J_{HH}$ 8.0 Hz, 1H, -CH-C*H*-CH-), 6.93 (bd, $^3J_{HH}$ 2.4 Hz, 1H, -C*H*-NH-), 6.88 (dd, $^3J_{HH}$ 8.0 Hz, $^4J_{HH}$ 1.3 Hz, 1H, -C*H*-CH-CH-C-OMe), 6.86 (dd, $^3J_{HH}$ 8.8 Hz, $^4J_{HH}$ 2.5 Hz, 1H, -C-CH-C*H*-C-

OMe), 6.76 (d, $^4J_{HH}$ 2.5 Hz, 1H, -C-C*H*-C-OMe), 6.69 (ddd, $^3J_{HH}$ 8.0 Hz, $^4J_{HH}$ 1.3 Hz, $^5J_{HH}$ 0.8 Hz, 1H, -CH-CH-C*H*-C-OMe), 6.40 (dd, $^2J_{HH}$ 1.7 Hz, $^4J_{HH}$ = 0.9 Hz, 1H, =C*H*H), 5.70 (dd, $^2J_{HH}$ 1.7 Hz, $^4J_{HH}$ 0.9 Hz, 1H, =CH*H*), 5.19 (bs, 1H, -C*H*-C=CH_2), 3.93 (s, 3H, -CH_3), 3.75 (s, 3H, -CH_3); δ_C (176 MHz, $CDCl_3$) 163.4 (O-*C*(O)), 154.1 (C_{Ar}), 147.9 (C_{Ar}), 140.2 (C_{Ar}), 135.9 (=*C*<), 132.2 (C_{Ar}), 128.7 (C_{Ar}H), 128.3 (=*C*H_2), 126.3 (C_{Ar}), 126.0 (C_{Ar}), 124.7 (C_{Ar}H), 124.4 (C_{Ar}H), 119.7 (C_{Ar}H), 113.5 (C_{Ar}), 112.5 (C_{Ar}H), 112.4 (C_{Ar}H), 111.4 (C_{Ar}H), 101.9 (C_{Ar}H), 56.3 (-OCH_3), 56.0 (-OCH_3), 40.5 (-C_{Ar}-*C*H-C_{Ar}).

6-Chloro-4-(5-methoxy-1*H*-indol-3-yl)-3-methylenechroman-2-one (**4f**). Colorless foam; Anal. calcd for $C_{19}H_{14}ClNO_3$: C, 67.16; H, 4.15; N, 4.12; Found C, 67.4; H, 4.1; N, 4.1; IR(ATR): 3404, 2996, 2939, 2899, 2830, 1738, 1478, 1217, 1172, 1131, 1106, 1083, 1049, 1024, 800, 530 cm^{-1}; δ_H (700 MHz, $CDCl_3$) 8.06 (bs, 1H, N*H*), 7.31 (dd, $^3J_{HH}$ 8.8 Hz, $^5J_{HH}$ 0.5 Hz, 1H, -N-C-C*H*-CH-C-OMe), 7.24 (ddd, $^3J_{HH}$ 8.7 Hz, $^4J_{HH}$ 2.5 Hz, $^5J_{HH}$ 0.6 Hz, 1H, -CCl-CH-C*H*-), 7.09 (d, $^3J_{HH}$ 8.7 Hz, 1H, -CCl-C*H*-CH-), 7.06 (dd, $^4J_{HH}$ 2.5 Hz, $^5J_{HH}$ 0.9 Hz, 1H, -C-CCl-C*H*-), 6.97 (bd, $^3J_{HH}$ 2.4 Hz, 1H, -C*H*-NH-), 6.89 (dd, $^3J_{HH}$ 8.8 Hz, $^4J_{HH}$ 2.5 Hz, 1H, -C-CH-C*H*-C-OMe), 6.71 (d, $^4J_{HH}$ 2.5 Hz, 1H, -C-C*H*-C-OMe), 6.45 (dd, $^2J_{HH}$ 1.9 Hz, $^4J_{HH}$ 0.8 Hz, 1H, =C*H*H), 5.71 (dd, $^2J_{HH}$ 1.9 Hz, $^4J_{HH}$ 0.8 Hz, 1H, =CH*H*), 5.18 (bs, 1H, -C*H*-C=CH_2), 3.76 (s, 3H, -CH_3); δ_C (176 MHz, $CDCl_3$) 163.3 (O-*C*(O)), 154.3 (C_{Ar}), 149.4 (C_{Ar}), 140.2(C_{Ar}), 135.9 132.2 (C_{Ar}), 128.7 (C_{Ar}H), 135.0 (=*C*<), 132.2 (C_{Ar}), 130.0 (C_{Ar}), 129.4 (=*C*H_2), 128.8 (C_{Ar}H), 128.2 (C_{Ar}H), 126.9 (C_{Ar}), 125.7 (C_{Ar}), 124.5 (C_{Ar}H), 118.6 (C_{Ar}H), 112.7 (C_{Ar}H), 112.5 (C_{Ar}H), 101.8 (C_{Ar}H), 56.0 (-OCH_3), 40.2 5 (-C_{Ar}-*C*H-C_{Ar}).

Diethyl (8-hydroxy-2-oxo-2*H*-chromen-3-yl)phosphonate (**7**). To a solution of 2,3-dihydroxybenzaldehyde (6.9 g, 50 mmol) **5** and triethyl phosphonoacetate **6** (11.2 g, 50 mmol) in toluene (100 mL) piperidine (0.5 mL) and acetic acid (1.0 mL) were added. The solution was then heated at reflux under a Dean-Stark trap until the starting materials were consumed (ca. 15 h, TLC and ^{31}P NMR monitoring). After evaporation of the solvent the residue was purified by chromatography using CH_2Cl_2/MeOH, 15:1, as eluent (R_F ~ 0.6) to yield desired phosphonate **7** (8.05 g, 54%). Colorless crystals, mp 126-128 °C; Anal. calcd for $C_{13}H_{15}O_6P$: C, 52.36; H, 5.07; Found C, 52.3; H, 5.1; IR(ATR): 3147, 2986, 2908, 1717, 1577, 1465, 1220, 1166, 1047, 1013, 994, 974, 957, 764, 632, 499 cm^{-1}; δ_H (700 MHz, acetone-d6) 9.22 (bs, 1H, -OH), 8.54 (d, $^2J_{PH}$ 17.3 Hz, 1H, *H*-CP), 7.32 (dd, $^3J_{HH}$ 7.3 Hz, $^4J_{HH}$ 1.4 Hz, 1H, C-C*H*-CH-), 7.28 (dd, $^3J_{HH}$ 7.3 Hz, $^4J_{HH}$ 1.4 Hz, 1H, C*H*-C(OH)-), 7.24 (t, $^3J_{HH}$ 7.3 Hz, 1H, -CH-C*H*-CH-), 4.17-4.30 (m, 4H, -CH_2-), 1.32 (t, $^3J_{HH}$ 7.1, 6H, -CH_3); δ_C (700 MHz, acetone-d6) 158.2 (d, $^2J_{PC}$ 15.1 Hz, O-*C*(O)), 154.4 (d, $^2J_{PC}$ 6.1 Hz, HC_{Ar}-C_{Ar}P), 145.4 (C_{Ar}), 144.6 (C_{Ar}), 125.4 (C_{Ar}H), 121.4 (C_{Ar}H), 121.2 (C_{Ar}H), 119.7 (d, $^3J_{PC}$ 14.0 Hz, -C_{Ar}), 118.9 (d, $^1J_{PC}$ 195.0 Hz, -C_{Ar}), 63.4 (d, $^2J_{PC}$ 5.6 Hz, CH_3-*C*H_2-OP), 16.7 (d, $^3J_{PC}$ 6.2 Hz, *C*H_3-CH_2-OP); δ_P (283.3 MHz, $CDCl_3$) 12.5ppm.

Diethyl (8-((*tert*-butyldimethylsilyl)oxy)-2-oxo-2*H*-chromen-3-yl)phosphonate (**8**). To a stirred solution of diethyl (8-hydroxy-2-oxo-2*H*-chromen-3-yl)phosphonate **7** (0.895 g, 3.0 mmol) and imidazole (0.408 g, 6.0 mmol) in CH_2Cl_2 (15 mL), *tert*-butyldimethylsilyl chloride (TBDMS-Cl) (0.497 g, 3.3 mmol) was added in one portion and the resulting mixture was stirred at rt for 24 h. Then solution was transferred into a separatory funnel and successively washed with 1M solution of citric acid (15 mL) and 1M solution of $NaHCO_3$ (15 mL). The organic layer was dried over $MgSO_4$ and evaporated. The crude product was purified by chromatography on silica gel using CH_2Cl_2/Me_2CO (10:1) as eluent (R_F ~ 0.7) to afford the desired silyl-protected coumarin **8** (1.126 g, 91%). Colorless crystals, mp 81-83 °C; Anal. calcd for $C_{19}H_{29}O_6PSi$: C, 55.32; H, 7.09; Found C, 55.2; H, 7.1; IR(ATR): 3363, 3186, 1767, 1666, 1569, 1384, 1367, 1309, 1139, 1124, 1034, 749, 734, 539, 505 cm^{-1}; δ_H (700 MHz, $CDCl_3$) 8.46 (d, $^3J_{PH}$ 17.2 Hz, 1H, *H*C_{Ar}-C_{Ar}P), 7.12-7.19 (m, 3H, C_{Ar}*H*-C_{Ar}), 4.20-4.33 (m, 4H, -CH_2-), 1.37 (t, $^3J_{HH}$ 7.1, $^4J_{PH}$ 0.5 Hz, 6H, -CH_2-CH_3), 1.03 (s, 9H, ^{t}Bu), 0.25 (s, 6H, Si(CH_3)$_2$); δ_C (176 MHz, $CDCl_3$) 157.9 (d, $^2J_{PC}$ 14.5 Hz, O-*C*(O)), 153.7 (d, $^2J_{PC}$ 6.5 Hz, HC_{Ar}-C_{Ar}P), 146.9 (C_{Ar}), 143.4 (C_{Ar}), 125.4 (C_{Ar}H), 124.9 (C_{Ar}H), 121.8 (C_{Ar}H), 119.2 (d, $^3J_{PC}$ 14.1 Hz, -C_{Ar}), 118.0 (d, $^1J_{PC}$ 196.4 Hz, -C_{Ar}), 63.6 (d, $^2J_{PC}$ 6.1 Hz, CH_3-*C*H_2-OP), 25.7 (-C-(*C*H_3)$_3$), 18.5(-*C*-(CH_3)$_3$), 16.5 (d, $^3J_{PC}$ 6.3 Hz, *C*H_3-CH_2-OP), -4.3 (-Si(*C*H_3)$_2$); δ_P (283.3 MHz, $CDCl_3$) 12.5ppm.

Diethyl ((3*R,4*S**)-8-((*tert*-butyldimethylsilyl)oxy)-4-(1*H*-indol-3-yl)-2-oxochroman-3-yl)phosphonate** (**9**). To a stirred solution of the silyl-protected coumarin **8** (0.412 g, 1.0 mmol) and indole **2a** (0.176 g, 1.5 mmol) in CH_2Cl_2 (10 mL), 1,5,7-triazabicyclo[4.4. 0]dec-5-ene (0.278 g, 2.0 mmol) was added in one portion. Stirring was continued at rt for 24 h. The resulting mixture was acidified with hydrochloric acid (5%, 10 mL) and separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated. The oily residue was subjected for column chromatography on silica gel using CH_2Cl_2/MeOH (20:1) as eluent (R_F ~ 0.60) to give pure phosphonate adduct **9** (0.281 g, 53%). Colorless crystals, mp 172-174 °C; Anal. calcd for $C_{27}H_{36}NO_6PSi$: C, 61.23; H, 6.85; N, 2.64; Found C, 61.3; H, 6.7; N, 2.7; IR(ATR): 3326, 2957, 2930, 2859, 1764, 1481, 1251, 1145, 1081, 1042, 1019, 867, 839, 825, 782, 738 cm^{-1}; δ_H (700 MHz, $CDCl_3$) 8.09 (bs, 1H, N*H*), 7.70 (bd, $^3J_{HH}$ 7.8 Hz, 1H, *H*-C_{Ar}), 6.86-7.36 (m, 6H, *H*-C_{Ar}), 6.56 (dd, $^3J_{HH}$ 2.5 Hz, $^4J_{HH}$ 0.9 Hz, 1H, -C*H*-NH-), 5.08 (bd, $^3J_{PH}$ 12.8 Hz, 1H, -C*H*-C_{Ar}), 4.12-4.21 (m, 2H, -CH_2-), 3.90-3.97 and 3.65-3.72 (m, 2H, -CH_2-), 3.83 (dd, $^2J_{PH}$ 25.2 Hz, $^3J_{HH}$ 1.1 Hz, 1H, *H*-C-P), 1.34 (t, $^3J_{HH}$ 7.1 Hz, 3H, CH_3-), 1.02-1.06 (m, 12H, ^{t}Bu and CH_3-CH_2-), 0.26 (s, 3H, -Si(CH_3)$_2$), 0.25 (s, 3H, -Si(CH_3)$_2$); δ_C (176 MHz, $CDCl_3$) 163.1 (d, $^2J_{PC}$ 5.2 Hz, O-*C*(O)), 143.6 (*C*$_{Ar}$), 143.1 (*C*$_{Ar}$), 136.8 (*C*$_{Ar}$), 125.3 (*C*$_{Ar}$), 125.0 (*C*$_{Ar}$H), 124.6 (*C*$_{Ar}$), 122.9 (*C*$_{Ar}$H), 122.1 (*C*$_{Ar}$H), 121.3 (*C*$_{Ar}$H), 120.9 (*C*$_{Ar}$H), 120.3 (*C*$_{Ar}$H), 118.4 (*C*$_{Ar}$H), 116.9 (d, $^3J_{PC}$ 18.1 Hz, -*C*$_{Ar}$-C_{Ar}H-N), 111.7 (*C*$_{Ar}$H), 63.4 (d, $^2J_{PC}$ 6.7 Hz, CH_3-*C*H_2-OP), 63.2 (d, $^2J_{PC}$ 6.7 Hz, CH_3-*C*H_2-OP), 47.5 (d, $^1J_{PC}$ 123.9 Hz, -*C*H-P), 34.8 (d, $^3J_{PC}$ 3.2 Hz, -C_{Ar}-*C*H-C_{Ar}), 25.8 (C-(*C*H3)$_3$), 25.8 (*C*-(CH3)$_3$), 16.4 (d, $^2J_{PC}$ 6.2 Hz, CH_3-*C*H_2-OP), 16.2 (d, $^2J_{PC}$ 6.2 Hz, CH_3-*C*H_2-OP), -4.3 (Si-*C*H_2), -4.4 (Si-*C*H_2); δ_P (283.3 MHz, $CDCl_3$) 18.9 ppm.

8-((*tert*-Butyldimethylsilyl)oxy)-4-(1*H*-indol-3-yl)-3-methylenechroman-2-one (**10**). A mixture of diethyl ((3*R**,4*S**)-8-((*tert*-butyldimethylsilyl)oxy)-4-(1*H*-indol-3-yl)-2-oxochroman-3-yl)phosphonate **9** (0.265 g, 0.5 mmol) and K_2CO_3 (0.207 g, 1.5 mmol) in THF (5 mL) was stirred at 0 °C for 15 min. Then aqueous formaldehyde (40%, 0.20 mL) was added and resulting suspension was stirred at 20 °C for an additional 3 h. The mixture was then concentrated *in vacuo* and the solid residue was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over $MgSO_4$ and evaporated. The oily residue was subjected for column chromatography on silica gel using CH_2Cl_2/Me_2CO (10:1) as eluent (R_F ~ 0.8) to afford methylenelactone **10** (0.122 g, 60%). Colorless foam; Anal. calcd for $C_{24}H_{27}NO_3Si$: C, 71.08; H, 6.71; N, 3.45; Found C, 71.3; H, 6.7; N, 3.5; IR(ATR): 3406, 2952, 2929, 2885, 2857, 1738, 1478, 1460, 1295, 1253, 1187, 1124, 860, 838, 802, 780, 738 cm^{-1}; δ_H (700 MHz, $CDCl_3$) 8.10 (bs, 1H, N*H*), 6.68-7.40 (m, 8H, *H*-C_{Ar}), 6.36 (dd, $^2J_{HH}$ 1.6 Hz, $^4J_{HH}$ 0.9 Hz, 1H, =C*H*H), 5.72 (dd, $^2J_{HH}$ 1.6 Hz, $^4J_{HH}$ 0.9 Hz, 1H, =CH*H*), 5.21 (bs, 1H, -C*H*-C=CH_2), 1.05 (s, 12H, ^{t}Bu and CH_3-CH_2-), 0.27 (s, 3H, -Si(CH_3)$_2$), 0.26 (s, 3H, -Si(CH_3)$_2$); δ_C (176 MHz, $CDCl_3$) 163.3 (O-*C*(O)), 143.9 (*C*$_{Ar}$), 142.3 (*C*$_{Ar}$), 137.0 (*C*$_{Ar}$), 136.4 (=*C*<), 127.9 (=*C*H_2), 126.8 (*C*$_{Ar}$), 125.6 (*C*$_{Ar}$), 124.7 (*C*$_{Ar}$H), 123.4 (*C*$_{Ar}$H), 122.6 (*C*$_{Ar}$H), 120.8 (*C*$_{Ar}$H), 120.6 (*C*$_{Ar}$H), 119.9 (*C*$_{Ar}$H), 119.7 (*C*$_{Ar}$H), 114.4 (*C*$_{Ar}$), 111.7 (*C*$_{Ar}$H), 40.75 (-C_{Ar}-*C*H-C_{Ar}), 25.9 (-C-(*C*H_3)$_3$), 18.6 (-*C*-(CH_3)$_3$), -4.4 (-Si(*C*H_3)$_2$).

8-Hydroxy-4-(1*H*-indol-3-yl)-3-methyl-2*H*-chromen-2-one (**11**). To a stirred solution of compound **10** (0.101 g, 0.25 mmol) in anhydrous THF (2 mL) was added a solution of TBAF in THF (1.1M, 0.45 mL, 0.50 mmol). The mixture was stirred at rt overnight until disappearance of the starting material (TLC). After evaporation *in vacuo* the residue was purified by flash chromatography (CH_2Cl_2/Me_2CO 10:1) to yield **11** (0.052 g, 71%). Colorless foam; Anal. calcd for $C_{18}H_{13}NO_3$: C, 74.22; H, 4.50; N, 4.81; Found C, 74.4; H, 4.5; N, 4.8; IR(ATR): 3363, 3187, 2983, 1668, 1570, 1420, 1384, 1369, 1310, 1139, 1092, 1036, 751, 735, 512 cm^{-1}; δ_H (700 MHz, acetone-d6) 10.80 (bs, 1H, N*H*), 8.81 (bs, 1H, O*H*), 7.58 (bd, $^3J_{HH}$ 8.2 Hz 1H, C_{Ar}*H*-C_{Ind}-C_{Ind}), 7.55 (s, 1H, *C*$_{Ar}$*H*-NH), 7.29 (bd, $^3J_{HH}$ 8.0 Hz, 1H, C_{Ar}*H*-C_{Ind}-NH), 7.22 (dt, $^3J_{HH}$ 7.6 Hz, $^4J_{HH}$ 0.8 Hz, 1H, C_{Ind}*H*-C_{Ind}H-C_{Ind}-C_{Ind}), 7.06-7.09 (m, 2H, *H*$_{Ar}$), 7.00 (t, $^3J_{HH}$ 7.7 Hz, 1H, C_{Ar}H-C_{Ar}*H*-C_{Ar}H), 6.81 (dt, $^3J_{HH}$ 8.0 Hz, $^4J_{HH}$ 1.3 Hz, 1H, *H*$_{Ar}$), 2.02 (s, 3H, -CH_3);δ_C (176 MHz, $CDCl_3$ + 10% CD_3OD) 163.2 (O-*C*(O)), 146.8 (*C*$_{Ar}$), 144.1 (*C*$_{Ar}$), 140.8 (*C*$_{Ar}$), 136.1 (*C*$_{Ar}$), 126.4 (*C*$_{Ar}$),

124.8 ($C_{Ar}H$), 124.0 ($C_{Ar}H$), 123.0 (C_{Ar}), 122.4 ($C_{Ar}H$), 121.8 (C_{Ar}), 120.1 ($C_{Ar}H$), 119.7 ($C_{Ar}H$), 118.4 ($C_{Ar}H$), 117.4 ($C_{Ar}H$), 111.7 ($C_{Ar}H$), 109.6 (C_{Ar}), 15.1 (-CH$_3$).

Supplementary Material

Supplementary material containing copies of IR, ^{1}H and ^{13}C NMR spectra associated with this paper can be found in the online version.

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