DOI: 10.1002/ejoc.200900207

"On-Water"-Promoted *C*-Alkylation of Indoles with 2-Aryl-3-nitro-2*H*-chromenes under Catalyst-Free Conditions

Pateliya Mujjamil Habib,[a] Veerababurao Kavala,[a] B. Rama Raju,[a] Chun-Wei Kuo,[a] Wen-Chang Huang,[a] and Ching-Fa Yao*[a]

Keywords: "On-water" chemistry / Alkylation / 2*H*-Chromenes / Indoles / Green chemistry / Synthetic methods

An environmentally benign method for the synthesis of indolyl(nitro)chromans from indoles and 2-aryl-3-nitro-2*H*-chromenes under catalyst-free conditions by use of an "on-water" concept is described. The salient features of the methodology are its clean reaction conditions, the eco-friendly medium, and the easy isolation and excellent diastereoselectivities of the products.

Introduction

Water-mediated reactions have received considerable attention in synthetic organic chemistry for environmental, economical, and safety-related reasons, because they display unique reactivities and selectivities that are not achieved in organic solvents.[1] Sharpless and his co-workers have described "on-water" conditions under which a substantial rate acceleration was observed when the organic reactants were insoluble in the aqueous phase.[2] This concept has been further explored by several other groups for various reactions.[3] In recent years, a great many efforts have been implemented in the development of catalyst-free processes employing water as a medium to accomplish cleaner syntheses.[4] Indeed, the increasing demands of environmental legislation require the minimization – or, preferably, the elimination – of waste production in chemical syntheses.[5] The development of efficient and convenient synthetic methodologies for "on-water" conditions is thus an important subject at present.[3]

2*H*-Chromene derivatives are an important class of compounds, widely distributed in nature.[6] Among 2*H*-chromene derivatives, 3-nitro-2*H*-chromenes have attracted considerable attention in recent years due to their use as phospholipase C inhibitors[7] and as intermediates for the synthesis of *N*-hydroxyspirolactams and aminochromans.[8] Recently, it was reported that 3-nitro-2*H*-chromene derivatives act as 2π components in 1,3-dipolar cycloadditions of azomethine ylides.[9] In addition, some 3-nitro-2*H*-chromene derivatives have been found to display efficient optical second-harmonic generation.[10] 3-Substituted indole derivatives are known to be valuable intermediates in pharmaceutical and biologically active compounds.[11] Fused heterocyclic systems containing both 2*H*-chromene and indole moieties have been found to exhibit biological activity.[12]

Syntheses of 3-substituted indole derivatives achieved through conjugate additions between indoles and Michael acceptors such as nitroalkenes and α,β-unsaturated carbonyl compounds, catalyzed by either protic or Lewis acids, are well documented in the literature.[13] There are only a small number of reports regarding the use of nitrochromenes as Michael acceptors for such reactions,[14] although Sosnovskikh's group have studied Michael additions of various nucleophiles to 3-nitro-2-trihalomethyl-2*H*-chromenes.[15] Indole additions with similar structural moieties such as 3-nitrocoumarin with the aid of $Mg(OTf)_2$ have been reported by Ye et al.[16]

In our previous article we reported on the iodine-catalyzed Michael addition between indole and 3-nitro-2*H*-chromene, which furnished two diastereomeric products in 72 h.[14a] In continuation of our research into nitro olefins,[17] we were in search of a method to accomplish the alkylation of indoles with nitrochromenes in an environmentally benign way. Recently, we have achieved alkylations of indoles with various nitrostyrenes in water under catalyst-free conditions, affording indolyl(nitro)styrenes in good yields.[18] This result prompted us to investigate reactions between 2-aryl-3-nitro-2*H*-chromenes and indoles in aqueous media further.

Results and Discussion

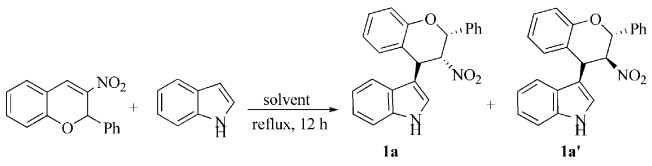
In our preliminary investigation, we treated indole with 3-nitro-2-phenyl-2*H*-chromene in water without any catalyst at room temperature. We were able to obtain only a ca. 15% yield of the product after 24 h. Upon increasing the reaction temperature to reflux conditions, however, there

[a] Department of Chemistry, National Taiwan Normal University, 88, Sec. 4, Tingchow Road, Taipei, Taiwan 116, R. O. C.
E-mail: cheyaocf@ntnu.edu.tw

was significant increase (91% yield) in the formation of the corresponding Michael adduct, 3-(3-nitro-2-phenylchroman-4-yl)-1*H*-indole (**1a** and **1a′**). The product obtained was a mixture of two diastereomers in a 7:3 ratio, determined by ^{1}H NMR analysis. The formation of two diastereomers is presumably due to *syn* or *anti* addition of indole with 3-nitro-2-phenyl-2*H*-chromene. These stereoisomers were separated by careful crystallization of the crude product from a mixture of ethyl acetate and hexane. The pure compounds (major and minor isomers) obtained were characterized by spectroscopic techniques and also by single-crystal XRD analysis, discussed in detail below.

In order to check the efficacy of water relative to organic solvents, we carried out the reaction between 3-nitro-2-phenyl-2*H*-chromene and indole in various solvents at reflux temperature without using any catalyst (Table 1). In organic solvents such as dichloromethane, acetonitrile, EtOH, or DMF, the yields of the alkylated products (**1a** and **1a′**) were very poor (Table 1, Entries 1, 2, 3, 4). None of the expected product was obtained in toluene, THF, or dichloroethane, even though the reaction systems were completely homogeneous (Table 1, Entries 5, 6, 7). It is interesting to note, however, that when water alone was used as solvent under the same conditions, the yield increased drastically to 91% (Table 1, Entry 9), which is better than in any of the organic solvents used (either polar or nonpolar). These results thus showed the superiority of water over the organic solvents (Table 1).

Table 1. Reaction between indole and 3-nitro-2*H*-chromene in various solvents.



1a **1a'**

Entry	Solvent	Yield (%)[a]	Major/minor[b]
1	CH_2Cl_2	10 (7)	77:23
2	MeCN	2	75:25
3	EtOH	36 (30)	66:34
4	DMF	32 (28)	71:29
5	toluene	0	–
6	THF	0	–
7	$Cl(CH_2)_2Cl$	0	–
8[c]	neat	18 (10)	68:32
9	H_2O	91 (87)	78:32

[a] All the reactions were conducted on a 1 mmol scale, and yields were determined from crude ^{1}H NMR spectra with toluene as internal standard. Isolated yields are shown in parentheses. [b] The major and minor diastereomers were determined from the crude ^{1}H NMR spectrum. [c] The reaction was conducted under inert conditions at 100 °C.

To explore the scope and limitations of this methodology further, we tested the alkylation of indole with various 3-nitro-2*H*-chromenes under optimized reaction conditions (Table 2). As can be seen, the alkylation of indole proceeded well with various 3-nitro-2*H*-chromenes to afford the Michael adducts in good yields. The product formation was governed by both electronic and steric factors, according to the nature of the substituent on the 3-nitro-2*H*-chromene. 3-Nitro-2*H*-chromene derivatives in which the phenyl rings were substituted with electron-withdrawing groups such as fluoro and chloro (Entries 1 and 4), for example, reacted efficiently through their 2-positions to afford the corresponding adducts in excellent yields. However, 3-nitro-2*H*-chromene derivatives in which the phenyl rings were substituted with electron-donating groups such as methyl and methoxy (Entries 2 and 3) required relatively longer reaction times to furnish the corresponding indolylchroman adducts. The diastereoselectivities of the products remained the same irrespective of the substituent at the 2-position in the 3-nitro-2*H*-chromene derivative.

Similarly, the nature of the substitution on the 3-nitro-2*H*-chromene had an effect on the progress of the reaction, as is evident from Table 2. A prolonged reaction time, for example, was observed with 6-methoxy-3-nitro-2-phenyl-2*H*-chromene (Entry 5), containing the electron-releasing OMe group, whereas the reaction between 6-bromo-3-nitro-2-phenyl-2*H*-chromene and indole (Entry 6) went to completion in a shorter reaction time to afford the Michael adduct in excellent yield.

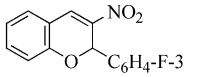
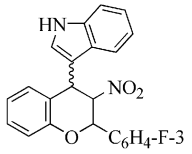
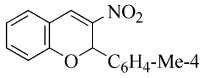
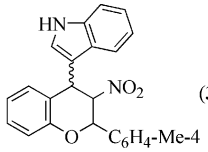
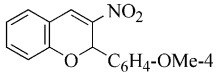
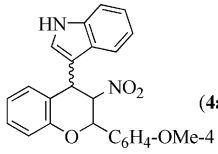
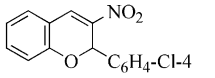
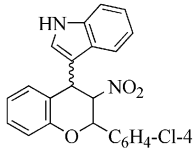
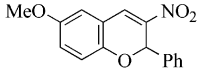
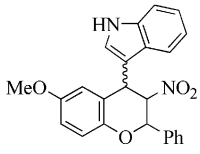
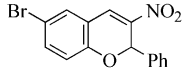
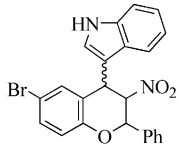
In order to assign the stereochemistries of the major and minor diastereomeric products, the Michael adduct 4-(indol-3-yl)-2-(4-methoxyphenyl)-3-nitro-2*H*-chromene (**4a**) was chosen as the model compound. The two diastereomers were separated by careful crystallization. The ^{1}H NMR spectrum of the isolated major product displayed three signals at δ = 5.32 ppm (s, 1 H), 5.29 ppm (s, 1 H), and 4.99 ppm (s, 1 H) for 2-H, 3-H, and 4-H, respectively. This is the characteristic pattern of a *cis,trans* diastereomer.[14]

NOE experiments were performed to assign the relative configurations of the two diastereomers. In the case of the major compound [**4a**; Figure 1 (right)], irradiation of 2-H showed an enhancement of 3.2% on 3-H. Similarly, irradiation of 3-H showed an enhancement of 6.9% on 2-H. We can hence deduce that 2-H and 3-H are in a *cis* orientation to one another and that the relative configuration of the major isomer is (2*S**,3*S**,4*R**). Further, this was also confirmed by single-crystal X-ray diffraction [Figure 1 (left)].

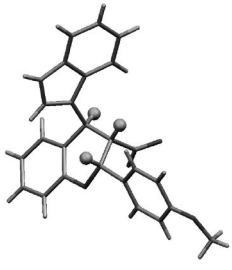
The ^{1}H NMR spectrum of the minor product showed a doublet at δ = 5.52 ppm (J = 9.2 Hz), a doublet of doublets at δ = 5.41 ppm (J = 9.2, 5.5 Hz), and a doublet at δ = 5.15 ppm (J = 5.5 Hz), for 2-H, 3-H, and 4-H, respectively. Comparison of the chemical shifts of *cis,trans* and *trans,cis* isomers showed the proton shifts of the latter lying downfield by ca. 0.15 ppm. This thus shows the pattern of a *trans,cis* diastereomer.[14]

In the case of the minor compound [**4a′**; Figure 2 (right)], irradiation of 3-H showed an enhancement of 4.6% on 4-H, whereas irradiation of 4-H showed an enhancement of 4% on 3-H. From the results obtained we can deduce that 3-H and 4-H are in a *cis* orientation to one another and that the relative configuration of the minor isomer is (2*S**,3*R**,4*R**). The stereochemistry of the minor product was further confirmed by single-crystal X-ray diffraction, as shown in Figure 2 (left).

Table 2. *C*-Alkylation of indole with various 2-aryl-3-nitro-2*H*-chromenes.

Entry	3-Nitrochromene derivative	Product		Time [h]	Yield [%][a,b]	Major/Minor[c]
1			(**2a**)	12	79	78:22
2			(**3a**)	12	81	73:27
3			(**4a**)	18	70	70:30
4			(**5a**)	12	82	75:25
5			(**6a**)	16	74	77:23
6			(**7a**)	10	84	71:29

[a] Isolated yields. [b] Mixture of diastereomers. [c] Ratio of major and minor diastereomers determined from the crude ^{1}H NMR spectrum.



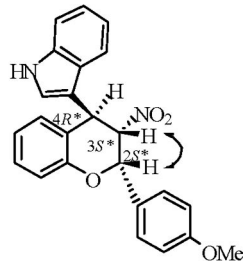
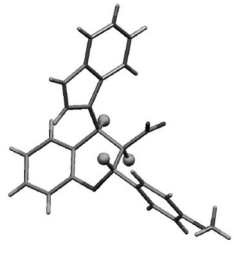


Figure 1. Crystal structure of **4a** (major diastereomer) (left).[19] NOE correlation of **4a** (right).



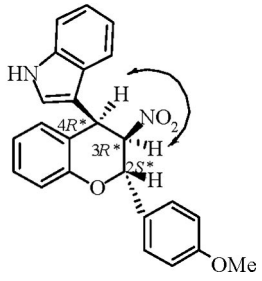
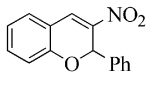
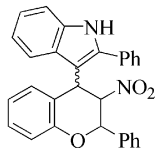
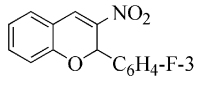
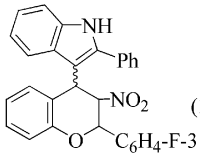
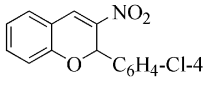
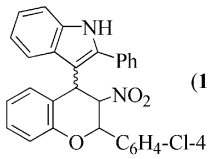
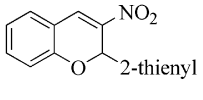
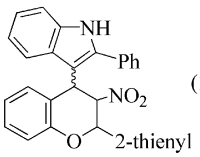
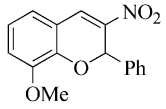
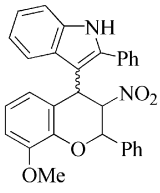
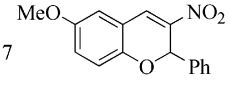
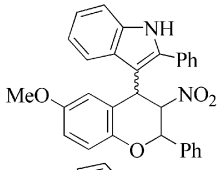
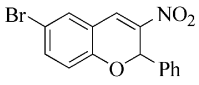
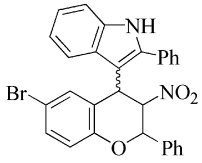
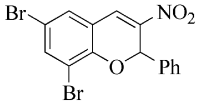
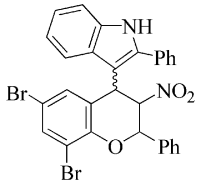
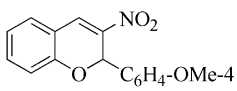
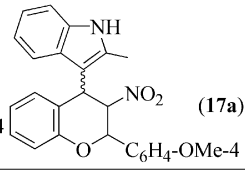


Figure 2. Crystal structure of **4a′** (minor diastereomer) (left).[19] NOE correlation of **4a′** (right).

Having successfully performed reactions between indole and an array of 3-nitro-2*H*-chromenes, we probed the feasibility of the reactions further with other substituted indole derivatives. The reaction between *N*-methylindole and 3-nitro-2-phenyl-2*H*-chromene furnished a mixture of diastereomers (**8a**, **8a′**) in a ratio of 65:35. Other indoles such as 5-bromoindole and 2-carboxyindole, however, did not react with 3-nitro-2-phenyl-2*H*-chromene under these reaction conditions.

It was observed that increasing the steric hindrance at the indole 2-position – the alkylation of 2-methyl- or 2-phenylindole, for example – resulted in reactions that pro-

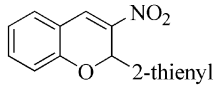
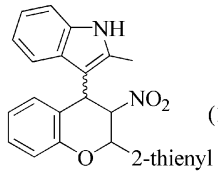
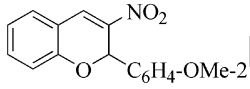
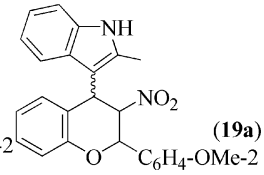
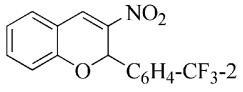
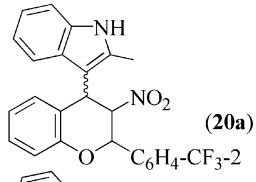
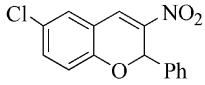
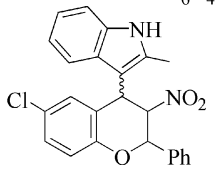
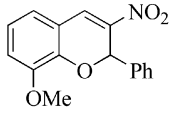
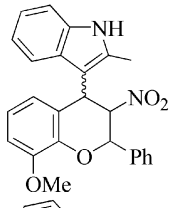
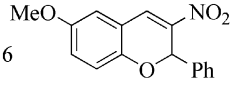
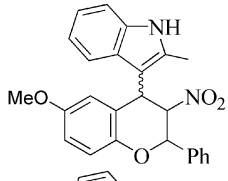
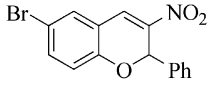
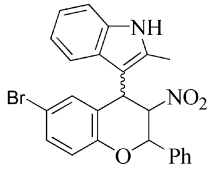
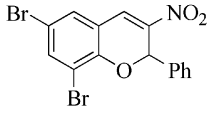
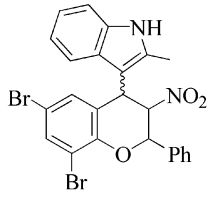
Table 3. *C*-Alkylation of 2-phenylindole and 2-methylindole with various 2-aryl-3-nitro-2*H*-chromenes (Entries 1–10, **9a**–**17a**).

Entry	3-Nitrochromene derivative	Product		Time [h]	Yield [%][a,b]	Major/Minor[c]
1			(**9a**)	12	73	>99:1
2			(**10a**)	12	83	>99:1
3			(**11a**)	12	81	>99:1
4			(**12a**)	12	76	96:4
6			(**13a**)	13	73	>99:1
7			(**14a**)	18	71	>99:1
8			(**15a**)	10	78	89:11
9			(**16a**)	10	81	96:4
10			(**17a**)	15	54	>99:1

[a] Isolated yields. [b] Mixture of diastereomers. [c] Ratio of major and minor diastereomers determined from the crude ^{1}H NMR spectrum.

ceeded efficiently at the 3-position with excellent diastereoselectivity. With this encouraging result to hand, we focused our attention on examining the reactions between 2-methyl- or 2-phenylindole and various 2-aryl-3-nitro-2*H*-chromenes. The results are shown in Tables 3 and 4. Alkylation of 2-phenylindole with 3-nitro-2-phenyl-2*H*-chromene (Table 3, Entry 1) proceeded well, affording the product in good yield. Similarly, 2-aryl-3-nitro-2*H*-chromenes containing various substituents, such as 3-fluorophenyl, 4-chlorophenyl, or 2-thienyl groups, at their 2-

Table 4. *C*-Alkylation of 2-phenylindole and 2-methylindole with various 2-aryl-3-nitro-2*H*-chromenes (Entries 11–18, **18a**–**25a**).

Entry	3-Nitrochromene derivative	Product		Time [h]	Yield [%][a,b]	Major/Minor[c]
11			(**18a**)	13	73	>99:1
12			(**19a**)	15	69	92:8
13			(**20a**)	15	78	>99:1
14			(**21a**)	12	79	94:6
15			(**22a**)	13	73	>99:1
16			(**23a**)	15	71	92:8
17			(**24a**)	15	82	>93:7
18			(**25a**)	12	86	99:1

[a] Isolated yields. [b] Mixture of diastereomers. [c] Ratio of major and minor diastereomers determined from crude ^{1}H NMR spectrum.

positions (Table 3, Entries 2, 3, and 4) reacted with 2-phenylindole to furnish the corresponding Michael adducts in excellent yields. Reactions between 2-phenylindole and 2-aryl-3-nitro-2*H*-chromenes containing an electron-releasing group (OMe, Entries 6, 7) required longer reaction times, whereas those with 6-bromo-3-nitro-2-phenyl-2*H*-chromene (Entry 8) or 6,8-dibromo-3-nitro-2-phenyl-2*H*-chromene (Entry 9), containing the electron-withdrawing Br group, required shorter reaction times. Excellent diastereoselectivities were observed with 2-aryl-3-nitro-2*H*-chromenes and 2-phenylindole as the substrates (Table 3, Entries 1–9).

We next turned our attention to reactions between 2-aryl-3-nitro-2*H*-chromenes and 2-methylindole. The reactions proceeded well, with degrees of selectivity as good as those obtained with 2-phenylindole. The reactions between 2-methylindole and 3-nitrochromenes containing electron-releasing groups (Table 3, Entry 10; Table 4, Entries 12, 15, and 16) were sluggish, whereas shorter reaction times were required with 3-nitrochromene derivatives containing electron-withdrawing groups (Table 4 Entries 13, 14, 17, and 18) to afford the products in good yields. We have thus examined the effect of 2-substituted indoles – mainly 2-methyl- and 2-phenylindole – and found them to play key roles with regard to the stereoselectivities of the reactions.

Moreover, Korotaev et al. reported that substitution at the 2-position of 3-nitro-2*H*-chromene with a bulkier system such as a CCl_3 group resulted in the loss of diastereoselectivity in additions to indole and *N*-methylindole.[14b]

To reinvestigate, we carried out the alkylation reaction of indole with the bulky substrate 2,2-dimethyl-3-nitrochromene (two methyl groups introduced at the 2-position of 3-nitro-2*H*-chromene), and we obtained a mixture of two diastereomers (**26a**, **26a′**) in a ratio of 1:1 (Scheme 1). It can thus be understood that the introduction of a bulky group at the 2-position in a 3-nitro-2*H*-chromene resulted in the loss of diastereoselectivity.

On the other hand, the reaction between 2,2-dimethyl-3-nitrochromene and 2-methylindole afforded the product as the single diastereomer (**27a**; Scheme 1). This experiment, together with the results shown in Tables 3 and 4, shows

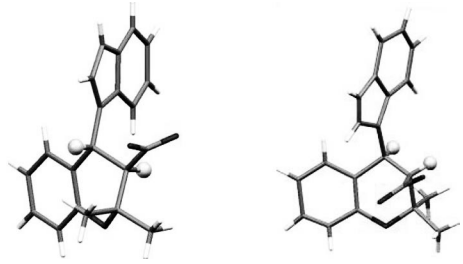
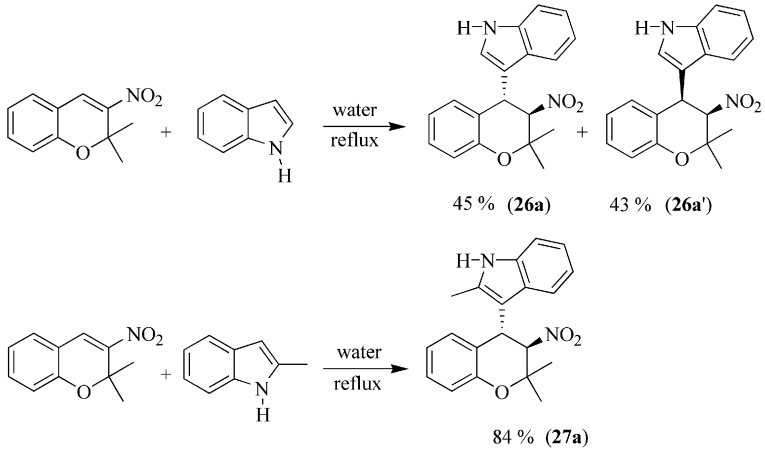
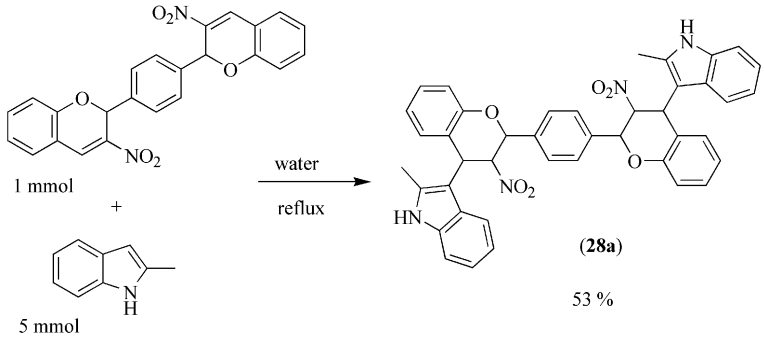


Figure 3. Crystal structure of **26a** (left). Crystal structure of **26a′** (right).



Scheme 1. Reaction of 2,2-dimethyl-3-nitro-*2H*-chromene with indole and 2-methylindole.



Scheme 2. Reaction between 2-methylindole and 1,4-bis(3-nitro-2*H*-chromen-2-yl)benzene.

that 2-substituted indoles exhibit good selectivity with 3-nitro-2*H*-chromene derivatives irrespective of any substituent at the 2-positions in the 3-nitro-2*H*-chromene systems. The diastereomers (**26a**, **26a′**) were separated by column chromatography and were characterized by ^{1}H NMR, ^{13}C NMR, LCMS, and HRMS analysis. The structures were also confirmed by single-crystal XRD analysis (Figure 3). The relative configuration of **26a** was assigned by crystallography as (3*R**,4*S**) and that of **26a′** as (3*S**,4*S**).

In order to extend the scope of the reaction, we treated 1,4-bis(3-nitro-2*H*-chromen-2-yl)benzene with 2-methylindole under these reaction conditions. We obtained the product as a mixture of diastereomers that were not separable, due to their insolubility in most organic solvents. However, treatment of 2-methylindole with 1,4-bis(3-nitro-2*H*-chromen-2-yl)benzene (**28a**) gave a single diastereomer in moderate yield (Scheme 2).

A plausible mechanism for the reaction can be postulated in nucleophilic 1,4-additions of electron-rich indoles to 3-nitro-2*H*-chromenes. We speculate that water may activate the nitro groups in 3-nitro-2*H*-chromene systems through hydrogen bonding, thereby generating electron-deficient centers at the 4-positions in the 3-nitro-2*H*-chromenes (Scheme 3). These species may undergo electrophilic substitution on indole to give intermediates **A**, which further lose protons to form intermediates **B**. Intermediates **B** further abstract protons either from water or from indole to afford indolyl(*aci*-nitro)chromans **C**. These indolyl(*aci*-nitro)chromans tautomerize to give the indolyl(nitro)chromans (**1a** or **1a′**; Scheme 1).

To pursue our speculation further, we conducted the Michael addition between 3-nitro-2-phenyl-2*H*-chromene

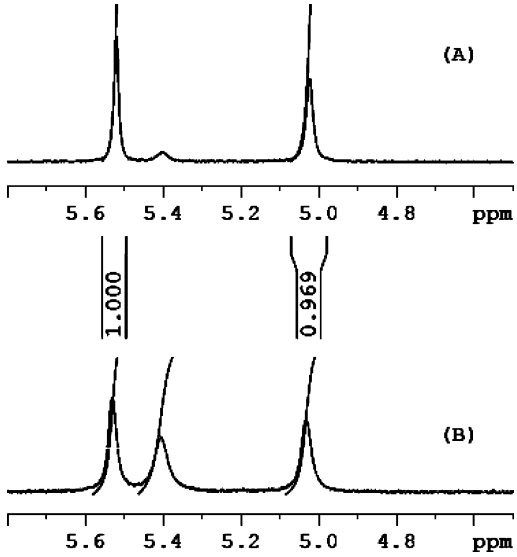
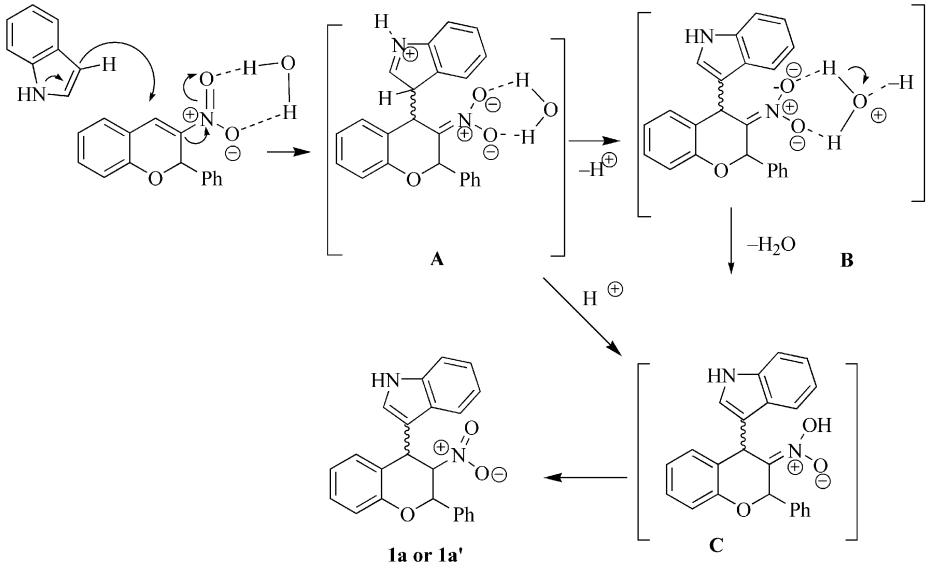
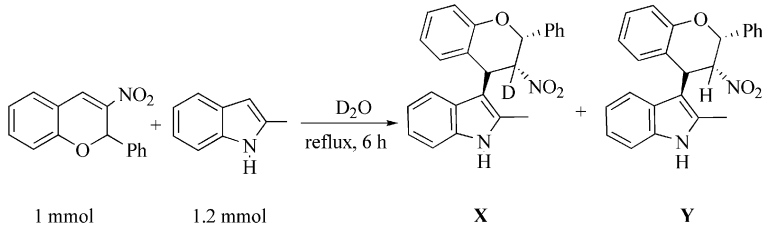


Figure 4. ^{1}H NMR spectra of deuterated indolylchroman (A) and undeuterated indolylchroman (B).



Scheme 3. Plausible mechanism for the *C*-alkylation of indole with 2-aryl-3-nitro-2*H* chromenes.



Scheme 4. Reaction between 3-nitro-2-phenyl-2*H*-chromene and 2-methylindole in D_2O.

and 2-methylindole in D_2O (Scheme 4). We were able to obtain the deuterated (2-methylindolyl)chroman **X** along with trace amounts of undeuterated (2-methylindolyl)-chroman **Y**, which was detected by ^1H NMR (Figure 4). From this experiment it was evident that water played a significant role in the reaction.

Conclusions

An efficient method for *C*-alkylation of indoles with 2-aryl-3-nitro-2*H*-chromenes "on-water" without the need for any catalyst or additives has been developed. The "on-water" conditions provided good yields of the indolylchroman derivatives within short reaction times. High diastereoselectivities were obtained with 2-substituted indoles. Simple experimental conditions, the green medium, and easy isolation of the products are the merits of this method. The fact that the reactions were clean, devoid of side reaction products, constitutes an additional attractive feature of this method. This method therefore represents a green procedure for the synthesis of indolylchromans.

Experimental Section

General: Unless otherwise mentioned, all commercial reagents and solvents were obtained from commercial suppliers and used without further purification. Thin-layer chromatography (TLC) was performed by using silica gel plates GF254 (0.25 mm thickness). For visualization, the TLC plates were either placed under ultraviolet light, or stained with iodine vapour. All purifications were carried out by flash chromatography using 230–400 mesh silica gel. All the melting points were determined with a microscope hot-stage apparatus and are uncorrected. High-resolution mass spectra were recorded in the EI mode with a JEOL JMS-D300 or JEOL JMS-HX 110 spectrometer. ^1H and ^{13}C NMR spectra were recorded with a Bruker Avance EX 400 FT spectrometer (^1H at 400.00 MHz and ^{13}C at 100.00 MHz) in [D_6]DMSO or $CDCl_3$ by using TMS as the internal reference. Crystallographic measurements were made with a Bruker Kappa Apex II CCD area detector with graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å). The structure was solved by direct methods (SHELXS-97), and additional atoms were located in the difference Fourier map and refined on *F*2 (SHELXL-97).

Typical Experimental Procedure: A mixture of indole (1.2 mmol) and 3-nitro-2-phenyl-2*H*-chromene (1 mmol) was suspended in water (2 mL) and heated at reflux. The progress of the reaction was monitored by TLC. After completion, the reaction mixture was extracted with ethyl acetate (3 × 10 mL). The organic layer was separated, dried with anhydrous magnesium sulfate, and concentrated under reduced pressure to provide a crude mixture. This was purified by flash chromatography to afford the mixture of diastereoisomers. The diastereoisomers were separated by careful crystallization from varying amounts of ethyl acetate and hexane. The ethyl acetate/hexane ratio used for crystallization was different for each compound, and the exact ratio for each pure product is given in the spectroscopic data. Compounds **9a**–**27a** were obtained as single diastereomers.

3-[(2*S,3*S**,4*R**)-3-Nitro-2-phenylchroman-4-yl]-1*H*-indole (1a):** Colorless solid; m.p. 245–247 °C, 0.322 g, 87%. Mixture (**1a** + **1a′**) crystallized from 80% hexane and 20% ethyl acetate (5 mL). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.15 (s, 1 H), 7.60 (d, *J* = 8.0 Hz, 1 H), 7.40 (d, *J* = 8.0 Hz, 1 H), 7.32–7.19 (m, 9 H), 7.12 (d, *J* = 8.4 Hz, 1 H), 7.02 (t, *J* = 7.4 Hz, 1 H), 6.69 (s, 1 H), 5.36 (s, 1 H), 5.32 (s, 1 H), 5.01 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.3, 136.9, 135.9, 130.7, 128.9, 128.8, 128.7, 126.0, 125.5, 125.4, 123.3, 122.1, 120.8, 120.2, 118.3, 117.9, 117.2, 112.0, 87.7, 72.8, 37.3 ppm. MS (EI): *m*/*z* (%) = 370 (35) $[M]^+$, 323 (70), 246 (40), 207 (100), 130 (10). HRMS (EI): calcd. for $C_{23}H_{18}N_2O_3$ $[M]^+$ 370.1312; found 370.1308.

3-[(2*S,3*R**,4*R**)-3-Nitro-2-phenylchroman-4-yl]-1*H*-indole (1a′):** Colorless solid; m.p. 213–215 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.20 (s, 1 H), 7.44–7.41 (m, 2 H), 7.38–7.35 (m, 4 H), 7.29–7.23 (m, 4 H), 7.06–7.03 (m, 2 H), 6.95–6.91 (m, 2 H), 5.60 (d, *J* = 8.9 Hz, 1 H), 5.43 (dd, *J* = 8.9, 5.5 Hz, 1 H), 5.15 (d, *J* = 5.5 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.5, 136.8, 136.3, 130.3, 129.5, 129.0, 128.9, 127.9, 127.2, 125.0, 122.8, 121.9, 121.9, 120.5, 118.4, 116.9, 113.7, 111.7, 87.4, 74.5, 37.7 ppm. MS (EI): *m*/*z* (%) = 370 (50) $[M]^+$, 323 (15), 246 (15), 220 (100), 207 (80), 165 (20), 132 (70), 77 (20). HRMS (EI): calcd. for $C_{23}H_{18}N_2O_3$ (M^+) 370.1312; found 370.1315.

3-[(2*S,3*S**,4*R**)-2-(3-Fluorophenyl)-3-nitrochroman-4-yl]-1*H*-indole (2a):** Colorless solid; m.p. 203–205 °C. 0.306 g, 79%. Mixture (**2a** + **2a′**) crystallized from 80% hexane and 20% ethyl acetate (5 mL). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.16 (s, 1 H), 7.65 (d, *J* = 7.8 Hz, 1 H), 7.44 (d, *J* = 8.1 Hz, 1 H), 7.30–7.18 (m, 5 H), 7.13–6.99 (m, 5 H), 6.67 (s, 1 H), 5.34 (s, 1 H), 5.31 (s, 1 H), 5.02 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.2 (d, $J_{C,F}$ = 245.0 Hz), 153.8, 138.5 (d, $J_{C,F}$ = 7.0 Hz), 136.8, 130.6,130.3 (d, $J_{C,F}$ = 9.0 Hz), 128.7, 125.4, 125.3, 123.3, 122.2, 121.4, 120.7,120.1, 118.0, 117.5, 117.2, 115.7 (d, $J_{C,F}$ = 21.0 Hz), 113.3 (d, $J_{C,F}$ = 26.0 Hz), 112.1, 87.4, 71.9, 37.3 ppm. MS (EI): *m*/*z* (%) = 389 (5) $[M + 1]^+$, 388 (20) $[M]^+$, 341 (40), 246 (40), 225 (100), 220 (50), 204 (10), 130 (20), 109 (10). HRMS (EI): calcd. for $C_{23}H_{17}FN_2O_3$ $[M]^+$ 388.1218; found 388.1225.

3-[(2*S,3*R**,4*R**)-2-(3-Fluorophenyl)-3-nitrochroman-4-yl]-1*H*-indole (2a′):** Colorless solid; m.p. 174–176 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.21 (s, 1 H), 7.38–7.14 (m, 8 H), 7.07–7.03 (m, 3 H), 6.96–6.92 (m, 1 H), 6.90 (d, *J* = 2.5 Hz, 1 H), 5.59 (d, *J* = 9.2 Hz, 1 H), 5.39 (dd, *J* = 9.2, 5.5 Hz, 1 H), 5.16 (d, *J* = 4.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.2 (d, $J_{C,F}$ = 245.0 Hz), 153.2, 139.2 (d, $J_{C,F}$ = 7.0 Hz), 136.3, 130.6 (d, $J_{C,F}$ = 8.0 Hz), 130.4, 129.2, 127.2, 125.0, 123.7, 122.9, 122.2, 121.8, 120.6, 118.4, 116.9, 116.5 (d, $J_{C,F}$ = 21.0 Hz), 115.3 (d, $J_{C,F}$ = 22.0 Hz), 113.5, 111.7, 87.3, 73.8, 37.9 ppm. MS (EI): *m*/*z* (%) = 389 (5) $[M + 1]^+$, 388 (20) $[M]^+$, 225 (60), 220 (100), 165 (5), 132 (30). HRMS (EI): calcd. for $C_{23}H_{17}FN_2O_3$ $[M]^+$ 388.1218; found 388.1221.

3-[(2*S,3*S**,4*R**)-3-Nitro-2-*p*-tolylchroman-4-yl]-1*H*-indole (3a):** Colorless solid; m.p. 210–212 °C. 0.310 g, 81%. Mixture (**3a** + **3a′**) crystallized from 80% hexane and 20% ethyl acetate (5 mL). ^1H NMR (400 MHz, $CDCl_3$): δ = 8.11 (s, 1 H), 7.62 (d, *J* = 7.8 Hz, 1 H), 7.41 (d, *J* = 8.0 Hz, 1 H), 7.42–7.09 (m, 9 H), 6.97 (t, *J* = 7.4 Hz, 1 H), 6.66 (s, 1 H), 5.32 (s, 1 H), 5.39 (s, 1 H), 4.98 (s, 1 H), 2.30 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.1, 138.6, 136.7, 132.7, 130.5, 129.5, 129.3, 128.5, 125.7, 125.2, 123.1, 121.8, 120.5, 120.1, 118.1, 117.7, 117.1, 112.0, 87.7, 72.7, 37.1, 21.2 ppm. MS (EI): *m*/*z* (%) = 384 (5) $[M]^+$, 337 (10), 246 (15), 222 (20), 221 (100), 165 (20), 130 (10), 117 (25), 91 (15), 77 (5). HRMS (EI): calcd. for $C_{24}H_{20}N_2O_3$ $[M]^+$ 384.1468; found 384.1475.

3-[(2*S,3*R**,4*R**)-3-Nitro-2-*p*-tolylchroman-4-yl]-1*H*-indole (3a′):** Colorless solid; m.p. 217–219 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.18 (s, 1 H), 7.35–7.22 (m, 5 H), 7.20–7.12 (m, 4 H), 7.04 (t, *J*

= 7.6 Hz, 2 H), 6.93–6.88 (m, 2 H), 5.56 (d, *J* = 9.0 Hz, 1 H), 5.43 (dd, *J* = 8.8, 5.5 Hz, 1 H), 5.14 (d, *J* = 5.3 Hz, 1 H), 2.33 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.6, 139.4, 136.3, 133.7, 130.3, 129.7, 128.9, 127.7, 127.3, 125.0, 122.8, 122.0, 121.9, 120.4, 118.4, 116.9, 113.7, 111.7, 87.4, 74.4, 37.9, 21.4 ppm. MS (EI): *m*/*z* (%) = 384 (10) $[M]^+$, 337 (5), 246 (10), 222 (15), 219 (100), 204 (20), 165 (15), 117 (20), 105 (15), 77 (50). HRMS (EI): calcd. for $C_{24}H_{20}N_2O_3$ $[M]^+$ 384.1468; found 384.1476.

3-[(2*S,3*S**,4*R**)-2-(*p*-Methoxyphenyl)-3-nitrochroman-4-yl]-1*H*-indole (4a):** Colorless solid, m.p. 201–203 °C. 0.280 g, 70%. Mixture (**4a** + **4a′**) crystallized from 80% hexane and 20% ethyl acetate (5 mL). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (s, 1 H), 7.63 (d, *J* = 7.88 Hz, 1 H), 7.40 (d, *J* = 8.2 Hz, 1 H), 7.32–7.17 (m, 6 H), 7.09 (d, *J* = 8.16 Hz, 1 H), 6.98 (t, *J* = 7.2 Hz, 1 H), 6.84 (d, *J* = 9.7 Hz, 2 H), 6.71 (d, *J* = 2.6 Hz, 1 H), 4.99 (s, 1 H), 5.32 (s, 1 H), 5.29 (s, 1 H), 3.79 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.0, 154.3, 136.9, 130.7, 128.6, 127.9, 127.3, 125.4, 125.3, 123.2, 121.9, 120.7, 120.2, 118.3, 117.9, 117.2, 114.2, 112.0, 87.8, 72.7, 55.5, 37.2 ppm. MS (EI): *m*/*z* (%) = 400 (10) $[M]^+$, 353 (30), 246 (15), 237 (80), 220 (100), 165 (15), 121 (15), 117 (25), 77 (10). HRMS (EI): calcd. for $C_{24}H_{20}N_2O_4$ $[M]^+$ 400.1418; found 400.1424.

3-[(2*S,3*R**,4*R**)-2-(*p*-Methoxyphenyl)-3-nitrochroman-4-yl]-1*H*-indole (4a′):** Colorless solid; m.p. 185–187 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (s, 1 H), 7.35–6.86 (m, 13 H), 5.52 (d, *J* = 9.2 Hz, 1 H), 5.41 (dd, *J* = 9.2, 5.5 Hz, 1 H) 5.15 (d, *J* = 5.5 Hz, 1 H), 3.79 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.2, 153.3, 136.0, 130.2, 129.0, 128.8, 128.5, 127.0, 124.8, 122.5, 121.8, 121.7, 120.2, 118.2, 116.7, 114.1, 113.6, 111.4, 87.2, 73.8, 55.2, 37.8 ppm. MS (EI): *m*/*z* (%) = 400 (10) $[M]^+$, 353 (30), 246 (15), 237 (80), 220 (100), 165 (15), 121 (15), 117 (25), 77 (10). HRMS (EI): calcd. for $C_{24}H_{20}N_2O_4$ $[M]^+$ 400.1418; found 400.1427.

3-[(2*S,3*S**,4*R**)-2-(4-Chlorophenyl)-3-nitrochroman-4-yl]-1*H*-indole (5a):** Colorless solid; m.p. 213–215 °C. 0.330 g, 82%. Mixture (**5a** + **5a′**) crystallized from 70% hexane and 30% ethyl acetate (5 mL). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (s, 1 H), 7.64 (d, *J* = 7.8 Hz, 1 H), 7.45 (d, *J* = 8.0 Hz, 1 H), 7.32–7.28 (m, 4 H), 7.24–7.18 (m, 4 H), 7.12 (d, *J* = 8.2 Hz, 1 H), 7.02–6.98 (m, 1 H), 6.69 (d, *J* = 1.6 Hz, 1 H), 5.33 (s, 1 H), 5.29 (t, *J* = 2.0 Hz, 1 H), 5.02 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.8, 136.7, 134.6, 134.3, 130.5, 128.8, 128.5, 127.2, 125.2, 125.1, 123.2, 122.0, 120.7, 119.8, 118.0, 117.7, 117.0, 111.8, 87.2, 72.0, 37.0 ppm. MS (EI): *m*/*z* (%) = 406 (2) $[M + 2]^+$, 404 (5) $[M]^+$, 357 (20), 246 (35), 241 (100), 220 (90), 204 (35), 165 (30), 125 (25), 102 (15), 89 (10). HRMS (EI): calcd. for $C_{23}H_{17}ClN_2O_3$ $[M]^+$ 404.0922; found 404.0933.

3-[(2*S,3*R**,4*R**)-2-(4-Chlorophenyl)-3-nitrochroman-4-yl]-1*H*-indole (5a′):** Colorless solid; m.p. 141–143 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (s, 1 H), 7.38–7.32 (m, 5 H), 7.27–7.24 (m, 2 H), 7.19 (t, *J* = 8.0 Hz, 1 H), 7.15 (d, *J* = 7.6 Hz, 1 H), 7.05 (t, *J* = 8.4 Hz, 2 H), 6.94 (t, *J* = 7.4 Hz, 1 H), 6.89 (d, *J* = 2.4 Hz, 1 H), 5.54 (d, *J* = 9.4 Hz, 1 H), 5.37 (dd, *J* = 9.4, 5.5 Hz, 1 H), 5.17 (d, *J* = 5.5 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.1, 136.1, 135.3, 135.1, 130.3, 129.3, 129.0, 128.9, 126.9, 124.8, 122.7, 121.9, 121.7, 120.4, 118.2, 116.7, 113.4, 111.5, 87.2, 73.5, 37.9 ppm. MS (EI): *m*/*z* (%) = 406 (3) $[M + 2]^+$, 404 (10) $[M]^+$, 241 (50), 220, (100), 204 (10), 132 (30), 124 (10). HRMS (EI): calcd. for $C_{23}H_{17}{}^{35}ClN_2O_3$ $[M]^+$ 404.0922; found 404.0933, and for $C_{23}H_{17}{}^{37}ClN_2O_3$ $[M + 2]^+$ 406.0893; found 406.0914.

3-[(2*S,3*S**,4*R**)-6-Methoxy-3-nitro-2-phenylchroman-4-yl]-1*H*-indole (6a):** Colorless solid; m.p. 205–207 °C; 0.296 g, 74%. Mixture (**6a** + **6a′**) crystallized from 70% hexane and 30% ethyl acetate (5 mL). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (s, 1 H), 7.65 (d, *J* = 7.8 Hz, 1 H), 7.44 (d, *J* = 8 Hz, 1 H), 7.29–7.19 (m, 7 H), 7.06 (d, *J* = 8.9 Hz, 1 H), 6.89–6.86 (m, 1 H), 6.72 (d, *J* = 8.7 Hz, 2 H), 5.32 (s, 1 H), 5.27 (s, 1 H), 4.99 (s, 1 H), 3.70 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.3, 148.1, 136.9, 135.9, 128.6, 128.5, 125.7, 125.5, 125.2, 122.6, 120.8, 120.1, 117.7, 117.6, 116.7, 115.2, 114.2, 112.1, 87.7, 72.6, 55.6, 37.5 ppm. MS (EI): *m*/*z* (%) = 400 (100) $[M]^+$, 359 (90), 276 (20), 237 (90). HRMS (EI): calcd. for $C_{24}H_{20}N_2O_4$ $[M]^+$ 400.1423; found 400.1422.

3-[(2*S,3*R**,4*R**)-6-Methoxy-3-nitro-2-phenylchroman-4-yl]-1*H*-indole (6a′):** Colorless solid; m.p. 211–212 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22 (s, 1 H), 7.45–7.42 (m, 2 H), 7.39–7.32 (m, 5 H), 7.21 (t, *J* = 7.2 Hz, 1 H), 7.08 (t, *J* = 7.2 Hz, 1 H), 7.01 (d, *J* = 8.9 Hz, 1 H), 6.95 (d, *J* = 2.4 Hz, 1 H), 6.87–6.84 (m, 1 H), 6.66 (d, *J* = 2.8 Hz, 1 H), 5.59 (d, *J* = 8.8 Hz, 1 H), 5.46 (dd, *J* = 8.8, 5.5 Hz, 1 H), 5.12 (d, *J* = 5.4 Hz, 1 H), 3.69 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.5, 147.5, 136.9, 136.2, 129.4, 128.9, 127.8, 127.3, 125.1, 122.8, 122.4, 120.5, 118.4, 117.7, 115.9, 113.9, 113.5, 111.7, 87.5, 74.6, 55.9, 37.8 ppm. MS (EI): *m*/*z* (%) = 400 (100) $[M]^+$, 353 (30), 250 (65), 237 (25), 205 (5), 132 (5). HRMS (EI): calcd. for $C_{24}H_{20}N_2O_4$ $[M]^+$ 400.1423; found 400.1422.

3-[(2*S,3*S**,4*R**)-6-Bromo-3-nitro-2-phenylchroman-4-yl]-1*H*-indole (7a):** Colorless solid; m.p. 232–234 °C; 0.372 g, 83%. Mixture (**7a** + **7a′**) crystallized from 60% hexane and 40% ethyl acetate (5 mL). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (s, 1 H), 7.64 (d, *J* = 7.8 Hz, 1 H), 7.46 (d, *J* = 8.1 Hz, 1 H), 7.40 (d, *J* = 8 Hz, 1 H), 7.34–7.31 (m, 5 H), 7.25–7.20 (m, 3 H), 7.03 (d, *J* = 8.7 Hz, 1 H), 6.73 (s, 1 H), 5.34 (s, 1 H), 5.28 (s, 1 H), 4.98 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.4, 136.2, 134.6, 132.1, 130.4, 127.9, 127.8, 125.0, 124.9, 124.3, 122.3, 121.7, 119.1, 118.1, 116.7, 114.9, 112.9, 111.6, 86.6, 71.8, 36.1 ppm. MS (EI): *m*/*z* (%) = 450 (50) $[M + 2]^+$, 448 (55) $[M]^+$, 403 (90), 401 (85), 326 (10), 324 (15), 287 (90), 285 (95), 206 (10), 132 (10). (%). HRMS (EI): calcd. for $C_{23}H_{17}BrN_2O_3$ $[M]^+$ 448.0423; found 448.0424.

3-[(2*S,3*R**,4*R**)-6-Bromo-3-nitro-2-phenylchroman-4-yl]-1*H*-indole (7a′):** Colorless solid; m.p. 244–246 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.22 (s, 1 H), 7.55–7.53 (m, 2 H), 7.41–7.36 (m, 5 H), 7.26–7.24 (m, 2 H), 7.10–7.06 (m, 2 H), 7.00–6.98 (d, *J* = 8.8 Hz, 1 H), 6.96 (t, *J* = 7.4 Hz, 1 H), 6.10 (dd, *J* = 9.4, 5.8 Hz,1 H), 5.59 (d, *J* = 9.4 Hz, 1 H), 4.99 (d, *J* = 5.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.37, 136.9, 136.5, 132.9, 131.6, 129.7, 129.1, 128.7, 127.2, 126.4, 125.8, 121.8, 119.6, 119.1, 118.2, 113.0, 112.3, 112.2, 85.6, 74.3, 37.2 ppm. MS (EI): *m*/*z* (%) = 450 (98) $[M + 2]^+$, 448 (100) $[M]^+$, 403 (35), 401 (30), 326 (10), 301 (15), 298 (25), 287 (50), 285 (45), 206 (10), 132 (85). HRMS (EI): calcd. for $C_{23}H_{17}BrN_2O_3$ $[M]^+$ 448.0423; found 448.0423.

1-Methyl-3-[(2*S,3*S**,4*R**)-3-nitro-2-phenylchroman-4-yl]-1*H*-indole (8a):** Colorless solid; m.p. 243–245 °C. 0.372 g, 83%. Mixture (**8a** + **8a′**) crystallized from 80% hexane and 20% ethyl acetate (5 mL). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 7.6 Hz, 1 H), 7.62–7.19 (m, 10 H), 7.14 (d, *J* = 8.4 Hz, 1 H), 7.01 (d, *J* = 7.2 Hz, 1 H), 6.55 (s, 1 H), 5.37 (s, 1 H), 5.32 (s, 1 H), 5.10 (s, 1 H), 3.73 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.2, 137.7, 135.9, 130.7, 129.8, 128.9, 128.8, 128.6, 126.1, 125.8, 122.8, 122.0, 120.3, 120.2, 118.4, 117.2, 116.3, 110.1, 87.8, 72.7, 37.3, 33.1 ppm. MS (EI): *m*/*z* (%) = 384 (50) $[M]^+$, 336 (10), 259 (10), 232 (100), 206 (50), 145 (90), 130 (5). HRMS (EI): calcd. for $C_{24}H_{20}N_2O_3$ $[M]^+$ 384.1468; found 384.1470.

1-Methyl-3-[(2*S,3*R**,4*R**)-3-nitro-2-phenylchroman-4-yl]-1*H*-indole (8a′):** Colorless solid; m.p. 178–180 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 (d, *J* = 7.3 Hz, 1 H), 7.43–7.14 (m, 10 H), 7.05–7.03 (d, *J* = 8.0 Hz, 1 H), 6.94 (t, *J* = 7.4 Hz, 1 H), 6.74 (s, 1 H), 5.60 (d, *J* = 8.9 Hz, 1 H), 5.44–5.40 (dd, *J* = 12.5, 8.9 Hz, 1 H),

5.13 (d, J = 5.4 Hz, 1 H), 3.74 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.5, 136.8, 130.3, 129.6, 129.4, 129.1, 129.0, 128.8, 127.9, 126.0, 125.8, 122.3, 121.9, 120.0, 118.4, 116.9, 111.9, 109.8, 87.5, 74.53, 37.7, 33.1 ppm. MS (EI): *m/z* (%) = 384 (50) $[M]^+$, 355 (10), 234 (100), 206 (50), 145 (55). HRMS (EI): calcd. for $C_{24}H_{20}N_2O_3$ $[M]^+$ 384.1468; found 384.1466.

3-[(2*S,3*S**,4*R**)-3-Nitro-2-phenylchroman-4-yl]-2-phenyl-1*H*-indole (9a):** Colorless solid; m.p. 198–200 °C. 0.325 g, 73%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.26 (s, 1 H), 7.44–7.38 (m, 6 H), 7.31–7.24 (m, 7 H), 7.18 (t, J = 7.2 Hz, 1 H), 7.07–7.02 (m, 2 H), 6.96 (t, J = 7.4 Hz, 1 H), 6.91 (t, J = 7.6 Hz, 1 H), 5.70 (s, 1 H), 5.40 (s, 1 H), 5.05 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.7, 136.9, 135.9, 135.5, 131.9, 129.9, 129.1, 128.8, 128.8, 128.7, 128.6, 128.5, 128.4, 125.8, 122.6, 122.2, 121.2, 120.5, 119.4, 116.8, 111.5, 111.3, 89.7, 75.0, 35.8 ppm. MS (EI): *m/z* (%) = 446 (10) $[M]^+$, 399 (15), 322 (20), 296 (40), 282 (30), 220 (40), 207 (100), 165 (45), 152 (15), 115 (10), 103 (25), 77 (35). HRMS (EI): calcd. for $C_{29}H_{22}N_2O_3$ $[M]^+$ 446.1625; found 446.1624.

3-[(2*S,3*S**,4*R**)-2-(3-Fluorophenyl)-3-nitrochroman-4-yl]-2-phenyl-1*H*-indole (10a):** Colorless solid; m.p. 196–198 °C. 0.385 g, 83%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30 (s, 1 H), 7.46–7.39 (m, 6 H), 7.32–7.20 (m, 2 H), 7.19 (t, J = 7.8 Hz, 1 H), 7.15 (d, J = 8.2 Hz, 1 H), 7.09–6.88 (m, 7 H), 5.68 (s, 1 H), 5.38 (s, 1 H), 5.08 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.0 (d, $J_{C,F}$ = 245.0 Hz), 153.4, 138.2 (d, $J_{C,F}$ = 7.0 Hz), 137.1, 136.0, 131.9, 130.3 (d, $J_{C,F}$ = 27.0 Hz) 130.2, 129.2, 128.9, 128.6, 127.1, 123.4 (d, $J_{C,F}$ = 24.0 Hz), 121.6 (d, $J_{C,F}$ = 3.0 Hz), 121.2, 120.7, 119.3, 116.9, 115.8 (d, $J_{C,F}$ = 21.0 Hz), 113.3 (d, $J_{C,F}$ = 24.0 Hz), 111.5, 111.4, 89.7, 74.3, 36.0 ppm. MS (EI): *m/z* (%) = 464 (10) $[M]^+$, 417 (20), 340 (10), 322 (20), 296 (30), 280 (10), 225 (100), 206 (30), 165 (10), 109 (10), 77 (5). HRMS (EI): calcd. for $C_{29}H_{21}FN_2O_3$ $[M]^+$ 464.1531; found 464.1533.

3-[(2*S,3*S**,4*R**)-2-(4-Chlorophenyl)-3-nitrochroman-4-yl]-2-phenyl-1*H*-indole (11a):** Colorless solid; m.p. 197–199 °C; 0.389 g, 81%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27 (s, 1 H), 7.44–7.38 (m, 6 H), 7.30–7.16 (m, 6 H), 7.11 (d, J = 8.1 Hz, 1 H), 7.07 (d, J = 7.6 Hz, 1 H), 6.99–6.88 (m, 3 H), 5.65 (s, 1 H), 5.35 (s, 1 H), 5.04 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.7, 137.2, 136.1, 134.9, 134.3, 132.1, 130.2, 129.4, 129.1, 128.0, 128.8, 127.5, 127.2, 122.9, 122.6, 121.3, 120.8, 119.5, 117.1, 111.6, 111.5, 89.8, 74.6, 36.0 ppm. MS (EI): *m/z* (%) = 482 (2) $[M + 2]^+$, 480 (5) $[M]^+$, 433 (5), 308 (10), 296 (35), 243 (30), 241 (100), 204 (30), 193 (40), 165 (30), 125 (40), 77 (15). HRMS (EI): calcd. for $C_{29}H_{21}{}^{35}ClN_2O_3$ $[M]^+$ 480.1235; found 480.1241, and for $C_{29}H_{21}{}^{37}ClN_2O_3$ $[M + 2]^+$ 482.1206; found 482.1229.

3-[(2*S,3*S**,4*R**)-3-Nitro-2-(thiophen-2-yl)chroman-4-yl]-2-phenyl-1*H*-indole (12a):** Colorless solid; m.p. 195–197 °C; 0.319 g, 76%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22 (s, 1 H), 7.49–7.36 (m, 6 H), 7.24–7.21 (m, 2 H), 7.17 (t, J = 7.6 Hz, 1 H), 7.12 (d, J = 7.6 Hz, 1 H), 7.00 (d, J = 8.0 Hz, 2 H), 6.98 (t, J = 7.6 Hz, 1 H), 6.93–6.89 (m, 3 H), 6.07 (d, J = 3.9 Hz, 1 H), 5.61–5.59 (m, 1 H), 5.30 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.3, 137.8, 136.7, 136.2, 132.3, 129.9, 129.2, 128.9, 128.8, 128.6, 127.2, 126.8, 126.7, 122.8, 122.7, 122.2, 120.6, 119.3, 117.5, 111.5, 110.3, 87.1, 73.1, 34.5 ppm. MS (EI): *m/z* (%) = 452 (5) $[M]^+$, 308 (10), 220 (20), 213 (100), 204 (20), 165 (15), 152 (10), 97 (15), 84 (5). HRMS (EI): calcd. for $C_{27}H_{20}N_2O_3S$ $[M]^+$ 452.1189; found 452.1186.

3-[(2*S,3*S**,4*R**)-8-Methoxy-3-nitro-2-phenylchroman-4-yl]-2-phenyl-1*H*-indole (13a):** Yellow solid; m.p. 248–250 °C; 0.302 g, 73%. ^{1}H NMR (400 MHz, $CDCl_3$ + $[D_6]$DMSO): δ = 10.09 (s, 1 H), 7.44–7.34 (m, 6 H), 7.29 (s, 5 H), 7.15 (t, J = 7.4 Hz, 1 H), 7.05 (s, 1 H), 6.92 (t, J = 7.4 Hz, 1 H), 6.86–6.79 (m, 2 H), 6.67 (d, J = 6.5 Hz, 1 H), 5.75 (s, 1 H), 5.43 (s, 1 H), 5.05 (s, 1 H), 3.94 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $[D_6]$DMSO): δ = 148.4, 143.6, 137.8, 136.8, 136.1, 132.7, 129.2, 129.1, 128.9, 128.8, 128.6, 127.0, 126.4, 122.9, 122.1, 122.0, 121.5, 119.9, 119.2, 112.3, 111.2, 109.9, 89.3, 75.1, 56.2, 36.3 ppm. MS (EI): *m/z* (%) = 476 (100) $[M]^+$, 428 (50), 325 (10), 282 (10), 237 (90), 205 (5). HRMS (EI): calcd. for $C_{30}H_{24}N_2O_4$ $[M]^+$ 476.1736; found 476.1737.

3-[(2*S,3*S**,4*R**)-6-Methoxy-3-nitro-2-phenylchroman-4-yl]-2-phenyl-1*H*-indole (14a):** Colorless solid; m.p. 203–205 °C; 0.338 g, 71%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.26 (s, 1 H), 7.44–7.39 (m, 6 H), 7.32–7.25 (m, 5 H), 7.19 (t, J = 8.8 Hz, 1 H), 7.08 (s, 1 H), 7.06 (d, J = 8.8 Hz, 1 H), 6.98 (t, J = 7.4 Hz, 1 H), 6.83 (dd, J = 8.7, 2.6 Hz, 1 H), 6.57 (d, J = 2.6 Hz, 1 H) 5.65 (s, 1 H), 5.36 (s, 1 H), 5.03 (s, 1 H), 3.62 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.7, 148.1, 137.0, 136.1, 135.8, 132.1, 129.2, 128.9, 128.8, 128.7, 127.2, 125.9, 122.7, 122.2, 120.6, 120.4, 119.6, 117.7, 114.7, 114.6, 111.5, 111.4, 90.2, 75.3, 55.7, 36.5 ppm. MS (EI): *m/z* (%) = 476 (100) $[M]^+$, 429 (55), 237 (70), 208 (40). HRMS (EI): calcd. for $C_{30}H_{24}N_2O_4$ $[M]^+$ 476.1736; found 476.1734.

3-[(2*S,3*S**,4*R**)-6-Bromo-3-nitro-2-phenylchroman-4-yl]-2-phenyl-1*H*-indole (15a):** Colorless solid; m.p. 214–216 °C; 0.408 g, 78%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30 (s, 1 H), 7.43–7.40 (m, 6 H), 7.33–7.32 (m, 4 H), 7.27–7.25 (m, 2 H), 7.23 (t, J = 7.7 Hz, 1 H), 7.16 (s, 1 H), 7.13 (s, 1 H), 7.02 (t, J = 8 Hz, 2 H), 5.68 (s, 1 H), 5.34 (s, 1 H), 5.00 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $[D_6]$DMSO): δ = 153.3, 138.0, 136.6, 135.7, 132.5, 132.4, 131.7, 129.4, 129.2, 128.9, 128.8, 127.8, 126.8, 126.3, 124.5, 122.1, 120.1, 119.2, 118.8, 113.7, 112.4, 109.3, 88.5, 74.7, 36.2 ppm. MS (EI): *m/z* (%) = 526 (98) $[M + 2]^+$, 524 (100) $[M]^+$, 481 (62), 479 (60), 400 (10), 287 (85), 285 (80), 208 (25), 193 (10). HRMS (EI): calcd. for $C_{29}H_{21}BrN_2O_3$ $[M]^+$ 524.0736; found 524.0737.

3-[(2*S,3*S**,4*R**)-6,8-Dibromo-3-nitro-2-phenylchroman-4-yl]-2-phenyl-1*H*-indole (16a):** Colorless solid; m.p. 186–188 °C; 0.489 g, 81%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.35 (s, 1 H), 7.62 (s, 1 H), 7.47–7.44 (m, 6 H), 7.36 (s, 5 H), 7.23 (d, J = 6.7 Hz, 1 H), 7.13–7.05 (m, 3 H), 5.78 (s, 1 H), 5.41 (s, 1 H), 5.02 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.8, 137.3, 135.9, 134.6, 134.5, 131.9, 131.6, 129.2, 129.1, 129.0, 128.8, 128.7, 126.7, 125.7, 124.2, 123.1, 121.1, 118.9, 114.1, 111.9, 111.6, 110.6, 89.0, 75.1, 36.8 ppm. MS (EI): *m/z* (%) = 606 (30) $[M + 4]^+$, 604 (70) $[M + 2]^+$, 602 (40) $[M]^+$, 558 (25), 556 (50), 554 (10), 366 (40), 364 (98), 362 (50), 282 (20), 207 (50), 193 (10). HRMS (EI): calcd. for $C_{29}H_{20}Br_2N_2O_3$ $[M]^+$ 601.9841; found 601.9843.

3-[(2*S,3*S**,4*R**)-2-(4-Methoxyphenyl)-3-nitrochroman-4-yl]-2-methyl-1*H*-indole (17a):** Colorless solid; m.p. 202–204 °C; 0.223 g, 54%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (s, 1 H), 7.29 (d, J = 8.6 Hz, 2 H), 7.19 (d, J = 8.6 Hz, 2 H), 7.12 (d, J = 8.0 Hz, 2 H), 7.05 (d, J = 6.7 Hz, 2 H), 6.92 (t, J = 7.3 Hz, 2 H), 6.85 (d, J = 8.6 Hz, 2 H), 5.51 (s, 1 H), 5.30 (s, 1 H), 4.92 (s, 1 H), 3.77 (s, 3 H), 2.19 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.0, 154.0, 135.4, 133.9, 130.3, 128.7, 127.8, 127.5, 127.1, 122.2, 121.8, 120.7, 120.2, 118.1, 117.0, 114.2, 110.8, 100.2, 88.6, 74.5, 55.4, 35.9, 12.3 ppm. MS (EI): *m/z* (%) = 414 (15) $[M]^+$, 352 (10), 250 (20), 236 (100), 220 (40), 194 (10), 165 (15), 131 (10), 77 (5). HRMS (EI): calcd. for $C_{25}H_{22}N_2O_4$ $[M]^+$ 414.1574; found 414.1578.

2-Methyl-3-[(2*S,3*S**,4*R**)-3-nitro-2-(thiophen-2-yl)chroman-4-yl]-1*H*-indole (18a):** Colorless solid; m.p. 241–243 °C; 0.285 g, 73%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (s, 1 H), 7.28–7.21 (m, 3 H), 7.11–7.06 (m, 2 H), 6.97–6.88 (m, 6 H), 6.02 (s, 1 H), 5.53 (s, 1 H), 5.10 (s, 1 H), 1.68 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.3, 135.9, 134.7, 133.7, 129.0, 127.4, 125.7, 125.6,

125.5, 125.4, 121.3, 120.6, 119.6, 118.1, 116.3, 116.0, 110.1, 107.0, 86.0, 71.0, 33.8, 10.8 ppm. MS (EI): *m*/*z* (%) = 390 (10) $[M]^+$, 246 (10), 234 (20), 220 (40), 213 (100), 204 (20), 165 (10), 130 (20), 97 (30), 84 (10), 77 (5). HRMS (EI): calcd. for $C_{22}H_{18}N_2O_3S$ $[M]^+$ 390.1033; found 390.1033.

3-[(2*S,3*S**,4*R**)-2-(2-Methoxyphenyl)-3-nitrochroman-4-yl]-2-methyl-1*H*-indole (19a):** Colorless solid, m.p. 193–195 °C; 0.286 g, 69%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (s, 1 H), 7.56 (d, J = 7.52 Hz, 1 H), 7.33–7.24 (m, 3 H), 7.14–7.04 (m, 3 H), 7.01–6.93 (m, 4 H), 6.80 (d, J = 8.2 Hz, 1 H), 5.80 (s, 1 H), 5.50 (s, 1 H), 5.00 (s, 1 H), 3.40 (s, 3 H), 2.08 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.7, 154.7, 135.3, 133.5, 130.3, 129.7, 128.5, 127.4, 127.0, 124.4, 122.2, 121.7, 121.4, 121.1, 120.1, 118.1, 117.1, 110.6, 110.2, 86.6, 70.1, 55.2, 36.8, 12.4 ppm. MS (EI): *m*/*z* (%) = 414 (50) $[M]^+$, 367 (70), 352 (50), 337 (10), 260 (15), 248 (20), 236 (100), 219 (50), 144 (35), 90 (10). HRMS (EI): calcd. for $C_{25}H_{22}N_2O_4$ $[M]^+$ 414.1574; found 414.1586.

2-Methyl-3-{(2*S,3*S**,4*R**)-3-nitro-2-[(trifluoromethyl)phenyl]chroman-4-yl}-1*H*-indole (20a):** Colorless solid; m.p. 188–190 °C; 0.357 g, 78%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (s, 1 H), 7.79 (d, J = 7.8 Hz, 1 H), 7.62 (t, J = 6.7 Hz, 2 H), 7.46 (t, J = 7.6 Hz, 1 H), 7.31 (t, J = 7.1 Hz, 2 H), 7.24–7.02 (m, 6 H), 5.72 (s, 1 H), 5.18 (s, 1 H), 5.08 (s, 1 H), 1.80 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$+[D$_6$]DMSO): δ = 154.6, 135.2, 134.4, 132.6, 130.4, 129.3, 128.5, 128.4, 127.3, 126.9 (q, $J_{C,F}$ = 30.0 Hz), 126.2 (q, $J_{C,F}$ = 5.0 Hz) 124.4 (q, $J_{C,F}$ = 272.0 Hz), 122.8, 121.9, 120.0, 120.2, 117.1, 116.8, 110.8, 110.4, 87.9, 70.1, 37.7, 12.2 ppm. MS (EI): *m*/*z* (%) = 452 (60) $[M]^+$, 405 (65), 390 (90), 288 (85), 275 (100), 234 (55), 219 (40), 203 (25), 144 (60), 129 (20), 115 (10). HRMS (EI): calcd. for $C_{25}H_{19}F_2N_2O_3$ $[M]^+$ 452.1342; found 452.1350.

3-[(2*S,3*S**,4*R**)-6-Chloro-3-nitro-2-phenylchroman-4-yl]-2-methyl-1*H*-indole (21a):** Colorless solid; m.p. 209–211 °C, 0.327 g, 79%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (s, 1 H), 7.32–7.23 (m, 8 H), 7.19 (s, 1 H), 7.10–7.01 (m, 3 H), 5.53 (s, 1 H), 5.28 (s, 1 H), 4.89 (s, 1 H), 2.22 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.0, 135.0, 134.8, 133.7, 129.1, 128.3, 128.0, 127.9, 126.2, 126.1, 125.2, 122.2, 120.5, 119.0, 117.7, 116.6, 110.7, 107.9, 87.7, 73.6, 35.7, 11.6 ppm. MS (EI): *m*/*z* (%) = 420 (5) $[M + 2]^+$, 418 (25) $[M]^+$, 371 (25), 356 (25), 294 (10), 254 (10), 239 (100), 219 (30), 143 (20), 130 (10), 77 (5). HRMS (EI): calcd. for $C_{24}H_{19}ClN_2O_3$ $[M]^+$ 418.1079; found 418.1085. and for $C_{24}H_{19}{}^{37}ClN_2O_3$ $[M + 2]^+$ 420.1049; found 420.1069.

3-[(2*S,3*S**,4*R**)-8-Methoxy-3-nitro-2-phenylchroman-4-yl]-2-methyl-1*H*-indole (22a):** Colorless solid; m.p. 229–231 °C; 0.302 g, 73%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (s, 1 H), 7.31–7.25 (m, 7 H), 7.11 (s, 1 H), 6.98 (s, 1 H), 6.87 (s, 2 H), 6.65 (s, 1 H), 5.64 (s, 1 H), 5.38 (s, 1 H), 4.92 (s, 1 H), 3.92 (s, 3 H), 2.22 (s, 3 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 147.8, 143.1, 135.9, 135.2, 134.3, 128.5, 128.4, 126.8, 125.8, 121.7, 121.5, 122.3, 120.4, 118.9, 117.2, 110.9, 110.4, 108.7, 88.2, 73.4, 55.6, 35.7, 11.7 ppm. MS (EI): *m*/*z* (%) = 414 (90) $[M]^+$, 367 (25), 352 (15), 237 (98), 219 (10). HRMS (EI) *m*/*z*. calcd. for $C_{25}H_{22}N_2O_4$ $[M]^+$ 414.1580; found 414.1581.

3-[(2*S,3*S**,4*R**)-6-Methoxy-3-nitro-2-phenylchroman-4-yl]-2-methyl-1*H*-indole (23a):** Colorless solid; m.p. 188–190 °C; 0.293 g, 71%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (s, 1 H), 7.31–7.24 (m, 7 H), 7.13–6.99 (m, 3 H), 6.87 (d, J = 8.8 Hz, 1 H), 6.60 (s, 1 H), 5.47 (s, 1 H), 5.26 (s, 1 H), 4.93 (s, 1 H), 3.64 (s, 3 H), 2.04 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.8, 148.0, 135.8, 135.2, 133.6, 129.3, 128.8, 128.7, 127.0, 125.9, 121.8, 121.2, 120.2, 117.7, 115.2, 114.2, 110.8, 110.2, 88.7, 74.5, 55.7, 36.6, 12.2 ppm. MS (EI) *m*/*z* (%) MS (EI): *m*/*z* (%) = 414 (100) $[M]^+$, 367 (30), 351 (25), 289 (5), 237 (70), 220 (5). HRMS (EI): calcd. for $C_{25}H_{22}N_2O_4$ $[M]^+$ 414.1580; found 414.1579.

3-[(2*S,3*S**,4*R**)-6-Bromo-3-nitro-2-phenylchroman-4-yl]-2-methyl-1*H*-indole (24a):** Colorless solid; m.p. 218–220 °C; 0.379 g, 82%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (s, 1 H), 7.40 (dd, J = 8.7, 2.0 Hz, 1 H), 7.34–7.31 (m, 4 H), 7.25 (m, 3 H), 7.21 (s, 1 H), 7.15 (s, 1 H), 7.05 (d, J = 8.7 Hz, 2 H), 5.53 (s, 1 H), 5.29 (s, 1 H), 4.90 (s, 1 H), 2.20 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ + [D$_6$]-DMSO): δ = 153.0, 135.5, 135.3, 134.4, 132.6, 131.4, 128.9, 128.6, 126.7, 125.8, 123.1, 121.2, 119.7, 118.7, 117.4, 114.1, 111.1, 108.8, 88.2, 74.1, 36.2, 12.2 ppm. MS (EI): *m*/*z* (%) = 464 (90) $[M + 2]^+$, 462 (100) $[M]^+$, 417 (30), 415 (30), 400 (20), 398 (15), 287 (98), 285 (99), 220 (35), 146 (30), 144 (10). HRMS (EI): calcd. for $C_{24}H_{19}BrN_2O_3$ $[M]^+$ 462.0579; found 462.0579.

3-[(2*S,3*S**,4*R**)-6,8-Dibromo-3-nitro-2-phenylchroman-4-yl]-2-methyl-1*H*-indole (25a):** Colorless solid; m.p. 218–220 °C; 0.466 g, 86%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (s, 1 H), 7.69 (s, 1 H), 7.35–7.31 (m, 7 H), 7.17 (s, 2 H), 7.03 (s, 1 H), 5.61 (s, 1 H), 5.30 (s, 1 H), 4.91 (s, 1 H), 2.22 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.7, 135.5, 134.7, 134.2, 134.1, 131.9, 128.9, 128.7, 126.6, 125.6, 124.3, 121.4, 119.9, 117.1, 113.9, 111.7, 111.2, 108.4, 87.9, 74.6, 36.7, 12.3 ppm. MS (EI): *m*/*z* (%) = 544 (40) $[M + 4]^+$, 542 (70) $[M + 2]^+$, 540 (40) $[M]^+$, 496 (18), 494 (20), 498 (22), 366 (30), 364 (98), 362 (65), 220 (20), 146 (25). HRMS (EI): calcd. for $C_{24}H_{18}Br_2N_2O_3$ $[M]^+$ 539.9684; found 539.9685.

3-[(3*R,4*S**)-2,2-Dimethyl-3-nitrochroman-4-yl)-1*H*-indole (26a):** Colorless solid; m.p. 212–214 °C. 0.1455 g, 45%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 (s, 1 H), 7.37 (d, J = 8 Hz, 1 H), 7.19–7.13 (m, 3 H), 6.96–6.93 (m, 4 H), 6.81 (t, J = 7.6 Hz, 1 H), 5.16 (d, J = 12 Hz, 1 H), 5.03 (d, J = 12 Hz, 1 H), 1.57 (s, 3 H), 1.56 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.6, 136.9, 129.6, 128.5, 125.3, 124.5, 122.4, 122.3, 121.7, 119.9, 119.4, 117.3, 112.6, 111.6, 93.4, 75.4, 36.9, 27.0, 19.5 ppm. MS (EI): *m*/*z* (%) = 322 (80) $[M]^+$, 275 (15), 260 (100), 158 (5). HRMS (EI): calcd. for $C_{19}H_{18}N_2O_3$ $[M]^+$ 322.1312; found 322.1307.

3-[(3*S,4*S**)-2,2-Dimethyl-3-nitrochroman-4-yl]-1*H*-indole (26a′):** Colorless solid; m.p. 197–199 °C. 0.138 g, 43%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (s, 1 H), 7.44 (d, J = 8.0 Hz, 1 H), 7.19–7.13 (m, 3 H), 6.96–6.93 (m, 4 H), 6.66 (d, J = 8 Hz, 1 H), 5.16 (d, J = 12 Hz, 1 H), 5.03 (d, J = 11.6 Hz, 1 H), 1.57 (s, 3 H), 1.56 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.9, 135.8, 128.8, 128.4, 127.1, 124.5, 122.5, 121.1, 120.5, 119.9, 117.4, 114.6, 111.8, 111.2, 90.6, 73.6, 33.6, 26.4, 25.2 ppm. MS (EI): *m*/*z* (%) = 322 (100) $[M]^+$, 260 (25), 220 (15), 132 (50). HRMS (EI): calcd. for $C_{19}H_{18}N_2O_3$ $[M]^+$ 322.1312; found 322.1312.

3-[(3*R,4*S**)-2,2-Dimethyl-3-nitro-2*H*-chromen-4-yl]-2-methyl-1*H*-indole (27a):** Colorless solid, m.p. 199–201 °C. 0.282 g, 84%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (s, 1 H), 7.23 (s, 1 H), 7.17 (t, J = 7.5 Hz, 1 H), 7.05 (t, J = 7.5 Hz, 1 H), 6.95 (d, J = 8.1 Hz, 1 H), 6.85 (t, J = 7.5 Hz, 2 H), 6.78 (t, J = 7.4 Hz, 1 H), 6.66 (d, J = 7.9 Hz, 1 H), 5.24 (d, J = 11.6 Hz, 1 H), 4.99 (d, J = 11.6 Hz, 1 H), 2.46 (s, 3 H), 1.58 (s, 3 H), 1.51 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.8,136.0, 134.6, 129.4, 128.4, 125.8, 122.5, 121.8, 121.4, 119.6, 118.7, 117.3, 110.7, 107.6, 92.3, 75.6, 36.0, 27.0, 19.54, 11.4 ppm. MS (EI): *m*/*z* (%) = 336 (80) $[M]^+$, 274 (100), 220 (10), 172 (5), 144 (5). HRMS (EI): calcd. for $C_{20}H_{20}N_2O_3$ $[M]^+$ 336.1468; found 336.1468.

1,4-Bis[4-(2-methyl-1*H*-indol-3-yl)-3-nitrochroman-2-yl]benzene (28a): Colorless solid, m.p. 306–308 °C; 0.366 g, 53%. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 11.09 (s, 2 H), 7.49–6.80 (m, 20 H), 5.54 (s, 2 H), 5.38 (s, 2 H), 5.02 (s, 2 H), 2.36 (s, 6 H) ppm. ^{13}C

NMR (100 MHz, [D$_6$]DMSO): δ = 153.4, 136.1, 135.1, 134.3, 130.1, 128.1, 126.8, 126.1, 125.9, 121.8, 121.0, 120.2, 118.8, 117.1, 116.3, 110.8, 88.1, 73.1, 35.6, 11.6 ppm. MS (EI): *m/z* (%) = 690 (10) [M]$^+$, 643 (5), 559 (30), 513 (25), 482 (20), 428 (15), 382 (80), 336 (50), 278 (10), 260 (20), 234 (40), 220 (50), 146 (65), 130 (100), 103 (10). HRMS (EI): calcd. for $C_{42}H_{34}N_4O_6$ [M]$^+$ 690.2473; found 690.2452.

Acknowledgments

Financial support for this work by the National Science Council of the Republic of China is gratefully acknowledged.

[1] a) R. Breslow, *Acc. Chem. Res.* **1991**, *24*, 159–164; b) C.-J. Li, T. H. Chang, *Organic Reactions in Aqueous Media*, Wiley, New York, **1997**; c) U. M. Lindström, *Chem. Rev.* **2002**, *102*, 2751–2771; d) K. Shu, M. Kei, *Acc. Chem. Res.* **2002**, *35*, 209–217; e) C.-J. Li, *Chem. Rev.* **2005**, *105*, 3095–3166; f) M. C. Pirrung, *Chem. Eur. J.* **2006**, *12*, 1312–1317; g) U. M. Lindström, *Organic reactions in water: Principles, Strategies and Applications*, Blackwell Publishers, New York, **2007**; h) V. Polshettiwar, R. S. Varma, *Acc. Chem. Res.* **2008**, *41*, 629–639.

[2] S. Narayan, J. Muldoon, M. G. Finn, V. V. Fokin, H. C. Kolb, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2005**, *44*, 3275–3279.

[3] a) J. E. Klijin, J. B. F. N. Engberts, *Nature* **2005**, *435*, 746–747; b) H. B. Zhang, L. Liu, Y. J. Chen, D. Wang, C.-J. Li, *Eur. J. Org. Chem.* **2006**, 869–873; c) D. Gonzalez-Cruz, D. Tejedor, P. deArmas, E. Q. Morales, F. Garcia-Tellado, *Chem. Commun.* **2006**, 2798–2800; d) A. K. Chakraborti, S. Rudrawar, K. B. Jadhav, G. Kaur, S. V. Chaneshwara, *Green Chem.* **2007**, *9*, 1335–1340; e) S. Guizzetti, M. Benaglia, L. Raimondi, G. Celentano, *Org. Lett.* **2007**, *9*, 1247–1250; f) C. Santi, S. Santoro, B. Battistelli, L. Testaferri, M. Tiecco, *Eur. J. Org. Chem.* **2008**, 5387–5390; g) F. Wang, H. Fu, Y. Jiang, Y. Zhao, *Adv. Synth. Catal.* **2008**, *350*, 1830–1834; h) Q.-Y. Zhang, B.-K. Liu, W.-Q. Chen, Q. Wu, X.-F. Lin, *Green Chem.* **2008**, *10*, 972–977; i) M. C. Pirrung, K. D. Sarma, J. Wang, *J. Org. Chem.* **2008**, *73*, 8323–8730.

[4] a) F. Bigi, M. L. Conforti, R. Maggi, A. Piccinno, G. Sartori, *Green Chem.* **2000**, *2*, 101–103; b) R. Maggi, F. Bigi, S. Carloni, A. Mazzacani, G. Sartori, *Green Chem.* **2001**, *3*, 173–174; c) F. Bigi, S. Carloni, L. Ferrari, R. Maggi, A. Mazzacani, G. Sartori, *Tetrahedron Lett.* **2001**, *42*, 5203–5205; d) D. Amantini, F. Fringuelli, F. Pizzo, *J. Org. Chem.* **2002**, *67*, 7238–7243; e) D. Mimeau, O. Delacroix, A.-C. Gaumont, *Chem. Commun.* **2003**, 2928–2929; f) D. Astley, H. Sayg, S. Gezer, S. T. Astley, *Tetrahedron Lett.* **2004**, *45*, 7315–7317; g) M. L. Deb, P. J. Bhuyan, *Tetrahedron Lett.* **2005**, *46*, 6453–6456; h) S. B. Bandgar, B. P. Bandgar, B. L. Korbad, J. V. Totre, S. Patil, *Aust. J. Chem.* **2007**, *60*, 305–307; i) N. M. Abd El-Rahman, A. A. El-Kateb, M. F. Mady, *Synth. Commun.* **2007**, *37*, 3961–3970; j) J. J. Shrikhande, M. B. Gawande, R. V. Jayaram, *Tetrahedron Lett.* **2008**, *49*, 4799–4803.

[5] R. A. Sheldon, *Chem. Ind. (London)* **1997**, 12–15.

[6] a) G. P. Ellis, *Chromenes, Chromanones and Chromones – The Chemistry of Heterocyclic Compounds*, Wiley, New York, NY, **1977**, p. 31; b) W. S. Bowers, T. Ohta, J. S. Cleere, P. A. Marsella, *Science* **1976**, *193*, 542–547; c) R. Bergmann, R. Gericke, *J. Med. Chem.* **1990**, *33*, 3023–3027; d) R. Gericke, J. Harting, I. Lues, C. Schittenhelm, *J. Med. Chem.* **1991**, *34*, 3074–3085.

[7] F. W. Penella, S.-F. Chen, D. L. Behrens, R. F. Kaltenbach, S. P. Seitzg, *J. Med. Chem.* **1994**, *37*, 2232–2237.

[8] S. Subramanian, U. R. Desai, G. K. Trivedi, *Synth. Commun.* **1990**, *20*, 1733–1742.

[9] a) M. Nyerges, A. Virányi, G. Marth, A. Dancsó, G. Blaskó, L. Tőkea, *Synlett* **2004**, 2761–2765; b) A. Virányi, G. Marth, A. Dancsó, G. Blaskó, L. Tőke, M. Nyerges, *Tetrahedron* **2006**, *62*, 8720–8730.

[10] N. Ono, K. Sugi, T. Ogawaa, S. Aramaki, *J. Chem. Soc., Chem. Commun.* **1993**, 1781–1782.

[11] a) R. J. Sundberg, *Indoles*, Academic Press, New York, **1996**; b) R. J. Sundberg, *The Chemistry of Indoles*, Academic Press, New York, **1970**; c) K. S. Para, C. J. Stankovic, M. Visnick, US patent 7074814, **2006**; d) C. J. Swain, R. Baker, C. Kneen, J. Moseley, J. Saunders, E. M. Seward, G. Stevenson, M. Beera, J. Staton, K. Watling, *J. Med. Chem.* **1991**, *34*, 140–151; e) G. R. Martinez, A. A. M. Walker, D. R. Hirschfeld, P. J. Moloney, D. S. Yang, R. P. Rosenkranz, *J. Med. Chem.* **1989**, *32*, 890–897.

[12] a) R. Gericke, J. Harting, I. Lues, C. Schittenhelm, *J. Med. Chem.* **1991**, *34*, 3074–3085; b) G. Burrell, F. Cassidy, J. M. Evans, D. Lightowler, G. Stemp, *J. Med. Chem.* **1990**, *33*, 3023–3027; c) V. A. Ashwood, R. E. Buckingham, F. Cassidy, J. M. Evans, E. A. Faruk, T. C. Hamilton, D. J. Nash, G. Stemp, K. Willcocks, *J. Med. Chem.* **1986**, *29*, 2194–2201.

[13] a) V. V. Perekalin, E. S. Lipina, V. M. Berestovitskaya, D. A. Efremov, *Nitroalkenes, Conjugated Nitro Compounds*, John Wiley & Sons, Ltd., Chichester, **1994**; b) S.-Y. Wang, S.-J. Ji, T.-P. Loh, *Synlett* **2003**, 2377–2379; c) S.-J. Ji, S.-Y. Wang, *Synlett* **2003**, 2074–2076; d) E. Marcantoni, L. Sambri, E. Torregiani, *J. Org. Chem.* **2003**, *68*, 4594–4597; e) I. Komoto, S. Kobayashi, *J. Org. Chem.* **2004**, *69*, 680–688; f) H. Firouzabadi, N. Iranpoor, F. Nowrouzi, *Chem. Commun.* **2005**, 789–791; g) R. Ballini, R. R. Clemente, A. Palmieri, M. Petrini, *Adv. Synth. Catal.* **2006**, *348*, 191–196; h) M. Kawatsura, S. Aburatani, J. Uenishi, *Tetrahedron* **2007**, *63*, 4172–4177; i) L.-T. An, J.-P. Zou, L. L. Zhang, Y. Zhang, *Tetrahedron Lett.* **2007**, *48*, 4297–4300; j) K. S. Babu, V. R. S. Rao, P. Sunitha, S. S. Babu, J. M. Rao, *Synth. Commun.* **2008**, *38*, 1784–1791; k) P. Wu, Y. Wan, J. Cai, *Synlett* **2008**, 1193–1198.

[14] a) C. Lin, J. Hsu, M. N. V. Sastry, H. Fang, Z. Tu, J.-T. Liu, C.-F. Yao, *Tetrahedron* **2005**, *61*, 11751–11757; b) V. Y. Korotaev, V. Y. Sosnovskikh, I. B. Kutyashev, *Russ. Chem. Bull., Int. Ed.* **2007**, *56*, 2054–2059.

[15] a) V. Y. Korotaev, I. B. Kutyashev, V. Y. Sosnovskikh, *Heteroat. Chem.* **2005**, *16*, 492–496; b) V. Y. Korotaev, V. Y. Sosnovskikh, I. B. Kutyashev, M. I. Kodess, *Russ. Chem. Bull., Int. Ed.* **2006**, *55*, 317–330; c) V. Y. Korotaev, V. Y. Sosnovskikh, I. B. Kutyashev, M. I. Kodess, *Russ. Chem. Bull., Int. Ed.* **2006**, *55*, 2020–2031; d) V. Y. Korotaev, I. B. Kutyashev, V. Y. Sosnovskikh, M. I. Kodess, *Mendeleev Commun.* **2007**, *17*, 52–53; e) V. Y. Korotaev, V. Y. Sosnovskikh, I. B. Kutyashev, A. Y. Bakov, Y. V. Shklyaev, *Tetrahedron Lett.* **2008**, *49*, 5376–5379.

[16] M.-C. Ye, Y.-Y. Yang, Y. Tang, X.-L. Sun, Z. Ma, W.-M. Qin, *Synlett* **2006**, *8*, 1240–1244.

[17] a) Z. Tu, B. R. Raju, T.-R. Liou, V. Kavala, C.-W. Kuo, Y. Jang, Y.-H. Shih, C.-C. Wang, C.-F. Yao, *Tetrahedron* **2009**, *65*, 2436–2442; b) Z. Tu, Y. Jang, C. Lin, J.-T. Liu, J. Hsu, M. N. V. Sastry, C.-F. Yao, *Tetrahedron* **2005**, *61*, 10541–10551; c) M.-C. Yan, Y.-J. Jang, J. Wu, Y.-F. Lin, C.-F. Yao, *Tetrahedron Lett.* **2004**, *45*, 3685–3688; d) C.-F. Yao, Y.-J. Jang, M.-C. Yan, *Tetrahedron Lett.* **2003**, *44*, 3813–3816; e) M.-C. Yan, Z. Tu, C. Lin, C.-F. Yao, *Tetrahedron Lett.* **2002**, *43*, 7991–7994.

[18] P. M. Habib, V. Kavala, C.-W. Kuo, C.-F. Yao, *Tetrahedron Lett.* **2008**, *49*, 7005–7007.

[19] CCDC-699101 (**4a**), -699102 (**4a′**) -728662 (**26a**), and -728663 (**26a′**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Received: February 28, 2009
Published Online: July 29, 2009

