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Highly diastereoselective synthesis of novel 2,3,4-trisubstituted chromanes via the reaction of 3-nitro-2-(trihalomethyl)- and 3-nitro-2-phenyl-2*H*-chromenes with 1-morpholinocyclopentene

Vladislav Y. Korotaev*, Igor B. Kutyashev, Alexey Y. Barkov, Vyacheslav Y. Sosnovskikh

Institute of Natural Sciences and Mathematics, Ural Federal University, 620000 Ekaterinburg, Russian Federation

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ABSTRACT

The reaction of 3-nitro-2-trifluoro(trichloro)methyl- and 3-nitro-2-phenyl-2*H*-chromenes with 1-morpholinocyclopentene under the conditions of kinetic or thermodynamic control led to the formation of products due to enamine addition at the C-4 atom of chromene as individual *cis,trans*- or *trans,trans*-isomers, differing by the position of double bond in the enamine moiety. Hydrolysis of these compounds in dilute HCl did not cause changes of pyran ring configuration and provided the respective 4-(cyclopentanon-2-yl)chromanes with *anti*-configuration of hydrogen atoms at the C-4 and C-2′ atoms. Stereochemistry of the obtained compounds was confirmed by X-ray structural analysis.

1. Introduction

Enamines that are based on cycloalkanones and secondary amines provide readily available nucleophilic reagents capable of diastereoselective addition at the activated double bonds of conjugated nitroalkenes under mild conditions in the absence of a catalyst. Depending on the ring size of ketone molecule, the structure of nitroalkene, and the reaction conditions, such processes can result in the formation of nitroalkylated enamines[1] (conjugated addition), 1,2-oxazine *N*-oxides[2] ([4 + 2] heterocyclization), or cyclobutanes[1b,2a,3] ([2 + 2] carbocyclization). At the same time, only very limited data are available in the literature about reactions of these enamines with 3-nitro-2*H*-chromenes, the chemical properties of which are primarily defined by the presence of a β-nitrostyrene moiety in the molecule.[4] It is only known[5] that catalytic reactions of 2-unsubstituted 3-nitro-2*H*-chromene with proline enamines of cyclopentanone and cyclohexanone, formed *in situ* from proline and the respective ketones in the presence of sodium acetate in methanol (enamine catalysis), after removal of the solvent and purification by flash chromatography provided mixtures of epimeric 3,4-*trans*-chromanes **1** in approximately equal amounts, differed by the relative configuration at the C-2′ atom (Scheme 1).

We have recently shown[6] that diastereoselective nucleophilic addition of 1-morpholinocyclohexene (**3**) at the double bond C-4 atom of 3-nitro-2-trifluoro(trichloro)methyl-2*H*-chromenes **2** in acetonitrile at room temperature resulted in the isolation of either 1,2-oxazine-*N*-oxides **4** or *trans,trans*-Michael adducts **5** with tetrasubstituted double bond in the enamine moiety (Scheme 2).

In a continuation of our search for new stereoselective reactions involving 3-nitro-2*H*-chromenes,[6,7] we devoted the current work to studying the interaction of 2-(trihalomethyl)-3-nitro-2*H*-chromenes **2a**–**n** and 2-phenyl-3-nitro-2*H*-chromenes **2o**–**q** with 1-morpholinocyclopentene (**6**) under various conditions. This study resulted in the development of a diastereoselective synthesis leading to new representatives of 2,3,4-trisubstituted chromanes, including their stereochemical characterization and identification of some structural features of the obtained Michael adducts.

2. Results and discussion

We found that 2-CX_3-nitrochromenes **2a**–**n** reacted with 1-morpholinocyclopentene (**6**) under the conditions of kinetic control (−18 or 20°C) in anhydrous acetonitrile, forming adducts *ct*-**7a**–**n** as individual *cis,trans*-isomers (*ct*-isomers) with trisubstituted double bond in the enamine moiety, which gradually

* Corresponding author.
E-mail address: korotaev.vladislav@urfu.ru (V.Y. Korotaev).

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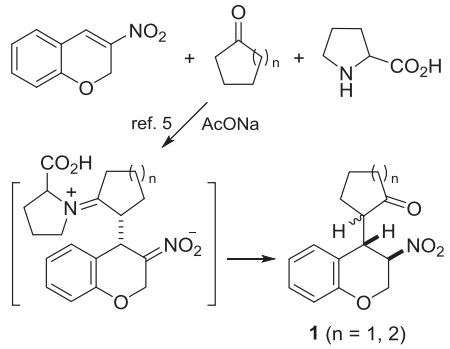
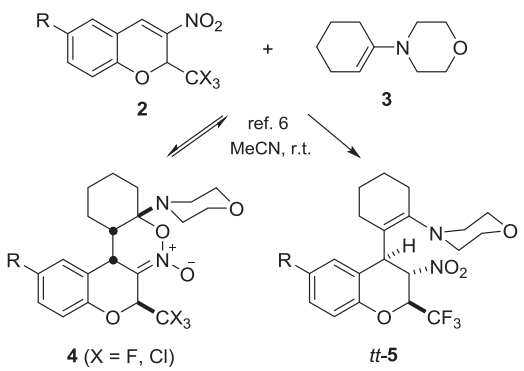
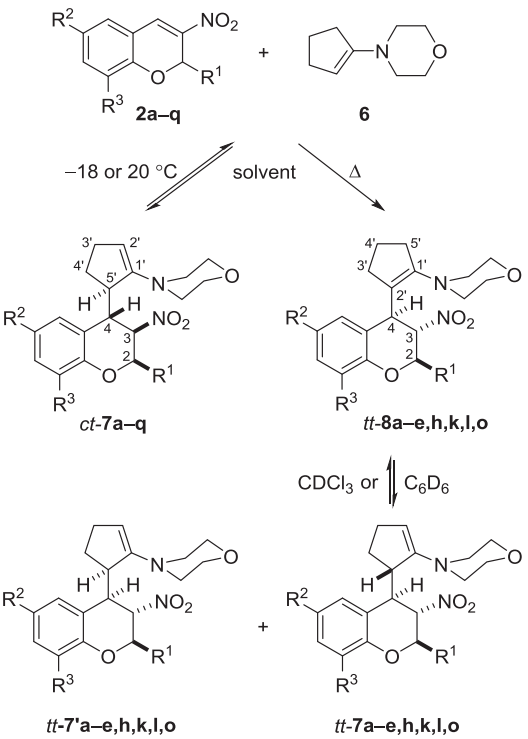


Scheme 1. Synthesis of chromanes **1**.



Scheme 2. Synthesis of compounds **4** and **5**.

crystallized from the reaction mixture as colorless prisms (Scheme 3, Table 1). This process is equilibrium, and the rate of formation and yields of products *ct*-**7** are primarily related to their solubility.



Scheme 3. Synthesis of chromanes **7** and **8**.

Therefore, the lower yields of 2-CF_3-chromanoenamines *ct*-**7** compared to their 2-CCl_3-analogs were caused by their higher solubility in acetonitrile. At the same time, the use of *tert*-butyl methyl ether, dichloromethane or methanol as solvent in the reaction of enamine **6** with chromene **2a** (−18°C, 48 h) decreased the yield of product *ct*-**7a** to 21–41%. Reduced yields of products *ct*-**7** upon substituting acetonitrile with another solvent were also observed in the series of 2-CCl_3-chromenes. For example, the reaction of enamine **6** with chromene **2h** in benzene, *tert*-butyl methyl ether, dichloromethane, and methanol (20°C, 24 h) gave chromane *ct*-**7h** in decreased yields (30–43%).

Similarly to the 2-CX_3-nitrochromenes **2a**–**n**, 3-nitro-2-phenyl-2*H*-chromenes **2o**–**q** reacted stereoselectively with enamine **6** at 20°C, forming the kinetically controlled products *ct*-**7o**–**q**. The highest yields (58–81%) after the shortest reaction duration (0.5–1 h) were obtained in *tert*-butyl methyl ether, due to the low solubility of the formed products in this solvent and rapid shifting of equilibrium towards the chromanoenamines *ct*-**7o**–**q** (Scheme 3, Table 1).

When the reaction of 2-CF_3-nitrochromenes **2a**–**e** with enamine **6** was performed in anhydrous methanol for 3–8 h at 35°C, the thermodynamically favored chromanoenamines *tt*-**8a**–**e** with *trans,trans*-configuration of substituents in the pyran ring and tetrasubstituted double bond in the enamine moiety were obtained in 39–78% yields (Scheme 3, Table 1). When the reaction was performed in acetonitrile, the yields of these compounds decreased by ~10%. Regardless of the selected solvent, chromanes *tt*-**8**, similarly to their isomers *ct*-**7**, gradually crystallized from the reaction mixtures as colorless prisms or white, fine crystalline powders. Increasing the reaction duration or raising the temperature to 40–60°C led to noticeable resinification in both solvents. It should be noted that chromanes *tt*-**8a**, *tt*-**8c**, and *tt*-**8d** were formed in 52, 39, and 40% yields, respectively, when chromenes **2a,c,d** were heated for 1 h with an excess of enamine **6** (1.5 equiv) under solvent-free conditions at 60°C.

Conversion of 2-trichloromethyl- and 2-phenyl-3-nitro-2*H*-chromenes to the respective *trans,trans*-chromanoenamines *tt*-**8** proceeded at a higher temperature (Scheme 3, Table 1). For example, 6-halosubstituted 2-CCl_3-chromanes *tt*-**8k,l** were synthesised in 54 and 46% yields by heating a solution of the respective chromene **2** and enamine **6** in methanol or acetonitrile for 6 h at 40°C, while 2-Ph-chromane *tt*-**8o** formed in acetonitrile after 4 h at 60°C. Product *tt*-**8h** could be obtained as a mixture with its *ct*-**8h** isomer only upon microwave irradiation of the starting materials in dichloromethane for 15 min at 100°C (69% combined yield). It is interesting to note that, unlike in the case of cyclohexanone enamine **3**, the formation of 1,2-oxazine-*N*-oxides of type **4** was not observed in any of the experiments.

Chromanoenamines *tt*-**8** in $CDCl_3$ or C_6D_6 solutions were in equilibrium with the epimeric chromanes *tt*-**7** and *tt*-**7′** containing a trisubstituted double bond in the enamine moiety, with the only difference between these compounds provided by the configuration at the C-5′ atom (Scheme 3). It was established that two new sets of ^{1}H NMR signals emerged 5 min after dissolving monocrystals of products *tt*-**8** in deuterated solvent. Each of these sets contained not only the proton signals of pyran ring, but also a characteristic broadened singlet of the vinyl proton, pointing to the presence of a trisubstituted double bond in chromanes *tt*-**7** and *tt*-**7'** (the assignment of compounds *tt*-**7** and *tt*-**7′** as *anti*- or *syn*-isomers and their preferred conformations in solution phase are described below). The equilibrium *tt*-**8** ⇌ *tt*-**7**+*tt*-**7′** in C_6D_6 solution was reached within approximately a day and favored the chromanoenamine *tt*-**8** containing a tetrasubstituted double bond. The isomeric chromanes *tt*-**8a–e,h**, *tt*-**7a**–**e,h**, and *tt*-**7'a–e,h** existed in C_6D_6 solution at room temperature in equilibrium mixtures that

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Table 1
Reaction conditions and yields of chromanoenamines *ct*-**7** and *tt*-**8**.

Chromene	R^1	R^2	R^3	Solvent	Time, h	Temp., °C	Chromane	Yield, %
2a	CF_3	H	H	MeCN	48	−18	*ct*-**7a**	58
2b	CF_3	MeO	H	MeCN	48	−18	*ct*-**7b**	50
2c	CF_3	H	EtO	MeCN	48	−18	*ct*-**7c**	49
2d	CF_3	Cl	H	MeCN	48	−18	*ct*-**7d**	64
2e	CF_3	Br	H	MeCN	48	−18	*ct*-**7e**	72
2f	CF_3	Cl	Cl	MeCN	6	20	*ct*-**7f**	71
2g	CF_3	Br	Br	MeCN	6	20	*ct*-**7g**	66
2h	CCl_3	H	H	MeCN	24	20	*ct*-**7h**	68
2i	CCl_3	MeO	H	MeCN	48	20	*ct*-**7i**	62
2j	CCl_3	H	EtO	MeCN	48	20	*ct*-**7j**	52
2k	CCl_3	Cl	H	MeCN	24	20	*ct*-**7k**	74
2l	CCl_3	Br	H	MeCN	24	20	*ct*-**7l**	77
2m	CCl_3	Cl	Cl	MeCN	24	20	*ct*-**7m**	78
2n	CCl_3	Br	Br	MeCN	24	20	*ct*-**7n**	83
2o	Ph	H	H	*t*-BuOMe	1	20	*ct*-**7o**	72
2p	Ph	MeO	H	*t*-BuOMe	0.5	20	*ct*-**7p**	58
2q	Ph	Br	H	*t*-BuOMe	0.5	20	*ct*-**7q**	82
2a	CF_3	H	H	MeOH	5	35	*tt*-**8a**	78
2b	CF_3	MeO	H	MeOH	8	35	*tt*-**8b**	59
2c	CF_3	H	EtO	MeOH	8	35	*tt*-**8c**	39
2d	CF_3	Cl	H	MeOH	3	35	*tt*-**8d**	51
2e	CF_3	Br	H	MeOH	3	35	*tt*-**8e**	47
2h	CCl_3	H	H	CH_2Cl_2	15 min	100[a]	*tt*-**8h**	69[b]
2k	CCl_3	Cl	H	MeOH	6	40	*tt*-**8k**	54
2l	CCl_3	Br	H	MeCN	6	40	*tt*-**8l**	46
2o	Ph	H	H	MeCN	4	60	*tt*-**8o**	34

[a] Upon microwave irradiation.
[b] A mixture of isomers in the ratio *tt*-**8h**:*ct*-**8h** = 64:36.

were characterised by ^{1}H and ^{19}F NMR spectroscopy, as shown in Table 2.

The thermodynamically favored adducts *tt*-**8** with equatorial configuration of all three bulky substituents in the benzopyran system and a tetrasubstituted double bond in the enamine moiety were formed from the less stable kinetically favored products *ct*-**7** featuring a *trans*-diaxially oriented nitro group and bulky enamine moiety, as a result of a retro-Michael reaction with cleavage of the C(4)–C(2′) bond. This confirmed the results obtained by studying the behaviour of compound *ct*-**7a** in C_6D_6 solution in NMR ampule by using ^{19}F NMR spectroscopy. Thus, the reaction mixture after a day at room temperature contained 38% of chromene **2a** and 3% of *tt*-isomers (*tt*-**8** + *tt*-**7a** + *tt*-**7′a**). The amount of chromane *ct*-**7a** decreased by almost three times after 3 days, while the content of chromene **2a** and the total amount of *tt*-isomers increased to 52 and 12%, respectively. The maximum content of *tt*-isomers in the mixture (27%) was observed after 8 days, while the conversion of chromane *ct*-**7a** reached 86%.

^{1}H NMR spectra of compounds *ct*-**7a**–**q** contained characteristic signals of H-2, H-3, and H-4 protons of the pyran ring, as well as a broadened singlet of the vinylic H-2′ proton, indicating the presence of a trisubstituted double bond in the five-membered ring. The *cis,trans*-configuration of chromanes *ct*-**7a**–**q** was evidenced by the small values of spin-spin coupling constants $J_{2,3}$ = 1.2–2.3 Hz and $J_{3,4}$ = 0–1.0 Hz.[7a,c] It should be noted that ^{1}H NMR spectra of 2-CF_3-chromanes *ct*-**7a**–**g** and 2-Ph-chromanes *ct*-**7o**–**q**, which were acquired in $CDCl_3$ solution, showed the presence of 8–19% of the respective chromenes **2** and enamine **6** due to a retro-Michael reaction that occurred in this solvent. NMR spectra of the indicated compounds were free of these impurities when acquired in a nonpolar solvent (C_6D_6).

In order to confirm the structure of chromanoenamines *ct*-**7a**–**q** proposed on the basis of ^{1}H NMR spectral data, as well as for establishing the relative configuration of substituents at the C-5′ atom, we performed monocrystal X-ray structural study of chromane *ct*-**7h**, which identified this compound as the *cis,trans*-isomer with H-4 and H-5′ hydrogen atoms in *anti*-configuration (Fig. 1). The trichloromethyl group in this molecule occupied an equatorial position, while the nitro group and enamine moiety had a *trans*-diaxial relationship. The pyran ring assumed a slightly twisted half-

Table 2
The equilibrium compositions for tautomeric mixtures of chromanes. *tt*-**8a**–**e,h**, *tt*-**7a**–**e,h**, and *tt*-**7′a**–**e,h** in C_6D_6 at 22°C

Isomers in equilibrium mixture	Content of each isomer, %		
	tt-8	*tt*-7	*tt*-7′
tt-**8a**:*tt*-**7a**:*tt*-**7′a**	67	21	12
tt-**8b**:*tt*-**7b**:*tt*-**7′b**	61	27	12
tt-**8c**:*tt*-**7c**:*tt*-**7′c**	61	27	12
tt-**8d**:*tt*-**7d**:*tt*-**7′d**	61	24	15
tt-**8e**:*tt*-**7e**:*tt*-**7′e**	59	26	16
tt-**8h**:*tt*-**7h**:*tt*-**7′h**	67	17	16

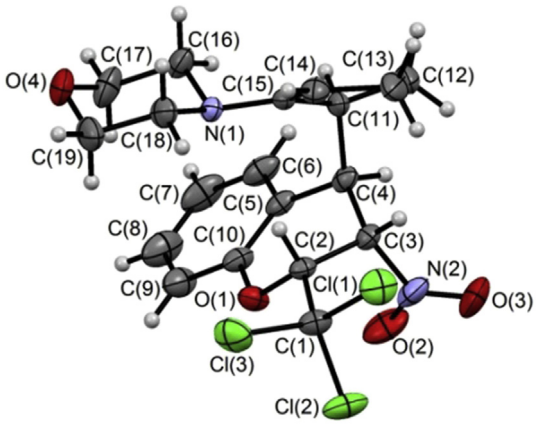

Fig. 1. Molecular structure of *ct*-**7h** (ORTEP drawing, 50% probability level).

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chair conformation. The dihedral angle H(11)–C(11)–C(4)–H(4) was equal to 63.5°, in agreement with the observed vicinal constants $J_{4,5'} = 2.3–3.1$ Hz in ^{1}H NMR spectra of chromanes *ct*-**7a**–**q**.

^{1}H NMR spectra of compounds *tt*-**8** contained characteristic signals of pyran ring protons, with the H-4 proton appearing as a doublet resulting from spin-spin coupling with only the H-3 proton. This fact, along with the lack of ^{1}H NMR signal due to vinylic proton, pointed to the presence of a tetrasubstituted double bond in the enamine moiety. The *trans,trans*-configuration of substituents at C-2, C-3, and C-4 atoms in chromanes *tt*-**8** was deduced from the large values of coupling constants $J_{2,3}$ = 7.7–10.1 Hz and $J_{3,4} = 10.2–11.0$ Hz.[7b,8]

The *trans,trans*-configuration and double bond position in the enamine moiety of chromanoenamines *tt*-**8** was confirmed by monocrystal X-ray structural analysis of compound *tt*-**8a** (Fig. 2). All substituents in the pyran ring of molecule *tt*-**8a** were arranged in a transoid configuration and occupied equatorial positions. The pyran ring was in a half-chair conformation, with the dihedral angles H(2)–C(2)–C(3)–H(3) and H(3)–C(3)–C(4)–H(4) equal to −176 (2)° and 172 (2)°, respectively. The double bond in the five-membered ring was localised between the C(11) and C(15) atoms.

Hydrolysis of chromanoenamines *ct*-**7a**–**q** in aqueous methanol under mild conditions (dilute HCl, 20°C, 24 h for 2-CF_3-chromanes *ct*-**7a**–**g** and 50°C, 5 h for 2-CCl_3- and 2-Ph-chromanes *ct*-**7h**–**q**) led to the respective chromanoketones *ct*-**9a**–**q** with preservation of configuration at the C-2, C-3, C-4, and C-2′ atoms (C-2′ is equivalent to the C-5′ atom in chromanes *ct*-**7**) (Scheme 4, Table 3). The hydrolysis of 2-CF_3-chromanoenamines *ct*-**7** at 50°C was accompanied by the formation of 2-CF_3-chromenes **2** in a retro-Michael reaction; moreover, in a range of cases the 2-CF_3-chromanoketones *ct*-**9** were epimerised to the isomers *tc*-**9** via the *aci*-form, already previously observed for the *ct*-isomers of 2,3,4-trisubstituted chromanes.[7a,c]

The *cis,trans*-configuration of pyran ring and the *anti*-orientation of H-4 and H-2′ hydrogen atoms in the hydrolysis products *ct*-**9a**–**q** were established by monocrystal X-ray structural analysis of chromane *ct*-**9l** (Fig. 3). The molecular geometry of chromanoketones *ct*-**9l** was closely related to the chromanoenamine *ct*-**7h** (Fig. 1), with the CCl_3 group also occupying equatorial position, the nitro group and enamine moiety being in a *trans*-diaxial relationship, and the pyran ring in half-chair configuration. These data are in a good agreement with the observed values of ^{1}H NMR coupling constants $J_{2,3} = 1.5–2.6$ Hz and $J_{3,4} = 1.2–1.9$ Hz for the hydrolysis products obtained from enamines *ct*-**7a**–**q**. At the same time, the absolute value of dihedral angle H(15)–C(15)–C(4)–H(4) in the molecule of compound *ct*-**9l** was larger (−86.3°) than in the

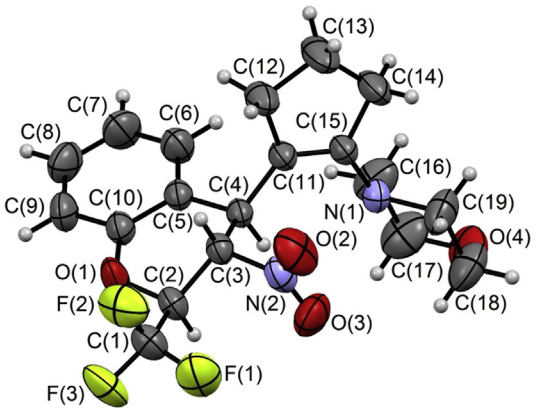
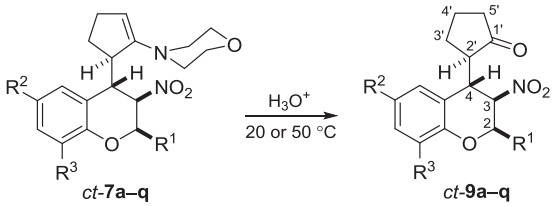


Fig. 2. Molecular structure of *tt*-**8a** (ORTEP drawing, 50% probability level).



Scheme 4. Hydrolysis of chromanes *ct*-**7a**–**q**.

Table 3
Yields of chromanes *ct*-**9**.

Chromane	R^1	R^2	R^3	Yield, %
ct-**9a**	CF_3	H	H	90
ct-**9b**	CF_3	MeO	H	71
ct-**9c**	CF_3	H	EtO	78
ct-**9d**	CF_3	Cl	H	83
ct-**9e**	CF_3	Br	H	80
ct-**9f**	CF_3	Cl	Cl	85
ct-**9g**	CF_3	Br	Br	89
ct-**9h**	CCl_3	H	H	71
ct-**9i**	CCl_3	MeO	H	70
ct-**9j**	CCl_3	H	EtO	87
ct-**9k**	CCl_3	Cl	H	99
ct-**9l**	CCl_3	Br	H	91
ct-**9m**	CCl_3	Cl	Cl	84
ct-**9n**	CCl_3	Br	Br	81
ct-**9o**	Ph	H	H	94
ct-**9p**	Ph	MeO	H	91
ct-**9q**	Ph	Br	H	84

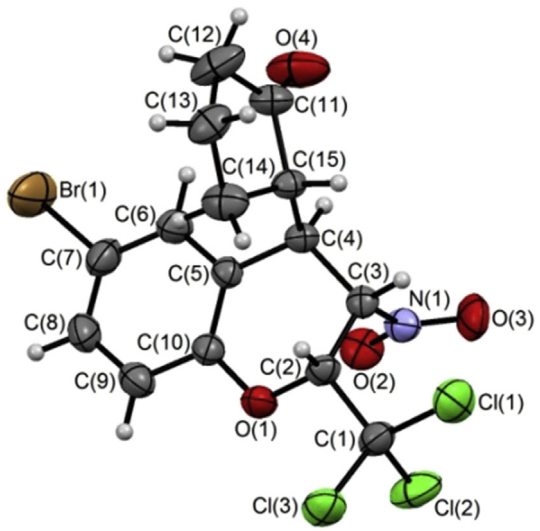


Fig. 3. Molecular structure of *ct*-**9l** (ORTEP drawing, 50% probability level).

chromane *ct*-**7h** (63.5°), increasing the vicinal $J_{4,2'}$ constants in chromanoketones *ct*-**9a**–**q** to 4.7–6.2 Hz, compared to the chromanoenamines *ct*-**7a**–**q** ($J_{4,2'} = 2.3–3.1$ Hz).

Acidic hydrolysis of chromanoenamines *tt*-**8** under non-epimerising conditions (dilute HCl, 20°C, 24 h) led to high yields of chromanoketones *tt*-**9** and *tt*-**9′**, which differed only by the configuration at C-2′ atom. The major component was the more stable epimer *tt*-**9** with *anti*-configuration of H-4 and H-2′ hydrogen atoms (Scheme 5, Table 4). When the hydrolysis of chromanes *tt*-**8a,b,d,k** was performed for 5 h at 50°C, the content of the respective epimers *tt*-**9** increased to 81–90%, but the yield of 6-chlorosubstituted chromane *tt*-**9d** at the same time decreased to

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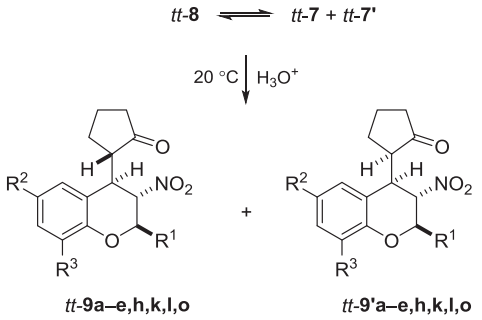


Scheme 5. Hydrolysis of chromanes *tt*-**8**.

Table 4
Yields of chromanes *tt*-**9** and *tt*-**9'**.

Chromane	R^1	R^2	R^3	Yield, %	*tt*-9:*tt*-9′ ratio, %
tt-**9a** + *tt*-**9'a**	CF_3	H	H	80	69:31
tt-**9b** + *tt*-**9'b**	CF_3	MeO	H	77	75:25
tt-**9c** + *tt*-**9'c**	CF_3	H	EtO	92	79:21
tt-**9d** + *tt*-**9'd**	CF_3	Cl	H	73	74:26
tt-**9e** + *tt*-**9'e**	CF_3	Br	H	84	71:29
tt-**9h** + *tt*-**9'h**	CCl_3	H	H	51[a]	100:0[a]
tt-**9k** + *tt*-**9'k**	CCl_3	Cl	H	94	71:29
tt-**9l** + *tt*-**9'l**	CCl_3	Br	H	96	63:37
tt-**9o** + *tt*-**9'o**	Ph	H	H	87	76:24

[a] After purification by column chromatography.

55% due to a retro-Michael side reaction. It is important to note that epimerisation at the C-3 atom was not observed, while ketones *tt*-**9** can be purified from an impurity of the minor epimer *tt*-**9′** by a simple recrystallisation from hexane. Hydrolysis of the mixture containing isomers *tt*-**8h** and *ct*-**8h**, which was obtained upon microwave irradiation, followed by purification of the reaction product by column chromatography, gave the stereoisomer *tt*-**9h** as an individual compound in 51% yield.

We propose that the ratio of hydrolysis products *tt*-**9** and *tt*-**9′** under conditions not conductive to epimerisation (Table 4) was affected by the content of tautomers *tt*-**8**, *tt*-**7** and *tt*-**7′** in the solution. An additional amount of the more stable epimer *tt*-**9** with *anti*-configuration of H-4 and H-2′ atoms was apparently formed during the heating from the less stable chromane *tt*-**9′**, as a result of epimerisation at the C-2′ atom. It should be mentioned in particular that the attempt to synthesise chromanoketones **9a,h** from chromenes **2a,h** and cyclopentanone under the conditions developed by Yan and coworkers[5] for the 2-unsubstituted analogs **1** produced a complex mixture of unidentified products in both cases.

The major isomers of chromanoketones *tt*-**9** were stereochemically identified by monocrystal X-ray structural analysis of compounds *tt*-**9c** and *tt*-**9h** (Figs. 4 and 5). As shown in Fig. 4, the pyran ring in the molecule of 2-CF_3-chromane *tt*-**9c** in the solid state assumed a half-chair conformation, with all substituents having transoid relationships and occupying equatorial positions. The molecule of 2-CCl_3-chromanoketone *tt*-**9h** (Fig. 5) also had a *trans,trans*-configuration, but its pyran ring assumed a twist-boat conformation with the O(1), C(3), and C(4) atoms deviating from the plane of other atoms by 0.516, 0.348, and 0.687 Å, respectively. For this reason, the bulky trichloromethyl group in the molecule of compound *tt*-**9h** occupied an equatorial position, while the nitro group and ketone moiety were oriented axially. The difference in molecular conformations of compounds *tt*-**9c** and *tt*-**9h** was associated with a decrease of dihedral angles H(2)–C(2)–C(3)–H(3) and H(3)–C(3)–C(4)–H(4) from 178 (2) and −157 (2)° in chromane *tt*-**9c** to 131 (2) and −85 (3)° in chromane *tt*-**9h**.

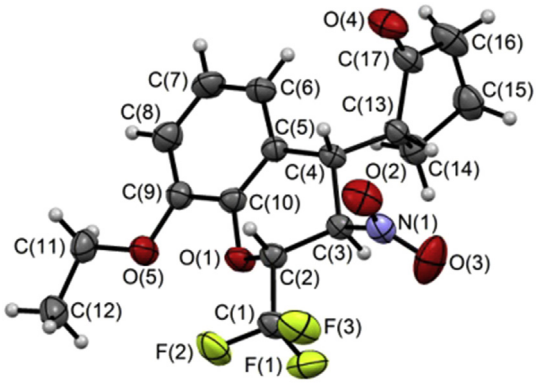


Fig. 4. Molecular structure of *tt*-**9c** (ORTEP drawing, 50% probability level).

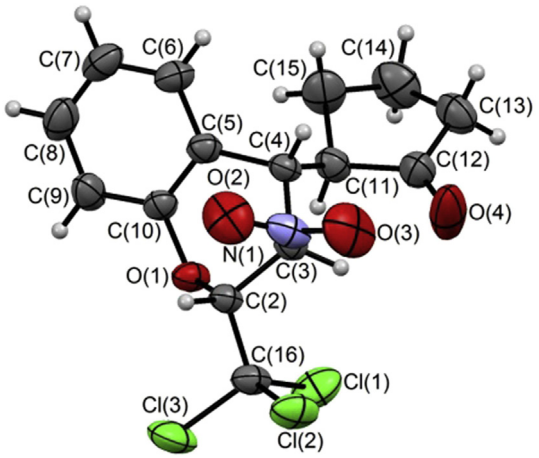
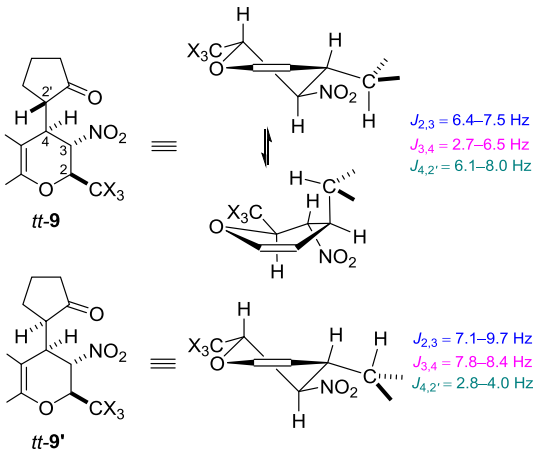


Fig. 5. Molecular structure of *tt*-**9h** (ORTEP drawing, 50% probability level).

Apparently, 2-CX_3-chromanoketones *tt*-**9** existed in $CDCl_3$ and C_6D_6 solutions as a dynamic equilibrium mixture of half-chair and boat conformers (Scheme 6), resulting in a decrease of vicinal coupling constants to $J_{2,3}$ = 6.4–7.5 Hz and $J_{3,4}$ = 2.7–6.5 Hz compared to the chromanoenamines *tt*-**8** ($J_{2,3}$ = 7.7–10.1 Hz, $J_{3,4}$ = 10.2–11.0 Hz). However, the half-chair conformation was predominant in solutions of 2-Ph-substituted chromane *tt*-**9o**, with



Scheme 6. The preferred conformations of epimeric chromanes *tt*-**9** and *tt*-**9′** in solution.

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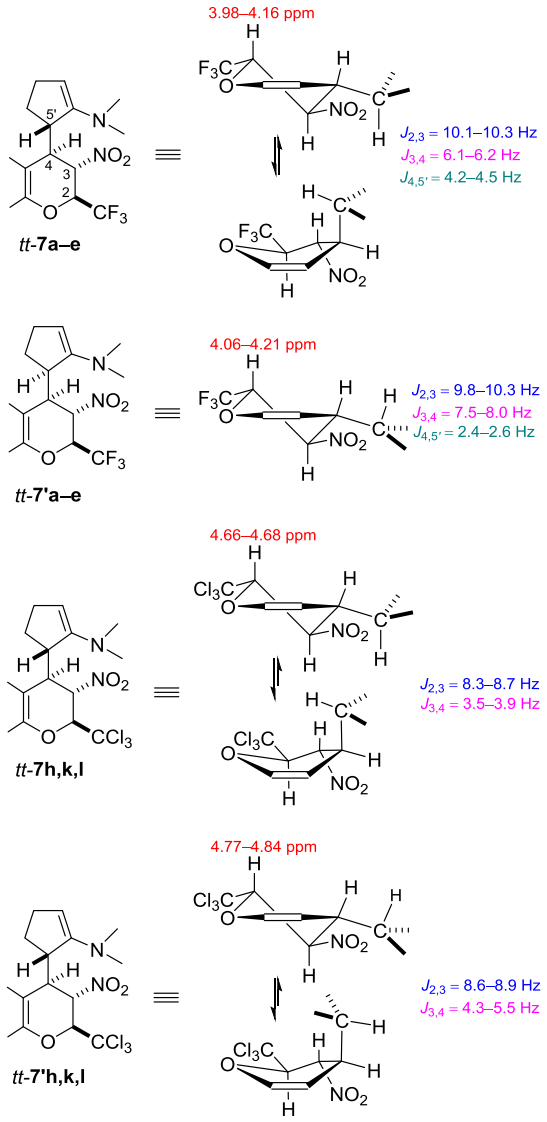

Scheme 7. The preferred conformations of epimeric chromanes *tt*-**7** and *tt*-**7′** in solution.

the observed values of $J_{2,3}$ = 9.6 Hz and $J_{3,4}$ = 9.8 Hz.

The proposed *trans,trans*-configuration of pyran ring in the minor isomers *tt*-**9′**, which in solution assumed a half-chair conformation with equatorial orientation of all substituents, was supported by the large values of $J_{2,3}$ = 7.1–9.8 Hz and $J_{3,4}$ = 7.5–9.8 Hz in their ^{1}H NMR spectra, as well as the data obtained from a 2D ^{1}H–^{1}H NOESY experiment for a mixture of 2-CCl_3-chromanoketones *tt*-**9l** and *tt*-**9'l**, where both isomers showed cross-peaks between the H-2 and H-4 atoms. The *syn*-orientation of H-4 and H-2′ hydrogen atoms in epimers *tt*-**9′** was indicated by the smaller vicinal coupling constant $J_{4,2'}$ (2.8–4.0 Hz), compared to the epimers *tt*-**9** with *anti*-orientation of these atoms ($J_{4,2'}$ = 6.1–8.0 Hz) (Scheme 6). The exception was the 2-Ph-chromane **9o** again, for which both epimers had the value of $J_{4,2'}$ = 2.4 Hz.

As shown above, the hydrolysis of compounds *tt*-**8** under mild conditions occurred without changing the configuration of pyran ring. Therefore, chromanoenamines *tt*-**7** and *tt*-**7′**, which existed in solution as an equilibrium mixture with compounds *tt*-**8**, were *trans,trans*-isomers similarly to the chromanoketones *tt*-**9** and *tt*-**9′** and their only difference was the configuration of substituents at the C-5′ atom. ^{1}H NMR characterization of the epimeric 2-CX_3-chromanes *tt*-**7** and *tt*-**7′**, regardless of the selected deuterated solvent, revealed the same trends as for chromanoketones *tt*-**9** and *tt*-**9′**, the stereochemistry of which was established unequivocally by X-ray structural analysis. Therefore, the preferred conformations of epimeric chromanes *tt*-**7** and *tt*-**7′** in $CDCl_3$ or C_6D_6 solutions, as well as the *syn*- or *anti*-configurations of H-4 and H-5′ hydrogen atoms could be deduced from the respective vicinal coupling constants.

Similarly to ketones *tt*-**9** and *tt*-**9′**, the *anti*-isomers of 2-CF_3-chromanoenamines *tt*-**7a**–**e** existed in solutions as two conformers, while for the *syn*-isomers *tt*-**7'a**–**e** the only stable conformation was half-chair with lower values of $J_{4,5'}$ constants compared to the *anti*-isomers *tt*-**7a**–**e** (Scheme 7). In the series of 2-CCl_3-substituted epimeric chromanoenamines *tt*-**7h,k,l** and *tt*-**7'h,k,l**, the contribution of the boat conformer to the overall conformational equilibrium in $CDCl_3$ or C_6D_6 solutions was observed for both epimers, leading to a decrease of $J_{3,4}$ constants to 3.5–3.9 Hz in *anti*- and 4.3–5.5 Hz in *syn*-isomers. Since the signal of H-4 proton in the spectra of these compounds was not observed due to overlap, the assignment of epimers was based on the different chemical shifts of H-2 proton, the signal of which, as in the case of 2-CF_3-substituted analogs, was better shielded in epimers *tt*-**7**, regardless of the deuterated solvent used. In analogy to 2-CF_3-chromanes *tt*-**7a**–**e**, the epimers *tt*-**7h,k,l** with *anti*-configuration of hydrogen atoms differed from the *syn*-isomer with their lower values of $J_{3,4}$ constant (Scheme 7, chemical shifts of H-2 atom are reported for solutions of compounds *tt*-**7** and *tt*-**7′** in C_6D_6).

Both of the epimeric 2-Ph-chromanes *tt*-**7o** and *tt*-**7'o** exhibited similar chemical shifts of pyran ring protons and large values of $J_{2,3}$ = 10.0–10.2 Hz and $J_{3,4}$ = 7.5–7.6 Hz, indicating that they existed in C_6D_6 solution exclusively in the half-chair conformation. For this reason, we were unable to reliably assign these epimers as *anti*- or *syn*-isomers, while the *anti*-configuration of H-4 and H-5′ hydrogen atoms was postulated for the predominant epimer in the solution (the tautomeric ratio *tt*-**8o**:*tt*-**7o**:*tt*-**7'o** = 75:14:11).

3. Conclusion

Thus, 2-(trihalomethyl)- and 2-phenylsubstituted 3-nitro-2*H*-chromenes reacted stereoselectively with 1-morpholinocyclopentene and, depending on the reaction temperature, formed Michael adducts **7** or **8** as individual *cis,trans*- or *trans,trans*-isomers. Acidic hydrolysis of these compounds under non-epimerising conditions proceeded with preservation of the pyran ring configuration and led to the respective 4-(cyclopentanon-2-yl)chromane stereoisomers **9** with *anti*-configuration of H-4 and H-2′ hydrogen atoms. The obtained 2,3,4-trisubstituted chromanes are clearly of interest as starting materials for further diastereoselective syntheses. For example, ketones **9** can be used for the preparation of individual stereoisomers of annulated pyrroline-*N*-oxides and pyrrolidines as a result of reduction of the nitro group.[5,9]

4. Experimental

4.1. General

NMR spectra were recorded on Bruker DRX-400 (^{1}H–400 MHz and ^{19}F–376 MHz) and AVANCE-500 (^{1}H–500 MHz, ^{19}F–471 MHz and ^{13}C–126 MHz) spectrometers in $CDCl_3$ or C_6D_6 with TMS and C_6F_6 as internal standards. IR spectra were recorded on a Nicolet 6700 instruments (FTIR mode, ZnSe crystal). Mass spectra were recorded on a Waters Xevo Q-ToF mass spectrometer (ESI) with Acquity UPLC system and maxis mass spectrometer Impact HD

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Bruker Daltonik GmbH. Elemental analyses were performed at the Microanalysis Services of the Institute of Organic Synthesis, Ural Branch, Russian Academy of Sciences. Melting points were determined on a Stuart SMP40 apparatus. All solvents used were dried and distilled per standard procedures. The starting nitrochromenes **2a**–**n** and **2o**–**q** were prepared according to described procedures.[10,11]

4.2. General procedure for the synthesis of 2-CX_3-chromanes ct-7a–n

The appropriate chromene **2** (1.0 mmol) was dissolved in anhydrous acetonitrile (0.15 mL for 2-CF_3-chromenes or 0.50 mL for 2-CCl_3-chromenes) and treated by the addition of freshly distilled 1-morpholinocyclopentene (**6**) (0.16 g, 1.0 mmol), then maintained at −18 or 20°C for the time indicated in Table 1. In the case if chromanes *ct*-**7a**–**e** did not precipitate within 24 h, the solution was seeded with the respective chromane *ct*-**7** or triturated, then maintained at −18°C for the rest of the time. The precipitate that formed was collected by filtration and washed with cold acetonitrile (3 × 0.1 mL). Chromanes *ct*-**7a**–**n** were isolated as colourless prisms.

4.2.1. 4-{(5R*)-[(2S*,3R*,4S*)-3-Nitro-2-(trifluoromethyl)chroman-4-yl]cyclopent-1-yl}morpholine (ct-7a)

Yield 0.23 g (58%), m.p. 117–118 °C (decomp.). IR (ATR): 1626, 1557, 1490, 1453, 1377, 1336 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 1.31–2.13 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.74–2.90 (m, 3H, H-5′, $O(CHH)_2$), 2.94 (br d, J = 2.5 Hz, 1H, H-4), 3.08 (ddd, J = 11.2, 6.6, 2.9 Hz, 2H, $O(CHH)_2$), 4.29 (br s, 1H, =CH), 4.85 (qd, J = 6.6, 2.0 Hz, 1H, H-2), 4.97 (dd, J = 2.0, 0.7 Hz, 1H, H-3), 6.59 (dd, J = 7.9, 1.5 Hz, 1H, H-8), 6.64 (td, J = 7.8, 1.2 Hz, 1H, H-7), 6.79 (td, J = 8.0, 1.5 Hz, 1H, H-6), 6.85 (dd, J = 8.1, 1.2 Hz, 1H, H-5); ^{19}F NMR (376 MHz, C_6D_6) δ 87.5 (d, J = 6.6 Hz, CF_3); ^{13}C NMR (101 MHz, C_6D_6) δ 28.9, 29.3, 43.7, 47.1, 50.0, 65.8, 71.9 (q, J = 34.1, C-2), 77.6, 106.5, 117.4, 121.1, 122.4, 123.1 (q, J = 280.4, CF_3), 128.4, 129.0, 150.7, 152.8. Anal. Calcd. for $C_{19}H_{21}F_3N_2O_4$: C, 57.28; H, 5.31; N, 7.03. Found: C, 57.21; H, 5.41; N, 6.96.

4.2.2. 4-{(5R*)-[(2S*,3R*,4S*)-6-Methoxy-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (ct-7b)

Yield 0.21 g (50%), m.p. 120–121 °C (decomp.). IR (ATR): 1627, 1558, 1496, 1469, 1450, 1426, 1379, 1333 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 1.20–2.23 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.82–2.89 (1H, m, H-5′), 2.90–2.98 (m, 2H, $O(CHH)_2$), 3.00 (br d, J = 2.5 Hz, 1H, H-4), 3.14 (ddd, J = 11.4, 6.6, 2.8 Hz, 2H, $O(CHH)_2$), 3.26 (s, 3H, MeO), 4.30 (br s, 1H, =CH), 4.86 (qd, J = 6.6, 1.9 Hz, 1H, H-2), 4.97 (dd, J = 1.9, 0.9 Hz, 1H, H-3), 6.39 (dd, J = 9.0, 2.9 Hz, 1H, H-7), 6.50 (d, J = 2.9 Hz, 1H, H-5), 6.79 (d, J = 9.0 Hz, 1H, H-8); ^{19}F NMR (376 MHz, C_6D_6) δ 87.6 (d, J = 6.6 Hz, CF_3); ^{13}C NMR (101 MHz, C_6D_6) δ 28.9, 29.3, 43.7, 47.2, 50.1, 55.5, 65.9, 71.7 (q, J = 31.5 Hz, C-2), 77.7, 106.5, 113.6, 114.5, 118.0, 123.2 (q, J = 279.8 Hz, CF_3), 124.6, 147.2, 150.7, 155.3. HRMS (ESI): calcd. for 429.1632 $[M+H]^+$ $C_{20}H_{24}F_3N_2O_5$, found 429.1636.

4.2.3. 4-{(5R*)-[(2S*,3R*,4S*)-8-Ethoxy-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (ct-7c)

Yield 0.22 g (49%), m.p. 118–119 °C (decomp.). IR (ATR): 1620, 1589, 1563, 1474, 1450, 1399, 1378, 1340 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 1.08 (t, J = 7.0 Hz, 3H, Me), 1.34–2.19 (8H, m, 2 CH_2, $N(CH_2)_2$), 2.87–2.99 (m, 3H, $O(CHH)_2$, H-5′), 3.03 (1H, d, J = 2.4 Hz, H-4), 3.15 (ddd, J = 11.0, 6.6, 2.8, 2H, $O(CHH)_2$), 3.63 (dq, J = 9.5, 7.0 Hz, 1H, $OCHH$), 3.69 (dq, J = 9.5, 7.0 Hz, 1H, $OCHH$), 4.30 (br s, 1H, =CH), 4.90 (qd, J = 6.6, 1.8 Hz, 1H, H-2), 5.00 (br d, J = 1.8, 1H, H-3), 6.36 (d, J = 7.7 Hz, 1H, H-5/H-7), 6.51 (d, J = 7.8 Hz, 1H, H-7/H-5), 6.67 (t, J = 7.8 Hz, 1H, H-6); ^{19}F NMR (376 MHz, C_6D_6) δ 87.7 (d, J = 6.6 Hz, CF_3). HRMS (ESI): calcd. for 443.1788 $[M+H]^+$ $C_{21}H_{26}F_3N_2O_5$, found 443.1787.

4.2.4. 4-{(5R*)-[(2S*,3R*,4S*)-6-Chloro-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (ct-7d)

Yield 0.28 g (64%), m.p. 121–122 °C (decomp.). IR (ATR): 1630, 1555, 1481, 1455, 1443, 1415, 1373, 1326 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 1.26–2.07 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.59–2.65 (m, 1H, H-5′), 2.77 (br d, J = 2.6 Hz, 1H, H-4), 2.79–2.90 (m, 2H, $O(CHH)_2$), 3.05 (ddd, J = 11.2, 6.7, 2.9 Hz, 2H, $O(CHH)_2$), 4.25 (br s, 1H, =CH), 4.72 (qd, J = 6.6, 2.0 Hz, 1H, H-2), 4.88 (dd, J = 2.0, 0.8 Hz, 1H, H-3), 6.55 (d, J = 8.5 Hz, 1H, H-8), 6.71 (d, J = 2.5 Hz, 1H, H-5), 6.73 (dd, J = 8.5, 2.5 Hz, 1H, H-7); ^{19}F NMR (376 MHz, C_6D_6) δ 87.5 (d, J = 6.6 Hz, CF_3); ^{13}C NMR (101 MHz, C_6D_6) δ 28.4, 29.0, 43.3, 46.9, 50.1, 65.8, 71.9 (q, J = 34.4 Hz, C-2), 77.1, 106.9, 118.6, 120.1, 122.9 (q, J = 280.9 Hz, CF_3), 125.9, 128.5, 128.7, 150.3, 151.2. Anal. Calcd. for $C_{19}H_{20}ClF_3N_2O_4$: C, 52.73; H, 4.66; N, 6.47. Found: C, 52.80; H, 4.77; N, 6.57.

4.2.5. 4-{(5R*)-[(2S*,3R*,4S*)-6-Bromo-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (ct-7e)

Yield 0.34 g (72%), m.p. 127–128 °C (decomp.). IR (ATR): 1629, 1555, 1477, 1453, 1410, 1374, 1327 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 1.25–2.11 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.58–2.65 (m, 1H, H-5′), 2.77 (br d, J = 2.7 Hz, 1H, H-4), 2.78–2.88 (m, 2H, $O(CHH)_2$), 3.06 (ddd, J = 11.2, 6.6, 2.8 Hz, 2H, $O(CHH)_2$), 4.25 (br s, 1H, =CH), 4.70 (qd, J = 6.6, 1.9 Hz, 1H, H-2), 4.88 (dd, J = 1.9, 1.0 Hz, 1H, H-3), 6.49 (d, J = 8.5 Hz, 1H, H-8), 6.84–6.89 (m, 2H, H-5, H-7); ^{19}F NMR (376 MHz, C_6D_6) δ 87.5 (d, J = 6.6 Hz, CF_3). Anal. Calcd. for $C_{19}H_{20}BrF_3N_2O_4$: C, 47.81; H, 4.22; N, 5.87. Found: C, 47.79; H, 4.14; N, 5.90.

4.2.6. 4-{(5R*)-[(2S*,3R*,4S*)-6,8-Dichloro-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (ct-7f)

Yield 0.36 g (71%), m.p. 147–148 °C (decomp.). IR (ATR): 1630, 1558, 1460, 1437, 1413, 1394, 1373, 1345, 1325 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 1.20–2.02 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.51–2.57 (m, 1H, H-5′), 2.73 (br d, J = 2.7 Hz, 1H, H-4), 2.80–2.90 (m, 2H, $O(CHH)_2$), 3.08 (ddd, J = 11.3, 6.6, 2.9 Hz, 2H, $O(CHH)_2$), 4.23 (br s, 1H, =CH), 4.70 (qd, J = 6.4, 2.1 Hz, 1H, H-2), 4.85 (dd, J = 2.1, 1.0 Hz, 1H, H-3), 6.53 (d, J = 2.1 Hz, 1H, H-5/H-7), 6.97 (d, J = 2.1 Hz, 1H, H-7/H-5); ^{19}F NMR (376 MHz, C_6D_6) δ 87.6 (d, J = 6.4 Hz, CF_3); ^{13}C NMR (101 MHz, C_6D_6) δ 28.4, 29.2, 43.4, 47.0, 50.0, 65.9, 72.2 (q, J = 34.6 Hz, C-2), 76.8, 107.4, 119.3, 121.3, 122.6 (q, J = 276.2 Hz, CF_3), 124.0, 127.1, 128.9147.3, 150.1. Anal. Calcd. for $C_{19}H_{19}Cl_2F_3N_2O_4$: C, 48.84; H, 4.10; N, 6.00. Found: C, 49.00; H, 4.30; N, 5.92.

4.2.7. 4-{(5R*)-[(2S*,3R*,4S*)-6,8-Dibromo-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (ct-7g)

Yield 0.37 g (66%), m.p. 137–138 °C (decomp.). IR (ATR): 1630, 1560, 1456, 1372 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 1.19–2.03 (m, 2 CH_2, 8H, $N(CH_2)_2$), 2.48–2.57 (m, 1H, H-5′), 2.71 (br d, J = 2.8 Hz, 1H, H-4), 2.76–2.95 (m, 2H, $O(CHH)_2$), 3.09 (ddd, J = 11.3, 6.6, 2.9 Hz, 2H, $O(CHH)_2$), 4.22 (br s, 1H, =CH), 4.68 (qd, J = 6.4, 2.2 Hz, 1H, H-2), 4.83 (dd, J = 2.2, 1.0 Hz, 1H, H-3), 6.73 (d, J = 2.1 Hz, 1H, H-5/H-7), 7.32 (d, J = 2.1 Hz, 1H, H-7/H-5). ^{19}F NMR (376 MHz, C_6D_6) δ 87.6 (d, J = 3.3 Hz, CF_3); ^{13}C NMR (101 MHz, C_6D_6) δ 28.4, 29.2, 43.4, 47.0, 50.0, 65.9, 72.3 (q, J = 34.8 Hz, C-2), 76.8, 107.4, 112.4, 114.5, 122.6 (q, J = 280.8 Hz, CF_3), 124.5, 130.7, 134.4, 148.6, 150.1. Anal. Calcd. for $C_{19}H_{19}Br_2F_3N_2O_4$: C, 41.03; H, 3.44; N, 5.04. Found: C, 41.07; H, 3.50; N, 5.02.

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4.2.8. 4-{(5R)-[(2S*,3R*,4S*)-3-Nitro-2-(trichloromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (ct-**7h**)*

Yield 0.30 g (68%), m.p. 151–152 °C (decomp.). IR (ATR): 1622, 1584, 1555, 1490, 1451, 1376, 1337 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.91–2.60 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.90–3.12 (m, 2H, $O(CHH)_2$), 3.21–3.30 (m, 2H, $O(CHH)_2$), 3.39 (d, J = 2.7 Hz, 1H, H-4), 3.49–3.56 (m, 1H, H-5′), 4.78 (br s, 1H, =CH), 5.04 (d, J = 1.4 Hz, 1H, H-2), 5.43 (d, J = 1.4 Hz, 1H, H-3), 7.04 (td, J = 7.5, 1.0 Hz, 1H, H-6), 7.13 (dd, J = 8.2, 1.0 Hz, 1H, H-8), 7.21–7.31 (m, 2H, H-5, H-7); ^{13}C NMR (126 MHz, $CDCl_3$) δ 29.2, 29.4, 46.2, 47.2, 49.7, 65.9, 77.9, 81.3, 96.0, 107.3, 117.2, 121.2, 122.4, 128.2, 128.5, 150.1, 153.3. Anal. Calcd. for $C_{19}H_{21}Cl_3N_2O_4$: C, 50.97; H, 4.73; N, 6.26. Found: C, 50.96; H, 4.77; N, 6.22.

4.2.9. 4-{(5R)-[(2S*,3R*,4S*)-6-Methoxy-3-nitro-2-(trichloromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (ct-**7i**)*

Yield 0.30 g (62%), m.p. 164–165 °C (decomp.). IR (ATR): 1631, 1556, 1495, 1449, 1424, 1378, 1332 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.92–2.59 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.97–3.16 (m, 2H, $O(CHH)_2$), 3.31 (ddd, J = 11.2, 6.5, 3.0 Hz, 2H, $O(CHH)_2$), 3.36 (d, J = 2.4 Hz, 1H, H-4), 3.47–3.53 (m, 1H, H-5′), 3.78 (s, 3H, MeO), 4.79 (br s, 1H, =CH), 5.03 (d, 1H, J = 1.4, H-2), 5.41 (d, J = 1.4 Hz, 1H, H-3), 6.80 (d, J = 2.8 Hz, 1H, H-5), 6.83 (dd, J = 8.8, 2.8 Hz, 1H, H-7), 7.07 (d, J = 8.8 Hz, 1H, H-8); ^{13}C NMR (101 MHz, $CDCl_3$) δ 29.3 (2C), 46.5, 47.2, 49.8, 55.8, 65.9, 77.8, 81.5, 96.0, 107.3, 113.3, 113.9, 117.8, 132.9, 147.5, 150.1, 154.9. Anal. Calcd for $C_{20}H_{23}Cl_3N_2O_5$: C, 50.28; H, 4.85; N, 5.86. Found: C, 50.26; H, 4.72; N, 5.86.

4.2.10. 4-{(5R)-[(2S*,3R*,4S*)-8-Ethoxy-3-nitro-2-(trichloromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (ct-**7j**)*

Yield 0.26 g (52%), m.p. 142–143 °C (decomp.). IR (ATR): 1629, 1583, 1556, 1486, 1467, 1450, 1378, 1349, 1337 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.43 (t, J = 7.0 Hz, 3H, Me), 1.89–2.60 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.95–3.17 (m, 2H, $O(CHH)_2$), 3.24–3.34 (m, 2H, $O(CHH)_2$), 3.47–3.55 (m, 1H, H-5′), 3.39 (d, J = 2.3 Hz, 1H, H-4), 4.13 (dq, J = 9.7, 7.0 Hz, 1H, OC*H*H), 4.16 (dq, J = 9.7, 7.0 Hz, 1H, OCH*H*), 4.78 (br s, 1H, =CH), 5.04 (d, J = 1.2 Hz, 1H, H-2); 5.42 (br s, 1H, H-3), 6.87 (dd, J = 7.5, 1.7 Hz, 1H, H-5/H-7), 6.90 (dd, J = 7.5, 1.7 Hz, 1H, H-7/H-5), 6.94 (t, J = 7.5 Hz, 1H, H-6); ^{13}C NMR (126 MHz, $CDCl_3$) δ 15.1, 29.3, 29.6, 46.3, 47.2, 50.0, 65.9, 66.1, 78.1, 82.0, 96.9, 106.9, 114.4, 120.9, 121.7, 122.6, 145.0, 148.4, 150.5. Anal. Calcd. for $C_{21}H_{25}Cl_3N_2O_5$: C, 51.29; H, 5.12; N, 5.70. Found: C, 50.99; H, 5.12; N, 5.75.

4.2.11. 4-{(5R)-[(2S*,3R*,4S*)-6-Chloro-3-nitro-2-(trichloromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (ct-**7k**)*

Yield 0.36 g (74%), m.p. 156–157 °C (decomp.). IR (ATR): 1631, 1555, 1483, 1449, 1376, 1333 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.92–2.58 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.94–3.15 (m, 2H, $O(CHH)_2$), 3.33 (ddd, J = 11.3, 6.6, 3.0 Hz, 2H, $O(CHH)_2$), 3.35 (d, J = 3.1 Hz, 1H, H-4), 3.46–3.52 (m, 1H, H-5′), 4.82 (br s, 1H, =CH), 4.98 (d, J = 1.5 Hz, 1H, H-2), 5.41 (d, J = 1.5 Hz, 1H, H-3), 7.09 (d, J = 8.8 Hz, 1H, H-8), 7.23 (dd, J = 8.8, 2.3 Hz, 1H, H-7), 7.29 (d, J = 2.3 Hz, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$) δ 29.1, 29.4, 46.0, 47.1, 49.9, 65.9, 77.5, 81.5, 95.7, 107.9, 118.6, 123.0, 128.1, 128.3, 134.5, 149.9, 152.0. Anal. Calcd. for $C_{19}H_{20}Cl_4N_2O_4$: C, 47.33; H, 4.18; N, 5.81. Found: C, 47.29; H, 4.11; N, 5.67.

4.2.12. 4-{(5R)-[(2S*,3R*,4S*)-6-Bromo-3-nitro-2-(trichloromethyl)chroman-4-y])cyclopenten-1-yl}morpholine (ct-**7l**)*

Yield 0.41 g (77%), m.p. 163–164 °C (decomp.). IR (ATR): 1631, 1554, 1479, 1461, 1449, 1375, 1329 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.92–2.57 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.95–3.15 (m, 2H, $O(CHH)_2$), 3.33 (ddd, J = 11.3, 6.6, 3.0 Hz, 2H, $O(CHH)_2$), 3.36 (d, J = 2.9 Hz, 1H, H-4), 3.47–3.52 (m, 1H, H-5′), 4.81 (br s, 1H, =CH), 4.97 (d, J = 1.5 Hz, 1H, H-2), 5.41 (d, J = 1.5 Hz, 1H, H-3), 7.04 (d, J = 8.7 Hz, 1H, H-8), 7.37 (dd, J = 8.7, 2.2 Hz, 1H, H-7), 7.44 (d, J = 2.2 Hz, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$) δ 29.1, 29.4, 45.8, 47.1, 49.9, 65.9, 77.4, 81.4, 95.6, 107.9, 114.5, 118.9, 123.5, 131.0, 131.1, 149.8, 152.5. Anal. Calcd. for $C_{19}H_{20}BrCl_3N_2O_4$: C, 43.33; H, 3.83; N, 5.32. Found: C, 43.33; H, 3.73; N, 5.29.

4.2.13. 4-{(5R)-[(2S*,3R*,4S*)-6,8-Dichloro-3-nitro-2-(trichloromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (ct-**7m**)*

Yield 0.40 g (78%), m.p. 194–195 °C (decomp.). IR (ATP): 1627, 1553, 1461, 1439, 1372, 1335 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.91–2.60 (m, 8H, 2 CH_2, $N(CH_2)_2$), 3.01–3.15 (m, 2H, $O(CHH)_2$), 3.32–3.36 (m, 2H, $O(CHH)_2$), 3.37 (d, J = 2.5 Hz, 1H, H-4), 3.43–3.49 (m, 1H, H-5′), 4.84 (br s, 1H, =CH), 4.97 (d, J = 1.2 Hz, 1H, H-2), 5.41 (br s, 1H, H-3), 7.20 (d, J = 2.1 Hz, 1H, H-5/H-7), 7.36 (d, J = 2.1 Hz, 1H, H-7/H-5); ^{13}C NMR (101 MHz, $CDCl_3$) δ 29.0, 29.3, 46.0, 47.3, 49.8, 66.0, 77.2, 81.6, 95.2, 108.4, 123.3, 124.3, 126.5, 127.0, 128.5, 147.9, 149.6. Anal. Calcd. for $C_{19}H_{19}Cl_5N_2O_4$: C, 44.17; H, 3.71; N, 5.42. Found: C, 44.25; H, 3.81; N, 5.62.

4.2.14. 4-{(5R)-[(2S*,3R*,4S*)-6,8-Dibromo-3-nitro-2-(trichloromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (ct-**7n**)*

Yield 0.50 g (83%), m.p. 169–170 °C (decomp.). IR (ATR): 1626, 1552, 1455, 1372, 1333 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.90–2.60 (m, 8H, 2 CH_2, $N(CH_2)_2$), 3.07 (br s, 2H, $O(CHH)_2$), 3.31–3.37 (m, 2H, $O(CHH)_2$), 3.38 (d, J = 3.0 Hz, 1H, H-4), 3.42–3.49 (m, 1H, H-5′), 4.84 (br s, 1H, =CH), 4.96 (d, J = 1.5 Hz, 1H, H-2), 5.39 (d, J = 1.5 Hz, 1H, H-3), 7.39 (d, J = 2.1 Hz, 1H, H-5/H-7), 7.66 (dd, J = 2.1 Hz, 1H, H-7/H-5); ^{13}C NMR (126 MHz, C_6D_6) δ 28.9, 29.4, 45.7, 47.0, 50.0, 66.0, 77.3, 82.1, 95.8, 107.9, 112.5, 114.2, 125.1, 130.4, 134.1, 149.8, 149.9. Anal. Calcd. for $C_{19}H_{19}Br_2Cl_3N_2O_4$: C, 37.69; H, 3.16; N, 4.63. Found: C, 37.56; H, 3.10; N, 4.62.

*4.3. General procedure for the synthesis of 2-Ph-chromanes ct-**7o**–q*

Freshly distilled 1-morpholinocyclopentene (**6**) (0.19 g, 1.2 mmol) was added to a solution of the appropriate chromene **2** (1.0 mmol) in anhydrous *t*-butyl methyl ether (0.50–0.75 mL) and the mixture was maintained at 20°C for the time indicated in Table 1. The precipitate that formed was collected by filtration and washed with cold acetonitrile (3 × 0.1 mL). Chromanes *ct*-**7o**–**q** were obtained as white powders.

4.3.1. 4-{(5R)-[(2R*,3R*,4S*)-3-Nitro-2-phenylchroman-4-yl]cyclopenten-1-yl}morpholine (ct-**7o**)*

Yield 0.29 g (72%), m.p. 137–138 °C (decomp.). IR (ATR): 1625, 1582, 1543, 1486, 1451, 1375, 1326 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 1.45–2.31 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.82–3.04 (m, 3H, H-5′, $O(CHH)_2$), 3.09 (ddd, J = 11.3, 6.7, 2.8 Hz, 2H, $O(CHH)_2$), 3.15 (d, J = 2.8 Hz, 1H, H-4), 4.42 (br s, 1H, =CH), 4.93 (d, J = 2.0 Hz, 1H, H-2), 5.42 (d, J = 2.0 Hz, 1H, H-3), 6.72 (td, J = 7.6, 1.0 Hz, 1H, H-7), 7.01 (dd, J = 7.8, 1.0 Hz, 1H, H-8), 6.95 (td, J = 7.6, 1.3 Hz, 1H, H-7), 7.07 (dd, J = 7.8, 1.3 Hz, 1H, H-5), 7.10 (tt, J = 7.4, 1.2 Hz, 1H, H_p), 7.20 (t, J = 7.5 Hz, 2H, H_m), 7.53 (br d, J = 7.6 Hz, 2H, H_o); ^{13}C NMR (126 MHz, C_6D_6) δ 29.5, 30.3, 44.1, 47.9, 50.8, 66.5, 75.0, 86.5, 105.6, 118.1, 121.9, 122.2, 126.6, 128.5, 129.4, 129.6, 129.7, 137.8, 152.7, 155.4. Anal. Calcd. for $C_{24}H_{26}N_2O_4$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.63; H, 6.43; N, 6.80.

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4.3.2. 4-{(5R)-[(2R*,3R*,4S*)-6-Methoxy-3-nitro-2-phenylchroman-4-yl]cyclopenten-1-yl}morpholine (ct-**7p**)*

Yield 0.25 g (58%), m.p. 149–150 °C (decomp.). IR (ATR): 1630, 1545, 1493, 1453, 1440, 1427, 1376, 1354, 1322 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 1.44–2.40 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.92–3.06 (m, 3H, H-5′, $O(CHH)_2$), 3.14 (ddd, *J* = 10.9, 6.6, 2.8 Hz, 2H, $O(CHH)_2$), 3.20 (d, *J* = 2.9 Hz, 1H, H-4), 3.33 (s, 3H, MeO), 4.42 (br s, 1H, =CH), 4.91 (d, *J* = 2.2 Hz, 1H, H-2), 5.42 (d, *J* = 2.2 Hz, 1H, H-3), 6.56 (dd, *J* = 8.9, 2.9 Hz, 1H, H-7), 6.64 (d, *J* = 2.9 Hz, 1H, H-5), 6.99 (d, *J* = 8.9 Hz, 1H, H-8), 7.11 (tt, *J* = 7.5, 1.2 Hz, 1H, H_p), 7.21 (t, *J* = 7.5 Hz, 2H, H_m), 7.54 (br d, *J* = 7.5 Hz, 2H, H_o). ^{13}C NMR (101 MHz, C_6D_6) δ 28.8, 29.7, 43.5, 47.6, 50.2, 55.4, 66.0, 74.7, 86.1, 105.1, 113.6, 114.5, 118.0, 122.2, 126.1, 128.9, 129.0, 137.4, 149.0, 152.1, 154.7. Anal. Calcd. for $C_{25}H_{28}N_2O_5$: C, 68.79; H, 6.47; N, 6.42. Found: C, 68.80; H, 6.50; N, 6.38.

4.3.3. 4-{(5R)-[(2R*,3R*,4S*)-6-Bromo-3-nitro-2-phenylchroman-4-yl]cyclopenten-1-yl}morpholine (ct-**7q**)*

Yield 0.40 g (82%), m.p. 183–184 °C (decomp.). IR (ATR): 1631, 1546, 1476, 1453, 1440, 1372, 1349, 1325 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 1.35–2.26 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.75–2.90 (m, 3H, H-5′, $O(CHH)_2$), 2.96 (d, *J* = 3.1 Hz, 1H, H-4), 3.08 (ddd, *J* = 10.8, 6.6, 2.8 Hz, 2H, $O(CHH)_2$), 4.37 (br s, 1H, =CH), 4.82 (d, *J* = 2.2 Hz, 1H, H-2), 5.27 (d, *J* = 2.2 Hz, 1H, H-3), 6.71 (d, *J* = 7.5 Hz, 1H, H-8), 7.01 (dd, *J* = 7.5, 2.3 Hz, 1H, H-7), 7.02 (d, *J* = 2.3 Hz, 1H, H-5), 7.09 (tt, *J* = 7.4, 1.2 Hz, 1H, H_p), 7.18 (t, *J* = 7.5 Hz, 2H, H_m), 7.18 (dd, *J* = 7.6, 1.2 Hz, 2H, H_o); ^{13}C NMR (126 MHz, C_6D_6) δ 29.0, 30.0, 43.4, 47.4, 50.6, 66.3, 75.0, 85.7, 105.8, 113.8, 119.6, 124.3, 126.3, 129.3, 129.4, 131.3, 132.1, 137.1, 152.1, 154.2. Anal. Calcd. for $C_{24}H_{25}BrN_2O_4$: C, 59.39; H, 5.19; N, 5.77. Found: C, 59.17; H, 5.15; N, 5.96.

4.4. General procedure for the synthesis of 2-CF_3-chromanes tt-8a–e

Freshly distilled 1-morpholinocyclopentene (**6**) (0.16 g, 1.0 mmol) was added to a solution of the appropriate chromene **2** (1.0 mmol) in acetonitrile or methanol (0.50 mL) and the mixture was maintained at 35 °C for the time indicated in Table 1. In the case if no precipitate was obtained within 1 h, the solution was seeded with the respective chromane *tt*-**8** or triturated, then maintained at 35 °C for the rest of the time. The precipitate that formed was collected by filtration and washed with cold acetonitrile or methanol (3 × 0.1 mL). Chromanes *tt*-**8a**–**e** were obtained as colourless prisms or white powders.

4.4.1. 4-{2-[(2S,3S*,4R*)-3-Nitro-2-(trifluoromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (tt-**8a**), 4-{(5S*)-[(2S*,3S*,4R*)-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (tt-**7a**) and 4-{(5R*)-[(2S*,3S*,4R*)-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (tt-**7'a**)*

Yield in MeOH 0.31 g (78%), yield in MeCN 0.27 g (68%), m.p. 164–165 °C (decomp.). IR (ATR): 1669, 1562, 1478, 1450, 1415, 1359, 1328 cm^{-1}. Ratio of tautomers *tt*-**8a**:*tt*-**7a**:*tt*-**7'a** = 87:9:4 in 5 min and 70:22:8 in 24 h (C_6D_6).

*4.4.1.1. Compound tt-**8a**.* ^1H NMR (500 MHz, C_6D_6) δ 1.43–2.05 (m, 6H, 3 CH_2), 2.37–2.46 (m, 4H, $N(CH_2)_2$), 3.54–3.62 (m, 4H, $O(CH_2)_2$), 4.27 (dq, *J* = 10.1, 5.4 Hz, 1H, H-2), 4.84 (d, *J* = 11.0 Hz, 1H, 4-CH), 4.98 (dd, *J* = 11.0, 10.1 Hz, 1H, H-3), 6.75 (td, *J* = 6.8, 1.0 Hz, 1H, H-6), 6.78–6.82 (m, 2H, H-5, H-8), 6.84–6.89 (m, 1H, H-7); ^{19}F NMR (471 MHz, C_6D_6) δ 85.9 (d, *J* = 5.4 Hz, CF_3); ^{13}C NMR (101 MHz, C_6D_6) δ 21.1, 28.4, 28.8, 40.1, 51.6, 67.0, 73.5 (q, *J* = 32.6 Hz, C-2), 80.5, 117.1, 120.7, 121.1, 123.0, 123.2 (q, *J* = 281.6 Hz, C-2), 127.9, 128.9, 151.8, 154.8.

*4.4.1.2. Compound tt-**7a**.* ^1H NMR (500 MHz, C_6D_6) δ 1.13–2.62 (m, 8H, 3 CH_2, $N(CH_2)_2$), 2.94–3.02 (m, 1H, H-5′), 3.80 (dd, *J* = 6.2, 4.4 Hz, 1H, H-4), 4.05 (dq, *J* = 10.2, 5.5 Hz, 1H, H-2), 4.51 (br s, 1H, =CH), 5.02 (dd, *J* = 10.2, 6.2 Hz, 1H, H-3) (signals of $O(CH_2)_2$ and aromatic protons are masked); ^{19}F NMR (471 MHz, C_6D_6) δ 86.3 (d, *J* = 5.5 Hz, CF_3); ^{13}C NMR (101 MHz, C_6D_6) δ 23.6, 29.1, 42.1, 48.8, 49.5, 66.5, 75.4 (q, *J* = 32.7 Hz, C-2), 81.1, 105.1, 117.6, 123.1 (q, *J* = 281.1 Hz, CF_3), 124.2, 124.9, 128.5, 149.9, 153.7 (one C is not observed).

*4.4.1.3. Compound tt-**7'a**.* ^1H NMR (500 MHz, C_6D_6) δ 1.13–2.44 (m, 8H, 3 CH_2, $N(CH_2)_2$), 3.03–3.09 (m, 1H, H-5′), 3.40 (t, *J* = 4.8 Hz, 4H, $O(CH_2)_2$), 3.70 (dd, *J* = 7.9, 2.5 Hz, 1H, H-4), 4.11 (dq, *J* = 10.3, 5.4 Hz, 1H, H-2), 4.43 (br s, 1H, =CH), 5.04 (dd, *J* = 10.3, 7.9 Hz, 1H, H-3) (signals of aromatic protons are masked); ^{19}F NMR (471 MHz, C_6D_6) δ 86.0 (d, *J* = 5.4 Hz, CF_3); ^{13}C NMR (101 MHz, C_6D_6) δ 23.1, 24.3, 42.6, 46.9, 50.0, 66.5, 74.2 (q, *J* = 32.8 Hz, C-2), 83.8, 100.2, 117.3, 122.3, 123.2 (q, *J* = 281.6 Hz, CF_3), 133.3, 129.3, 151.0, 153.5 (one C is not observed). Anal. Calcd. for $C_{19}H_{21}F_3N_2O_4$: C, 57.28; H, 5.31; N, 7.03. Found: C, 57.34; H, 5.17; N, 7.11.

4.4.2. 4-{2-[(2S,3S*,4R*)-6-Methoxy-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (tt-**8b**), 4-{(5S*)-[(2S*,3S*,4R*)-6-methoxy-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (tt-**7b**) and 4-{(5R*)-[(2S*,3S*,4R*)-6-methoxy-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (tt-**7'b**)*

Yield in MeOH 0.25 g (59%), yield in MeCN 0.18 g (42%), m.p. 150–151 °C (decomp.). IR (ATR): 1559, 1541, 1520, 1496, 1461, 1421, 1371, 1340 cm^{-1}. Ratio of tautomers *tt*-**8b**:*tt*-**7b**:*tt*-**7'b** = 76:17:7 in 5 min and 61:27:12 in 24 h (C_6D_6).

*4.4.2.1. Compound tt-**8b**.* ^1H NMR (500 MHz, C_6D_6) δ 1.40–2.05 (m, 6H, 3 CH_2), 2.37–2.46 (m, 4H, $N(CH_2)_2$), 3.24 (s, 3H, MeO), 3.53–3.61 (m, 4H, $O(CH_2)_2$), 4.31 (dq, *J* = 10.1, 5.4 Hz, 1H, H-2), 4.89 (d, *J* = 11.0 Hz, 1H, H-4), 5.02 (dd, *J* = 11.0, 10.1 Hz, 1H, H-3), 6.41 (dd, *J* = 8.9, 2.8 Hz, 1H, H-7), 6.59 (d, *J* = 2.8 Hz, 1H, H-5), 6.75 (d, *J* = 8.9 Hz, 1H, H-8); ^{19}F NMR (471 MHz, C_6D_6) δ 86.0 (d, *J* = 5.4 Hz, CF_3); ^{13}C NMR (101 MHz, C_6D_6) δ 21.2, 28.3, 28.8, 40.3, 51.6, 55.1, 67.0, 73.7 (q, *J* = 32.6 Hz, C-2), 80.9, 113.5, 113.7, 117.8, 121.3, 121.9, 123.3 (q, *J* = 281.5 Hz, CF_3), 145.7, 154.8, 155.8.

*4.4.2.2. Compound tt-**7b**.* ^1H NMR (500 MHz, C_6D_6) δ 1.18–2.49 (m, 8H, 3 CH_2, $N(CH_2)_2$), 3.00–3.06 (m, 1H, H-5′), 3.27 (s, 3H, MeO), 3.49–3.63 (m, 4H, $O(CH_2)_2$), 3.82 (br t, *J* = 5.2 Hz, 1H, H-4), 4.16 (dq, *J* = 10.3, 5.5 Hz, 1H, H-2), 4.51 (br s, 1H, =CH), 5.06 (dd, *J* = 10.3, 6.2 Hz, 1H, H-3), 6.38 (dd, *J* = 8.9, 2.8 Hz, 1H, H-7), 6.63 (d, *J* = 2.8 Hz, 1H, H-5), 6.77 (d, *J* = 8.9 Hz, 1H, H-8); ^{19}F NMR (471 MHz, C_6D_6) δ 86.4 (d, *J* = 5.5 Hz, CF_3); ^{13}C NMR (101 MHz, C_6D_6) δ 23.1, 29.1, 42.6, 49.5, 50.0, 55.2, 66.4, 75.9 (q, *J* = 32.5 Hz, C-2), 81.3, 105.2, 112.9, 114.4, 118.3, 123.2 (q, *J* = 281.3 Hz, CF_3), 126.2, 147.7, 150.0, 155.7.

*4.4.2.3. Compound tt-**7'b**.* ^1H NMR (500 MHz, C_6D_6) δ 1.18–2.59 (m, 8H, 3 CH_2, $N(CH_2)_2$), 3.07–3.11 (m, 1H, H-5′), 3.26 (s, 3H, MeO), 3.41–3.45 (m, 4H, $O(CH_2)_2$), 3.73 (dd, *J* = 8.0, 2.4 Hz, 1H, H-4), 4.17 (dq, *J* = 10.1, 5.5 Hz, 1H, H-2), 4.41 (br s, 1H, =CH), 6.49 (dd, *J* = 8.9, 2.8 Hz, 1H, H-7), 6.72 (d, *J* = 8.9 Hz, 1H, H-8), 6.76 (d, *J* = 2.8 Hz, 1H, H-5) (signal of H-3 is masked); ^{19}F NMR (471 MHz, C_6D_6) δ 86.1 (d, *J* = 5.5 Hz, CF_3); ^{13}C NMR (101 MHz, C_6D_6) δ 23.6, 23.8, 42.7, 46.8, 48.9, 55.0, 66.4, 74.5 (q, *J* = 32.6 Hz, C-2), 84.2, 100.2, 113.9, 114.1, 117.9, 122.7, 123.3 (q, *J* = 281.3 Hz, CF_3), 147.5, 151.0, 156.5. Anal. Calcd. for $C_{20}H_{23}F_3N_2O_5$: C, 56.07; H, 5.41; N, 6.54. Found: C, 56.13; H, 5.45; N, 6.36.

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4.4.3. 4-{2-[(2S,3S*,4R*)-8-Ethoxy-3-nitro-2-(trifluoromethyl) chroman-4-yl]cyclopenten-1-yl}morpholine (tt-**8c**), 4-{(5S*)-[(2S*,3S*,4R*)-8-ethoxy-3-nitro-2-(trifluoromethyl)chroman-4-yl] cyclopenten-1-yl}morpholine (tt-**7c**) and 4-{(5R*)-[(2S*,3S*,4R*)-8-ethoxy-3-nitro-2-(trifluoromethyl)chroman-4-y])cyclopenten-1-yl} morpholine (tt-**7'c**)*

Yield in MeOH 0.25 g (39%), yield in MeCN 0.18 g (41%), m.p. 137–138 °C (decomp.). IR (ATR): 1586, 1557, 1475, 1371 cm^{-1}. Ratio of tautomers *tt*-**8c**:*tt*-**7c**:*tt*-**7'c** = 75:21:4 in 5 min and 61:27:12 in 24 h (C_6D_6).

*4.4.3.1. Compound tt-**8c**.* ^{1}H NMR (500 MHz, C_6D_6) δ 1.12 (t, *J* = 6.9 Hz, 3H, Me), 1.47–2.07 (m, 6H, 3 CH_2), 2.39–2.49 (m, 4H, $N(CH_2)_2$), 3.54–3.67 (m, 6H, $O(CH_2)_2$, OCH_2Me), 4.37 (dq, *J* = 9.9, 5.4 Hz, 1H, H-2), 4.90 (d, *J* = 10.9 Hz, 1H, H-4), 5.03 (t, *J* = 10.4 Hz, 1H, H-3), 6.50–6.55 (m, 2H, H-5, H-7), 6.78 (t, *J* = 7.9 Hz, 1H, H-6); ^{19}F NMR (471 MHz, C_6D_6) δ 86.1 (d, *J* = 5.4 Hz, CF_3); ^{13}C NMR (101 MHz, C_6D_6) δ 14.7, 21.2, 28.5, 29.1, 40.2, 51.5, 65.0, 67.0, 73.8 (q, *J* = 32.9 Hz, C-2), 80.9, 113.4, 119.3, 121.4, 122.2, 122.8, 123.3 (q, *J* = 281.7 Hz, CF_3), 142.3, 148.6, 154.4.

*4.4.3.2. Compound tt-**7c**.* ^{1}H NMR (500 MHz, C_6D_6) δ 1.13 (t, *J* = 6.9 Hz, 3H, Me), 1.21–2.63 (m, 8H, 2 CH_2, $N(CH_2)_2$), 3.01–3.07 (m, 1H, H-5′), 3.49–3.71 (m, 6H, $O(CH_2)_2$, OCH_2Me), 3.86 (br t, *J* = 5.0 Hz, 1H, H-4), 4.12 (dq, *J* = 10.2, 5.5 Hz, 1H, H-2), 4.51 (br s, 1H, =CH), 5.07 (dd, *J* = 10.2, 6.2 Hz, 1H, H-3), 6.44 (d, *J* = 7.8 Hz, 1H, H-7), 6.51 (d, *J* = 8.0 Hz, 1H, H-7), 6.82 (t, *J* = 7.9 Hz, 1H, H-6); ^{19}F NMR (471 MHz, C_6D_6) δ 86.5 (d, *J* = 5.5 Hz, CF_3); ^{13}C NMR (101 MHz, C_6D_6) δ 14.7, 23.0, 29.1, 42.6, 46.5, 49.5, 66.4, 67.7, 75.9 (q, *J* = 32.9 Hz, C-2), 81.4, 105.1, 112.7, 119.5, 123.2 (q, *J* = 280.9 Hz, CF_3), 124.0, 124.7, 144.1, 148.9, 150.1.

*4.4.3.3. Compound tt-**7'c**.* ^{1}H NMR (500 MHz, C_6D_6) δ 1.13 (t, *J* = 6.9 Hz, 3H, Me), 1.21–2.62 (m, 8H, 2 CH_2, $N(CH_2)_2$), 3.07–3.11 (m, 1H, H-5′), 3.42 (t, *J* = 4.7 Hz, 4H, $O(CH_2)_2$), 3.73 (dd, *J* = 7.5, 2.6 Hz, 1H, H-4), 4.21 (dq, *J* = 10.0, 5.5 Hz, 1H, H-2), 4.47 (br s, 1H, =CH), 5.13 (dd, *J* = 10.0, 7.5 Hz, 1H, H-3), 6.72 (t, *J* = 7.9 Hz, 1H, H-6) (signals of OCH_2 and aromatic proton H-5, H-7 are masked); ^{19}F NMR (471 MHz, C_6D_6) δ 86.2 (d, *J* = 5.5 Hz, CF_3); ^{13}C NMR (101 MHz, C_6D_6) δ 14.7, 23.6, 28.8, 43.3, 47.3, 50.0, 64.9, 65.3, 74.8 (q, *J* = 33.2 Hz, C-2), 84.0, 100.2, 113.1, 119.9, 123.3 (q, *J* = 281.1 Hz, CF_3), 123.9, 124.3, 144.2, 149.2, 151.2. Anal. Calcd. for $C_{21}H_{25}F_3N_2O_5$: C, 57.01; H, 5.70; N, 6.33. Found: C, 56.64; H, 5.60; N, 6.26.

4.4.4. 4-{2-[(2S,3S*,4R*)-6-Chloro-3-nitro-2-(trifluoromethyl) chroman-4-yl]cyclopenten-1-yl}morpholine (tt-**8d**), 4-{(5S*)-[(2S*,3S*,4R*)-6-chloro-3-nitro-2-(trifluoromethyl)chroman-4-yl) cyclopenten-1-yl}morpholine (tt-**7d**) and 4-{(5R*)-[(2S*,3S*,4R*)-6-chloro-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopenten-1-yl} morpholine (tt-**7'd**)*

Yield in MeOH 0.22 g (51%), yield in MeCN 0.24 g (55%), m.p. 163–164 °C (decomp.). IR (ATR): 1669, 1561, 1479, 1450, 1414, 1367, 1341 cm^{-1}. Ratio of tautomers *tt*-**8d**:*tt*-**7d**:*tt*-**7'd** = 79:6:15 in 5 min and 61:24:15 in 24 h (C_6D_6).

*4.4.4.1. Compound tt-**8d**.* ^{1}H NMR (500 MHz, C_6D_6) δ 1.34–2.00 (m, 6H, 3 CH_2), 2.30–2.39 (m, 4H, $N(CH_2)_2$), 3.49–3.59 (m, 4H, $O(CH_2)_2$), 4.17 (dq, *J* = 10.1, 5.3 Hz, 1H, H-2), 4.73 (d, *J* = 11.0 Hz, 1H, H-4), 4.87 (dd, *J* = 11.0, 10.1 Hz,1H, H-3), 6.47 (d, *J* = 8.8 Hz, 1H, H-8), 6.79 (dd, *J* = 8.8, 2.1 Hz, 1H, H-7), 6.95 (dd, *J* = 2.1, 1.1 Hz, 1H, H-5); ^{19}F NMR (471 MHz, C_6D_6) δ 85.9 (d, *J* = 5.3 Hz, CF_3); ^{13}C NMR (101 MHz, C_6D_6) δ 21.1, 28.4, 28.7, 39.9, 51.5, 67.0, 73.6 (q, *J* = 32.9 Hz, C-2), 80.1, 118.6, 120.1, 122.7, 123.0 (q, *J* = 281.5 Hz, C-2), 127.5, 128.3, 129.1, 150.3, 155.6.

*4.4.4.2. Compound tt-**7d**.* ^{1}H NMR (500 MHz, C_6D_6) δ 1.24–2.45 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.73–2.81 (m, 1H, H-5′), 3.58–3.64 (m, 5H, $O(CH_2)_2$, H-4), 3.98 (dq, *J* = 10.2, 5.5 Hz, 1H, H-2), 4.46 (br s, 1H, =CH), 4.93 (dd, *J* = 10.2, 6.2 Hz, 1H, H-3), 6.48 (d, *J* = 8.8 Hz, 1H, H-8), 6.75 (dd, *J* = 8.8, 2.2 Hz, 1H, H-7), 6.87 (d, *J* = 2.2 Hz, 1H, H-5); ^{19}F NMR (471 MHz, C_6D_6) δ 86.4 (d, *J* = 5.5 Hz, CF_3); ^{13}C NMR (101 MHz, C_6D_6) δ 23.6, 28.9, 42.0, 48.5, 49.5, 66.4, 75.5 (q, *J* = 32.8 Hz, C-2), 80.7, 105.1, 119.0, 122.9 (q, *J* = 281.0 Hz, C-2), 126.8, 128.5, 129.3, 134.1, 149.7, 152.1.

*4.4.4.3. Compound tt-**7'd**.* ^{1}H NMR (500 MHz, C_6D_6) δ 1.19–2.51 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.96–3.02 (m, 1H, 5′–CH), 3.40 (t, *J* = 4.8 Hz, 4H, $O(CH_2)_2$), 4.06 (dq, *J* = 10.1, 5.4 Hz, 1H, H-2), 4.44 (br s, 1H, =CH), 4.91 (dd, *J* = 10.1, 7.5 Hz, 1H, H-3), 6.45 (d, *J* = 8.8 Hz, 1H, H-8), 6.76 (dd, *J* = 8.8, 2.1 Hz, 1H, H-7), 7.12 (d, *J* = 2.2 Hz, 1H, H-5) (signal of H-4 is masked); ^{19}F NMR (471 MHz, C_6D_6) δ 86.0 (d, *J* = 5.4 Hz, CF_3); ^{13}C NMR (101 MHz, C_6D_6) δ 23.1, 23.9, 42.2, 46.9, 49.9, 66.3, 74.3 (q, *J* = 32.8 Hz, C-2), 83.4, 100.2, 118.4, 122.9 (q, *J* = 281.3 Hz, C-2), 123.6, 128.4, 129.5, 133.3, 150.5, 152.0. Anal. Calcd. for $C_{19}H_{20}ClF_3N_2O_4$: C, 52.73; H, 4.66; N, 6.47. Found: C, 52.67; H, 4.58; N, 6.43.

4.4.5. 4-{2-[(2S,3S*,4R*)-6-Bromo-3-nitro-2-(trifluoromethyl) chroman-4-yl]cyclopenten-1-yl}morpholine (tt-**8e**), 4-{(5S*)-[(2S*,3S*,4R*)-6-bromo-3-nitro-2-(trifluoromethyl)chroman-4-yl] cyclopenten-1-yl}morpholine (tt-**7e**) and 4-{(5R*)-[(2S*,3S*,4R*)-6-bromo-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopent-1-yl} morpholine (tt-**7'e**)*

Yield in MeOH 0.22 g (47%), Yield in MeCN 0.25 g (52%), m.p. 154–155 °C (decomp.). IR (ATR): 1668, 1562, 1477, 1449, 1409, 1370 cm^{-1}. Ratio of tautomers *tt*-**8e**:*tt*-**7e**:*tt*-**7'e** = 71:20:9 in 5 min and 59:25:16 in 24 h (C_6D_6).

*4.4.5.1. Compound tt-**8e**.* ^{1}H NMR (400 MHz, C_6D_6) δ 1.35–2.01 (m, 6H, 3 CH_2), 2.29–2.41 (m, 4H, $N(CH_2)_2$), 3.54 (t, *J* = 4.7 Hz, 4H, $O(CH_2)_2$), 4.21 (dq, *J* = 10.0, 5.3 Hz, 1H, H-2), 4.73 (d, *J* = 10.9 Hz, 1H, H-4), 4.88 (dd, *J* = 10.9, 10.0 Hz, 1H, H-3), 6.42 (d, *J* = 8.8 Hz, 1H, H-8), 6.93 (dd, *J* = 8.8, 2.2 Hz, 1H, H-7), 7.10 (dd, *J* = 2.2, 1.1 Hz, 1H, H-5); ^{19}F NMR (376 MHz, C_6D_6) δ 85.8 (d, *J* = 5.3 Hz, CF_3).

*4.4.5.2. Compound tt-**7e**.* ^{1}H NMR (400 MHz, C_6D_6) δ 1.21–3.53 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.74–2.82 (m, 1H, H-5′), 3.58–3.67 (m, 5H, $O(CH_2)_2$, H-4), 3.99 (dq, *J* = 10.2, 5.6 Hz, 1H, H-2), 4.46 (br s, 1H, =CH), 4.92 (dd, *J* = 10.2, 6.2 Hz, 1H, H-3), 6.43 (d, *J* = 8.7 Hz, 1H, H-8), 6.91 (dd, *J* = 8.7, 2.1 Hz, 1H, H-7), 7.05 (d, *J* = 2.1 Hz, 1H, H-5); ^{19}F NMR (376 MHz, C_6D_6) δ 86.4 (d, *J* = 5.6 Hz, CF_3).

*4.4.5.3. Compound tt-**7'e**.* ^{1}H NMR (400 MHz, C_6D_6) δ 1.22–2.53 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.96–3.03 (m, 1H, H-5′), 3.41 (t, *J* = 4.8 Hz, 4H, $O(CH_2)_2$), 4.08 (dq, *J* = 10.1, 5.4 Hz, 1H, H-2), 4.44 (br s, 1H, =CH), 4.91 (dd, *J* = 10.1, 7.5 Hz, 1H, H-3), 6.39 (d, *J* = 8.7 Hz, 1H, H-8), 6.90 (dd, *J* = 8.7, 2.1 Hz, 1H, H-7), 7.27 (d, *J* = 2.1 Hz, 1H, H-5) (signal of H-4 is masked); ^{19}F NMR (376 MHz, C_6D_6) δ 86.0 (d, *J* = 5.4 Hz, CF_3). HRMS (ESI): calcd. for 477.0631 $[M+H]^+$ $C_{19}H_{21}BrF_3N_2O_4$, found 477.0634.

4.5. Synthesis of 2-CCl_3- and 2-Ph-chromanes tt-8h,k,l,o

4.5.1. 4-{2-[(2S,3S*,4R*)-3-Nitro-2-(trichloromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (tt-**8h**), 4-{(5S*)-[(2S*,3S*,4R*)-3-nitro-2-(trichloromethyl)chroman-4-yl]cyclopenten-1-yl} morpholine (tt-**7h**) and 4-{(5R*)-[(2S*,3S*,4R*)-3-nitro-2-(trichloromethyl)chroman-4-yl]cyclopenten-1-yl}morpholine (tt-**7'h**)*

These compounds were obtained as a mixture with *ct*-**7h** (*tt*-**8h**:*ct*-**7h** = 64:36) under microwave heating from chromene **2h**

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and enamine **6** in CH_2Cl_2 at 100 °C for 15 min. Yield 0.31 g (69%), white powder, m.p. 126–127 °C (decomp.). Ratio of tautomers *tt*-**8h**:*tt*-**7h**:*tt*-**7'h** = 66:20:14 in 5 min ($CDCl_3$) and 74:14:12 in 5 min (C_6D_6).

*4.5.1.1. Compound tt-**8h**.* ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.88–2.50 (m, 6H, 3 CH_2), 2.60–2.72 (m, 4H, $N(CH_2)_2$), 3.64–3.71 (m, 4H, $O(CH_2)_2$), 4.84 (d, *J* = 11.0 Hz, 1H, H-4), 5.11 (dd, *J* = 11.0, 7.8 Hz, 1H, H-3), 5.45 (d, *J* = 7.8 Hz, 1H, H-2), 6.98 (br d, *J* = 7.5 Hz, 1H, H-5), 7.03 (t, *J* = 7.4 Hz, 1H, H-6), 7.07 (d, *J* = 8.2 Hz, 1H, H-8), 7.10 (t, *J* = 7.8 Hz, 1H, H-7); ^{1}H NMR (500 MHz, C_6D_6) δ 1.42–2.40 (m, 6H, 3 CH_2), 2.43 (t, *J* = 4.6 Hz, 4H, $N(CH_2)_2$), 3.46–3.49 (m, 4H, $O(CH_2)_2$), 4.90 (br d, *J* = 10.4 Hz, 1H, H-4), 5.25 (dd, *J* = 10.2, 8.0 Hz, 1H, H-3), 5.28 (d, *J* = 8.0 Hz, 1H, H-2), 6.77–6.97 (m, 4H, H-5, H-6, H-7, H-8).

*4.5.1.2. Compound tt-**7h**.* ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.64–2.78 (m, 8H, 2 CH_2, $N(CH_2)_2$), 3.23–3.31 (m, 1H, H-5′), 3.50–3.60 (m, 4H, $O(CH_2)_2$, H-4), 4.79 (br s, 1H, =CH), 4.83 (d, *J* = 8.7 Hz, 1H, H-2), 5.21 (dd, *J* = 8.7, 3.8 Hz, 1H, H-3) (signals of aromatic protons are masked); ^{1}H NMR (500 MHz, C_6D_6) δ 1.19–2.48 (m, 8H, 2 CH_2, $N(CH_2)_2$), 3.65–3.75 (m, 4H, $O(CHH)_2$), 4.33 (br s, 1H, =CH), 4.68 (d, *J* = 8.7 Hz, 1H, H-2), 5.30 (dd, *J* = 8.7, 3.7 Hz, 1H, H-3) (signals of H-4, H-5′ and aromatic protons are masked).

*4.5.1.3. Compound tt-**7'h**.* ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.24–2.92 (m, 8H, 2 CH_2, $N(CH_2)_2$), 3.74 (t, *J* = 4.7 Hz, 4H, $O(CH_2)_2$), 4.77 (br s, 1H, =CH), 5.03 (d, *J* = 8.6 Hz, 1H, H-2), 5.28 (dd, *J* = 8.6, 4.8 Hz, 1H, H-3) (signals of H-4, H-5′ and aromatic protons are masked); ^{1}H NMR (500 MHz, C_6D_6) δ 1.19–2.48 (m, 8H, 2 CH_2, $N(CH_2)_2$), 4.40 (d, *J* = 8.8 Hz, 1H, 2-CH), 4.89 (br s, 1H, =CH), 5.32 (dd, *J* = 8.8, 4.3 Hz, 1H, H-3) (signals of H-4, H-5′, $O(CH_2)_2$ and aromatic protons are masked). Anal. Calcd. for $C_{19}H_{21}Cl_3N_2O_4$: C, 50.97; H, 4.73; N, 6.26. Found: C, 50.58; H, 4.60; N, 6.29.

4.5.2. 4-{2-[(2S,3S*,4R*)-6-Chloro-3-nitro-2-(trichloromethyl) chroman-4-yl]cyclopenten-1-yl}morpholine (tt-**8k**), 4-{(5S*)-[(2S*,3S*,4R*)-6-chloro-3-nitro-2-(trichloromethyl)chroman-4-yl] cyclopenten-1-yl}morpholine (tt-**7k**) and 4-{(5R*)-[(2S*,3S*,4R*)-6-chloro-3-nitro-2-(trichloromethyl)chroman-4-yl]cyclopenten-1-yl} morpholine (tt-**7'k**)*

This equilibrium mixture was obtained similarly to chromanes *tt*-**8a**–**e** in MeOH (0.5 mL) at 40 °C for 6 h. Yield 0.26 g (54%), light yellow prisms, m.p. 186–187 °C (decomp.). IR (ATR): 1661, 1643, 1562, 1476, 1451, 1412, 1372, 1355 cm^{-1}. Ratio of tautomers *tt*-**8k**:*tt*-**7k**:*tt*-**7'k** = 71:17:12 in 5 min ($CDCl_3$); 73:22:5 in 5 min and 67:17:16 in 24 h (C_6D_6).

*4.5.2.1. Compound tt-**8k**.* ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.90–2.53 (m, 6H, 3 CH_2), 2.61–2.73 (m, 4H, $N(CH_2)_2$), 3.63–3.73 (m, 4H, $O(CH_2)_2$), 4.80 (d, *J* = 11.1 Hz, 1H, H-4), 5.08 (dd, *J* = 11.1, 7.7 Hz, 1H, H-3), 5.46 (d, *J* = 7.7 Hz, 1H, H-2), 6.92 (br dd, *J* = 2.2, 1.0 Hz, 1H, H-5), 7.01 (d, *J* = 8.6 Hz, 1H, H-8), 7.22 (dd, *J* = 8.6, 2.2 Hz, 1H, H-7); ^{1}H NMR (500 MHz, C_6D_6) δ 1.45–2.31 (m, 6H, 3 CH_2), 2.35 (t, *J* = 4.6 Hz, 4H, $N(CH_2)_2$), 3.45 (dd, *J* = 6.3, 4.6 Hz, 4H, $O(CH_2)_2$), 4.81 (br d, *J* = 10.6 Hz, 1H, H-4), 5.16 (dd, *J* = 10.6, 7.8 Hz, 1H, H-3), 5.20 (d, *J* = 7.8 Hz, 1H, H-2), 6.63 (d, *J* = 8.6 Hz, 1H, H-8), 6.86 (ddd, *J* = 8.6, 2.3, 0.8 Hz, 1H, H-7), 7.05 (dd, *J* = 2.3, 1.1 Hz, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$) δ 21.1, 28.8, 28.9, 39.7, 51.2, 67.0, 84.7, 85.1, 98.6, 118.3, 118.8, 123.8, 126.6, 128.4, 129.0, 151.7, 155.6.

*4.5.2.2. Compound tt-**7k**.* ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.66–2.80 (m, 8H, 2 CH_2, $N(CH_2)_2$), 3.21–3.27 (m, 1H, H-5′), 3.45–3.59 (m, 4H, $O(CH_2)_2$), 4.78 (br s, 1H, =CH), 4.86 (d, *J* = 8.4 Hz, 1H, H-2), 5.21 (dd, *J* = 8.4, 3.6 Hz, 1H, H-3), 7.07 (d, *J* = 8.6 Hz, 1H, H-8), 7.12 (d, *J* = 2.3 Hz, 1H, H-5), 7.21 (dd, *J* = 8.6, 2.3 Hz, 1H, H-7) (signal of H-4 is masked); ^{1}H NMR (500 MHz, C_6D_6) δ 1.24–2.45 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.82–2.87 (m, 1H, H-5′), 3.33–3.51 (m, 5H, $O(CH_2)_2$, H-4), 4.51 (br s, 1H, =CH), 4.66 (d, *J* = 8.4 Hz, 1H, H-2), 5.26 (dd, *J* = 8.4, 3.9 Hz, 1H, H-3), 6.58 (d, *J* = 8.6 Hz, 1H, H-8), 6.80 (dd, *J* = 8.6, 2.4 Hz, 1H, H-7), 6.81 (d, *J* = 2.4 Hz, 1H, H-5); ^{13}C NMR (126 MHz, $CDCl_3$) δ 24.8, 28.3, 44.9, 47.8, 49.0, 66.4, 84.8, 86.7, 96.8, 105.0, 118.4, 118.9, 128.4, 128.5, 129.3, 150.7, 152.4.

*4.5.2.3. Compound tt-**7'k**.* ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20–2.94 (m, 8H, 2 CH_2, $N(CH_2)_2$), 3.39–3.44 (m, 1H, H-5′), 3.77 (t, *J* = 4.7 Hz, 4H, $O(CH_2)_2$), 4.71 (br s, 1H, =CH), 5.01 (d, *J* = 8.6 Hz, 1H, H-2), 5.24 (dd, *J* = 8.6, 5.0 Hz, 1H, H-3), 7.02 (d, *J* = 8.6 Hz, 1H, H-8), 7.08 (d, *J* = 2.3 Hz, 1H, H-5), 7.24 (dd, *J* = 8.6, 2.3 Hz, 1H, H-7) (signal of H-4 is masked); ^{1}H NMR (500 MHz, C_6D_6) δ 1.21–2.59 (m, 8H, 2 CH_2, $N(CH_2)_2$), 3.05–3.09 (m, 1H, H-5′), 4.40 (br s, 1H, =CH), 4.77 (d, *J* = 8.9 Hz, 1H, H-2), 6.56 (d, *J* = 8.6 Hz, 1H, H-8), 6.82 (dd, *J* = 8.6, 2.4 Hz, 1H, H-7), 7.05 (d, *J* = 2.4 Hz, 1H, H-5) (signals of H-3, H-4 and $O(CH_2)_2$ are masked); ^{13}C NMR (126 MHz, $CDCl_3$) δ 23.8, 28.6, 43.9, 48.5, 49.5, 66.6, 85.2, 87.3, 97.1, 106.7, 118.4, 118.9, 128.3, 128.6, 129.4, 150.2, 152.3. Anal. Calcd. for $C_{19}H_{20}Cl_4N_2O_4$: C, 47.33; H, 4.18; N, 5.81. Found: C, 47.05; H, 4.19; N, 5.83.

4.5.3. 4-{2-[(2S,3S*,4R*)-6-Bromo-3-nitro-2-(trichloromethyl) chroman-4-yl]cyclopenten-1-yl}morpholine (tt-**8l**), 4-{(5S*)-[(2S*,3S*,4R*)-6-bromo-3-nitro-2-(trichloromethyl)chroman-4-yl] cyclopenten-1-yl}morpholine (tt-**7l**) and 4-{(5R*)-[(2S*,3S*,4R*)-6-bromo-3-nitro-2-(trichloromethyl)chroman-4-yl]cyclopenten-1-yl} morpholine (tt-**7'l**)*

This equilibrium mixture was obtained similarly to chromanes *tt*-**8a**–**e** in MeCN (0.5 mL) at 40 °C for 6 h. Yield 0.24 g (46%), m.p. 192–193 °C (decomp.). IR (ATR): 1662, 1641, 1564, 1476, 1447, 1407, 1372, 1359 cm^{-1}. Ratio of tautomers *tt*-**8l**:*tt*-**7l**:*tt*-**7'l** = 69:17:14 in 5 min ($CDCl_3$) and 75:19:6 in 5 min (C_6D_6).

*4.5.3.1. Compound tt-**8l**.* ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.91–2.53 (m, 6H, 3 CH_2), 2.61–2.73 (m, 4H, $N(CH_2)_2$), 3.64–3.73 (m, 4H, $O(CH_2)_2$), 4.80 (d, *J* = 11.2 Hz, 1H, H-4), 5.07 (dd, *J* = 11.2, 7.7 Hz, 1H, H-3), 5.46 (d, *J* = 7.7 Hz, 1H, H-2), 6.96 (d, *J* = 8.6 Hz, 1H, H-8), 7.06 (d, *J* = 2.4 Hz, 1H, H-5), 7.36 (dd, *J* = 8.6, 2.4 Hz, 1H, H-7); ^{1}H NMR (500 MHz, C_6D_6) δ 1.45–2.09 (m, 6H, 3 CH_2), 2.35 (t, *J* = 4.6 Hz, 4H, $N(CH_2)_2$), 3.45 (t, *J* = 4.6 Hz, 4H, $O(CH_2)_2$), 4.81 (br d, *J* = 10.6 Hz, 1H, H-4), 5.15 (dd, *J* = 10.6, 7.9 Hz, 1H, H-3), 5.20 (d, *J* = 7.9 Hz, 1H, H-2), 6.57 (d, *J* = 8.6 Hz, 1H, H-8), 7.00 (ddd, *J* = 8.6, 2.3, 0.8 Hz, 1H, H-7), 7.20 (dd, *J* = 2.3, 1.1 Hz, 1H, H-5).

*4.5.3.2. Compound tt-**7l**.* ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.44–2.82 (m, 8H, 2 CH_2, $N(CH_2)_2$), 3.20–3.27 (m, 1H, H-5′), 3.45–3.60 (m, 4H, $O(CH_2)_2$), 4.78 (br s, 1H, =CH), 4.86 (d, *J* = 8.3 Hz, 1H, H-2), 5.21 (dd, *J* = 8.3, 3.5 Hz, 1H, H-3), 6.97 (d, *J* = 8.6 Hz, 1H, H-8), 7.25 (d, *J* = 2.4 Hz, 1H, H-5), 7.39 (dd, *J* = 8.6, 2.4 Hz, 1H, H-7) (signal of H-4 is masked); ^{1}H NMR (500 MHz, C_6D_6) δ 1.22–2.43 (m, 8H, 2 CH_2, $N(CH_2)_2$), 2.82–2.88 (m, 1H, H-5′), 3.32–3.50 (m, 5H, $O(CH_2)_2$, H-4), 4.50 (br s, 1H, =CH), 4.66 (d, *J* = 8.3 Hz, 1H, H-2), 5.25 (dd, *J* = 8.3, 3.9 Hz, 1H, H-3), 6.51 (d, *J* = 8.6 Hz, 1H, H-8), 6.95 (dd, *J* = 8.6, 2.4 Hz, 1H, H-7), 6.97 (d, *J* = 2.4 Hz, 1H, H-5).

*4.5.3.3. Compound tt-**7'l**.* ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.20–2.94 (m, 8H, 2 CH_2, $N(CH)_2$), 3.39–3.44 (m, 1H, H-5′), 3.77 (t, *J* = 4.6 Hz, 4H, $O(CH_2)_2$), 4.72 (br s, 1H, =CH), 5.01 (d, *J* = 8.9 Hz, 1H, H-2), 5.24 (dd, *J* = 8.9, 5.0 Hz, 1H, H-3), 7.01 (d, *J* = 8.6 Hz, 1H, H-8), 7.24 (d, *J* = 2.4 Hz, 1H, H-5), 7.35 (dd, *J* = 8.6, 2.4 Hz, 1H, H-7); ^{1}H NMR (500 MHz, C_6D_6) δ 1.22–2.60 (m, 8H, 2 CH_2, $N(CH)_2$), 3.04–3.09 (m, 1H, H-5′), 3.22–3.50 (m, 5H, $O(CH_2)_2$, H-4), 4.41 (br s, 1H, =CH), 4.77 (d, *J* = 8.9 Hz, 1H, H-2), 5.19 (dd, *J* = 8.9, 5.5 Hz, 1H, H-3), 6.49 (d, *J* = 8.6 Hz, 1H, H-8), 6.96 (dd, *J* = 8.6, 2.4 Hz, 1H, H-7), 7.21 (d,

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J = 2.4 Hz, 1H, H-5) (signals of H-3 и H-4 are masked). Anal. Calcd. for $C_{19}H_{20}BrCl_3N_2O_4$: C, 43.33; H, 3.83; N, 5.32. Found: C, 43.28; H, 3.63; N, 5.31.

4.5.4. 4-{2-[(2R,3S*,4R*)-3-Nitro-2-phenylchroman-4-yl] cyclopenten-1-yl}morpholine (tt-**8o**), 4-{(5S*)-[(2R*,3S*,4R*)-3-nitro-2-phenylchroman-4-yl]cyclopenten-1-yl}morpholine (tt-**7o**) and 4-{(5R*)-[(2R*,3S*,4R*)-3-nitro-2-phenylchroman-4-yl] cyclopenten-1-yl}morpholine (tt-**7'o**)*

This equilibrium mixture was obtained similarly to chromanes *tt*-**8a**–**e** in MeCN (0.5 mL) at 40 °C for 6 h. Yield 0.14 g (34%), light yellow prisms, m.p. 174–175 °C (decomp.). IR (ATR): 1662, 1630, 1581, 1548, 1482, 1455, 1374, 1347, 1331 cm^{-1}. Ratio of tautomers *tt*-**8o**:*tt*-**7o**:*tt*-**7'o** = 75:14:11 in 5 min (C_6D_6).

*4.5.4.1. Compound tt-**8o**.* ^1H NMR (500 MHz, C_6D_6) δ 1.50–2.24 (m, 6H, 3 CH_2), 2.46–2.56 (m, 4H, $N(CH_2)_2$), 3.59–3.70 (m, 4H, $O(CH_2)_2$), 5.02 (d, J = 9.7 Hz, 1H, H-2), 5.06 (t, J = 10.0, 7.9 Hz, 1H, H-3), 5.23 (br d, J = 10.3 Hz, 1H, H-4), 6.87 (td, J = 7.6, 1.4 Hz, 1H, H-6), 6.97 (dd. J = 8.0, 1.4 Hz, 1H, H-8), 6.99 (d, J = 7.7 Hz, 1H, H-5), 7.02–7.08 (m, 4H, H-7, H_m, H_p), 6.79 (dd, J = 8.0, 1.3 Hz, 2H, H_o); ^{13}C NMR (101 MHz, C_6D_6) δ 21.2, 28.4, 29.2, 41.8, 51.7, 67.1, 79.0, 88.1, 117.4, 121.8, 122.1, 127.3, 127.4, 128.5, 128.6, 128.9, 129.7, 135.9, 153.7, 154.6.

*4.5.4.2. Compound tt-**7o**.* ^1H NMR (500 MHz, C_6D_6) δ 1.24–2.65 (m, 8H, 2 CH_2, $N(CH_2)_2$), 3.23–3.16 (m, 1H, H-5′), 3.47–3.52 (m, 4H, $O(CH_2)_2$), 4.11–4.17 (m, 1H, H-4), 4.50 (br s, 1H, =CH), 4.79 (d, J = 10.0 Hz, 1H, H-2) (signals of H-3 and aromatic protons are masked); ^{13}C NMR (101 MHz, C_6D_6) δ 24.1, 27.1, 29.4, 42.3, 49.5, 66.4, 81.2, 89.2, 104.3, 117.8, 122.3, 122.8, 123.1, 125.4, 129.7, 129.0, 129.5, 136.4, 150.4, 156.4.

*4.5.4.3. Compound tt-**7'o**.* ^1H NMR (500 MHz, C_6D_6) δ 1.24–2.68 (m, 8H, 2 CH_2, $N(CH_2)_2$), 4.11–4.17 (m, 1H, H-4), 4.46 (br s, 1H, =CH), 4.79 (d, J = 10.0 Hz, 1H, H-2), 4.94 (dd, J = 10.2, 7.5 Hz, 1H, H-3), 3.44–3.64 (m, 4H, $O(CH_2)_2$) (signals aromatic protons are masked); ^{13}C NMR (101 MHz, C_6D_6) δ 22.9, 29.0, 31.9, 42.7, 50.1, 66.6, 79.7, 91.9, 100.2, 117.5, 122.3, 122.5, 123.1, 125.4, 129.6, 128.9, 129.4, 136.1, 151.6, 156.3. Anal. Calcd. for $C_{24}H_{26}N_2O_4$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.71; H, 6.75; N, 7.12.

4.6. General procedure for hydrolysis of chromanes 7 and 8

A mixture of the appropriate chromanoenamine **7** or **8** (1.0 mmol), MeOH (5 mL), H_2O (10 mL), and conc. HCl (0.25 mL) was stirred at room temperature (2-CF_3-chromanes) or 50 °C (the rest of the compounds) for 24 or 5 h, respectively. The precipitate was collected by filtration and washed with water (3 × 1 mL). Chromanes **9** were obtained as white powders. Products ***tt*-9a**–**d** were isolated as individual compounds by recrystallisation of the stereoisomeric mixture from hexane.

4.6.1. (2R)-[(2S*,3R*,4S*)-3-Nitro-2-(trifluoromethyl)chroman-4-yl]cyclopentan-1-one (ct-**9a**)*

Yield 0.30 g (90%), m.p. 94–95 °C. IR (ATR): 1730, 1587, 1559, 1489, 1474, 1396, 1373, 1322 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 1.58–2.51 (m, 7H, 3 CH_2, H-2′), 3.96 (br d, J = 5.1 Hz, 1H, H-4), 4.64 (qd, J = 5.7, 2.3 Hz, 1H, H-2), 5.57 (t, J = 1.9 Hz, 1H, H-3), 6.96–7.28 (m, 4H, Ar); ^{19}F NMR (376 MHz, $CDCl_3$) δ 86.9 (d, J = 5.7 Hz, CF_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 20.3, 27.9, 38.2, 38.4, 54.1, 70.8 (q, J = 34.5 Hz, C-2), 78.5, 117.2, 118.3, 122.0 (q, J = 281.7 Hz, CF_3), 122.9, 129.0, 129.1, 151.7, 216.8. HRMS (ESI): calcd. for 352.0767 $[M+Na]^+$ $C_{15}H_{14}F_3NNaO_4$, found 352.0770.

4.6.2. (2R)-[(2S*,3R*,4S*)-6-Methoxy-3-nitro-2-(trifluoromethyl) chroman-4-yl]cyclopentan-1-one (ct-**9b**)*

Yield 0.25 g (71%), m.p. 117–118 °C. IR (ATR): 1728, 1560, 1497, 1370, 1333 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 1.50–2.53 (m, 7H, 3 CH_2, H-2′), 3.73 (s, 3H, MeO), 3.97 (br d, J = 4.7 Hz, 1H, H-4), 4.58 (qd, J = 5.9, 2.4 Hz, 1H, H-2), 5.46 (t, J = 2.0 Hz, 1H, H-3), 6.48 (d, J = 2.9 Hz, 1H, H-5), 6.81 (dd, J = 9.0, 2.9 Hz, 1H, H-7), 6.96 (d, J = 9.0 Hz, 1H, H-8); ^{19}F NMR (376 MHz, $CDCl_3$) δ 86.8 (d, J = 5.9 Hz, CF_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 20.2, 27.6, 38.1, 38.4, 54.3, 55.6, 71.1 (q, J = 34.4 Hz, C-2), 78.9, 113.2, 115.1, 118.0, 118.9, 122.0 (q, J = 281.4 Hz, CF_3), 145.7, 155.0, 216.8. Anal. Calcd. for $C_{16}H_{16}F_3NO_5$: C, 53.49; H, 4.49; N, 3.90. Found: C, 53.57; H, 4.73; N, 3.87.

4.6.3. (2R)-[(2S*,3R*,4S*)-8-Ethoxy-3-nitro-2-(trifluoromethyl) chroman-4-yl]cyclopentan-1-one (ct-**9c**)*

Yield 0.29 g (78%), m.p. 96–97 °C. IR (ATR): 1733, 1578, 1557, 1484, 1470, 1406, 1367, 1312 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 1.43 (t, J = 7.0 Hz, 3H, Me), 1.52–2.51 (m, 7H, 3 CH_2, H-2′), 4.01 (dd, J = 4.7, 1.5 Hz, 1H, H-4), 4.07 (dd, J = 9.5, 7.0 Hz, 1H, OC*H*H), 4.08 (dd, J = 9.5, 7.0 Hz, 1H, OCH*H*), 4.68 (qd, J = 6.0, 2.6 Hz, 1H, H-2), 5.50 (t, J = 2.3 Hz, 1H, H-3), 6.54 (ddd, J = 7.7, 1.5, 0.5 Hz, 1H, H-5), 6.84 (dd, J = 8.2, 1.5 Hz, 1H, H-7), 6.90 (t, J = 7.9 Hz, 1H, H-6); ^{19}F NMR (376 MHz, $CDCl_3$) δ 87.2 (d, J = 6.0 Hz, CF_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.7, 20.3, 27.6, 38.1, 38.2, 54.2, 65.2, 71.0 (q, J = 34.5 Hz, C-2), 78.8, 113.6, 119.2, 120.5, 122.1 (q, J = 281.9 Hz, CF_3), 122.6, 142.1, 147.8, 216.8. HRMS (ESI): calcd. for 396.1029 $[M+Na]^+$ $C_{17}H_{18}F_3NNaO_5$, found 396.1031.

4.6.4. (2R)-[(2S*,3R*,4S*)-6-Chloro-3-nitro-2-(trifluoromethyl) chroman-4-yl]cyclopentan-1-one (ct-**9d**)*

Yield 0.30 g (83%), m.p. 95–96 °C. IR (ATR): 1735, 1560, 1480, 1367, 1332 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 1.50–2.56 (m, 7H, 3 CH_2, H-2′), 3.88 (br d, J = 5.7 Hz, 1H, H-4), 4.63 (qd, J = 5.9, 2.3 Hz, 1H, H-2), 5.59 (t, J = 1.9 Hz, 1H, H-3), 6.96–6.99 (m, 2H, H-5, H-8), 7.22 (dd, J = 8.7, 2.4 Hz, 1H, H-7); ^{19}F NMR (376 MHz, $CDCl_3$) δ 86.9 (d, J = 5.9 Hz, CF_3). HRMS (ESI): calcd. for 386.0377 $[M+Na]^+$ $C_{15}H_{13}ClF_3NNaO_4$, found 386.0377.

4.6.5. (2R)-[(2S*,3R*,4S*)-6-Bromo-3-nitro-2-(trifluoromethyl) chroman-4-yl]cyclopentan-1-one (ct-**9e**)*

Yield 0.33 g (80%), m.p. 110–111 °C. IR (ATR): 1738, 1562, 1479, 1368, 1340 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 1.57–2.54 (m, 7H, 3 CH_2, H-2′), 3.87 (br d, J = 5.4 Hz, 1H, H-4), 4.63 (qd, J = 5.9, 2.1 Hz, 1H, H-2), 5.60 (t, J = 2.1 Hz, 1H, H-3), 6.92 (d, J = 8.8 Hz, 1H, H-8), 7.13 (d, J = 2.3 Hz, 1H, H-5), 7.36 (dd, J = 8.8, 2.3 Hz, 1H, H-7); ^{19}F NMR (376 MHz, $CDCl_3$) δ 86.9 (d, J = 5.9 Hz, CF_3). HRMS (ESI): calcd. for 429.9872 $[M+Na]^+$ $C_{15}H_{13}BrF_3NNaO_4$, found 429.9869.

4.6.6. (2R)-[(2S*,3R*,4S*)-6,8-Dichloro-3-nitro-2-(trifluoromethyl) chroman-4-yl]cyclopentan-1-one (ct-**9f**)*

Yield 0.34 g (85%), m.p. 150–151 °C. IR (ATR): 1733, 1563, 1462, 1369, 1313 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 1.56–2.55 (m, 7H, 3 CH_2, H-2′), 3.88 (br d, J = 5.5 Hz, 1H, H-4), 4.71 (qd, J = 5.7, 2.6 Hz, 1H, H-2), 5.64 (t, J = 1.9 Hz, 1H, H-3), 6.91 (d, J = 2.3 Hz, 1H, H-5/H-7), 7.36 (d, J = 2.3 Hz, 1H, H-7/H-5); ^{19}F NMR (376 MHz, $CDCl_3$) δ 87.0 (d, J = 5.7 Hz, CF_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 20.1, 26.1, 37.0, 38.5, 49.6, 72.9 (q, J = 33.0 Hz, C-2), 80.1, 122.9 (q, J = 283.3 Hz, CF_3), 123.1, 123.8, 127.9, 128.8, 130.6, 146.8, 215.7. Anal. Calcd. for $C_{15}H_{12}Cl_2F_3NO_4$: C, 45.25; H, 3.04; N, 3.52. Found: C, 45.13; H, 3.03; N, 3.51.

4.6.7. (2R)-[(2S*,3R*,4S*)-6,8-Dibromo-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopentan-1-one (ct-**9g**)*

Yield 0.43 g (89%), m.p. 176–177 °C. IR (ATR): 1731, 1563, 1454, 1368 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 1.56–2.55 (m, 7H, 3 CH_2, H-

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2′), 3.86 (br d, J = 5.7 Hz, 1H, H-4), 4.72 (qd, J = 5.7, 2.5 Hz, 1H, H-2), 5.65 (t, J = 1.9 Hz, 1H, H-3), 7.09 (d, J = 2.3 Hz, 1H, H-5/H-7), 7.65 (d, J = 2.2 Hz, 1H, H-7/H-5); ^{19}F NMR (376 MHz, $CDCl_3$) δ 87.1 (d, J = 5.7 Hz, CF_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 20.2, 28.1, 38.1, 38.7, 53.6, 71.5 (q, J = 35.1 Hz, C-2), 77.5, 112.2, 114.9, 121.6 (q, J = 281.5 Hz, CF_3), 121.8, 130.7, 135.3, 147.7, 216.1. Anal. Calcd. for $C_{15}H_{12}Br_2F_3NO_4$: C, 36.99; H, 2.48; N, 2.88. Found: C, 37.01; H, 2.46; N, 2.92.

4.6.8. (2R)-[(2S*,3R*,4S*)-3-Nitro-2-(trichloromethyl)chroman-4-yl]cyclopentan-1-one (ct-**9h**)*

Yield 0.27 g (71%), m.p. 165–166 °C. IR (ATR): 1733, 1556, 1489, 1456, 1400, 1369, 1341 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.58–2.53 (m, 7H, 3 CH_2, H-2′), 3.94 (br d, J = 5.2 Hz, 1H, H-4), 4.62 (d, J = 1.5 Hz, 1H, H-2), 6.02 (t, J = 1.5 Hz, 1H, H-3), 6.97–7.02 (m, 2H, H-6, H-8), 7.11 (d, J = 8.2 Hz, 1H, H-5), 7.24–7.31 (m, 1H, H-7); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.3, 28.0, 38.2, 40.1, 54.5, 79.5, 80.9, 95.6, 117.2, 118.4, 122.8, 128.9, 129.0, 152.8, 216.7. Anal. Calcd. for $C_{15}H_{14}Cl_3NO_4 \cdot 0.25H_2O$: C, 47.02; H, 3.81; N, 3.66. Found: C, 47.12; H, 3.75; N, 3.67.

4.6.9. (2R)-[(2S*,3R*,4S*)-6-Methoxy-3-nitro-2-(trichloromethyl) chroman-4-yl]cyclopentan-1-one (ct-**9i**)*

Yield 0.29 g (70%), m.p. 155–156 °C. IR (ATR): 1727, 1557, 1497, 1359, 1316 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.56–2.53 (m, 7H, 3 CH_2, H-2′), 3.74 (s, 3H, MeO), 3.94 (br d, J = 4.8 Hz, 1H, H-4), 4.56 (d, J = 1.6 Hz, 1H, H-2), 5.90 (t, J = 1.6 Hz, 1H, H-3), 6.50 (d, J = 2.8 Hz, 1H, H-5), 6.84 (dd, J = 9.0, 2.8 Hz, 1H, H-7), 7.04 (d, J = 9.0 Hz, 1H, H-8). Anal. Calcd. for $C_{16}H_{16}Cl_3NO_5$: C, 47.03; H, 3.95; N, 3.43. Found: C, 46.95; H, 3.84; N, 3.44.

4.6.10. (2R)-[(2S*,3R*,4S*)-8-Ethoxy-3-nitro-2-(trichloromethyl) chroman-4-yl]cyclopentan-1-one (ct-**9j**)*

Yield 0.37 g (87%), m.p. 170–171 °C. IR (ATR): 1723, 1559, 1468, 1398, 1372, 1358, 1336 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (t, J = 7.0 Hz, 3H, Me), 1.56–2.51 (m, 7H, 3 CH_2, H-2′), 3.96 (br d, J = 4.8 Hz, 1H, H-4), 4.09 (dd, J = 9.2, 7.0 Hz, 1H, OC*H*H), 4.13 (dd, J = 9.2, 7.0 Hz, 1H, OCH*H*), 4.62 (d, J = 1.7 Hz, 1H, H-2), 5.95 (t, J = 1.5 Hz, 1H, H-3), 6.55–6.61 (m, 1H, H-7), 6.86–6.93 (m, 2H, H-5, H-6); ^{13}C NMR (126 MHz, $CDCl_3$) δ 15.0, 20.3, 27.9, 38.1, 40.1, 54.7, 65.9, 79.7, 81.1, 95.6, 114.9, 119.3, 120.9, 122.4, 143.7, 147.7, 216.7. Anal. Calcd. for $C_{17}H_{18}Cl_3NO_5 \cdot 0.33H_2O$: C, 47.63; H, 4.39; N, 3.27. Found: C, 47.62; H, 4.28; N, 3.27.

4.6.11. (2R)-[(2S*,3R*,4S*)-6-Chloro-3-nitro-2-(trichloromethyl) chroman-4-yl]cyclopentan-1-one (ct-**9k**)*

Yield 0.41 g (99%), m.p. 142–143 °C. IR (ATR): 1739, 1556, 1481, 1367, 1339 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.60–2.54 (m, 7H, 3 CH_2, H-2′), 3.85 (br d, J = 5.6 Hz, 1H, H-4), 4.61 (d, J = 1.8 Hz, 1H, H-2), 6.03 (t, J = 1.6 Hz, 1H, H-3), 6.99 (d, J = 2.4 Hz, 1H, H-5), 7.05 (d, J = 8.8 Hz, 1H, H-8), 7.24 (dd, J = 8.8, 2.4 Hz, 1H, H-7); ^{13}C NMR (101 MHz, $CDCl_3$) δ 20.2, 28.1, 38.1, 40.0, 54.2, 78.8, 81.0, 95.3, 118.5, 120.2, 127.7, 128.5, 129.1, 151.4, 216.3. Anal. Calcd. for $C_{15}H_{13}Cl_4NO_4$: C, 43.62; H, 3.17; N, 3.39. Found: C, 43.52; H, 2.89; N, 3.29.

4.6.12. (2-R)-[(2S*,3R*,4S*)-6-Bromo-3-nitro-2-(trichloromethyl) chroman-4-yl]cyclopentan-1-one (ct-**9l**)*

Yield 0.42 g (91%), m.p. 181–182 °C. IR (ATR): 1738, 1557, 1479, 1366, 1339 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.60–2.55 (m, 7H, 3 CH_2, H-2′), 3.84 (br d, J = 5.7 Hz, 1H, H-4), 4.61 (d, J = 1.8 Hz, 1H, H-2), 6.05 (t, J = 1.6 Hz, 1H, H-3), 7.00 (d, J = 8.8 Hz, 1H, H-8), 7.14 (d, J = 2.3 Hz, 1H, H-5), 7.38 (dd, J = 8.8, 2.3 Hz, 1H, H-7); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.3, 28.1, 38.2, 39.9, 54.2, 78.8, 80.9, 95.3, 115.0, 118.9, 120.7, 131.4, 132.0, 151.9, 216.3. Anal. Calcd. for $C_{15}H_{13}BrCl_3NO_4$: C, 39.38; H, 2.86; N, 3.06. Found: C, 39.36; H, 2.84; N, 3.04.

4.6.13. (2R)-[(2S*,3R*,4S*)-6,8-Dichloro-3-nitro-2-(trichloromethyl)chroman-4-yl]cyclopentan-1-one (ct-**9m**)*

Yield 0.38 g (84%), m.p. 157–158 °C. IR (ATR): 1731, 1559, 1459, 1362, 1340, 1311 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.57–2.56 (m, 7H, 3 CH_2, H-2′), 3.86 (br d, J = 5.7 Hz, 1H, H-4), 4.68 (d, J = 1.9 Hz, 1H, H-2), 6.07 (t, J = 1.6 Hz, 1H, H-3), 6.92 (d, J = 2.4 Hz, 1H, H-5/H-7), 7.37 (d, J = 2.4 Hz, 1H, H-7/H-5). Anal. Calcd. for $C_{15}H_{12}Cl_5NO_4 \cdot 0.67H_2O$: C, 39.21; H, 2.92; N, 3.05. Found: C, 39.00; H, 2.63; N, 3.05.

4.6.14. (2R)-[(2S*,3R*,4S*)-6,8-Dibromo-3-nitro-2-(trichloromethyl)chroman-4-yl]cyclopentan-1-one (ct-**9n**)*

Yield 0.43 g (81%), m.p. 167–168 °C. IR (ATR): 1731, 1556, 1454, 1400, 1366, 1352, 1338 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.58–2.56 (m, 7H, 2 CH_2, H-2′), 3.83 (br d, J = 5.9 Hz, 1H, H-4), 4.69 (d, J = 1.9 Hz, 1H, H-2), 6.08 (t, J = 1.6 Hz, 1H, H-3), 7.10 (d, J = 2.2 Hz, 1H, H-5/H-7), 7.67 (d, J = 2.2 Hz, 1H, H-7/H-5); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.2, 28.3, 38.1, 40.3, 54.0, 78.5, 81.4, 94.9, 112.2, 114.7, 121.9, 130.5, 135.1, 148.8, 216.0. Anal. Calcd. for $C_{15}H_{12}Br_2Cl_3NO_4$: C, 33.59; H, 2.25; N, 2.61. Found: C, 33.29; H, 2.58; N, 2.59.

4.6.15. (2R)-[(2R*,3R*,4S*)-3-Nitro-2-phenylchroman-4-yl] cyclopentan-1-one (ct-**9o**)*

Yield 0.32 g (94%), m.p. 168–169 °C. IR (ATR): 1740, 1547, 1487, 1454, 1373, 1336 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.68–2.52 (m, 7H, 3 CH_2, H-2′), 3.96 (br d, J = 5.8 Hz, 1H, H-4), 5.44 (d, J = 2.3 Hz, 1H, H-2), 5.95 (dd, J = 2.3, 1.8 Hz, 1H, H-3), 6.95 (td, J = 7.5, 1.0 Hz, 1H, H-6), 7.01 (dd, J = 7.8, 1.5 Hz, 1H, H-5), 7.04 (br d, J = 8.3 Hz, 1H, H-8), 7.24 (ddd, J = 8.3, 7.2, 1.5 Hz, 1H, H-7), 7.34–7.48 (m, 5H, Ph); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.4, 28.1, 38.6, 38.8, 54.4, 73.3, 86.0, 117.2, 118.7, 121.7, 125.6, 128.7, 128.8, 129.0, 135.7, 153.6, 217.6 (one C is not observed). Anal. Calcd. for $C_{20}H_{19}NO_4 \cdot 0.33H_2O$: C, 69.96; H, 5.77 8; N, 4.08. Found: C, 70.07; H, 5.37; N, 4.16.

4.6.16. (2R)-[(2R*,3R*,4S*)-6-Methoxy-3-nitro-2-phenylchroman-4-yl]cyclopentan-1-one (ct-**9p**)*

Yield 0.33 g (91%), m.p. 166–167 °C. IR (ATR): 1738, 1550, 1495, 1457, 1336 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.68–2.53 (m, 7H, 3 CH_2, H-2′), 3.74 (s, 3H, MeO), 3.99 (br d, J = 5.0 Hz, 1H, H-4), 5.37 (d, J = 2.5 Hz, 1H, H-2), 5.43 (dd, J = 2.5, 1.7 Hz, 1H, H-3), 6.53 (d, J = 2.9 Hz, 1H, H-5), 6.82 (d, J = 8.9, 2.9 Hz, 1H, H-7), 6.97 (d, J = 8.9 Hz, 1H, H-8), 7.35–7.45 (m, 5H, Ph); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.4, 28.0, 38.5, 38.8, 54.7, 55.7, 73.6, 86.5, 113.2, 114.9, 118.0, 119.3, 125.6, 128.7, 128.8, 135.8, 147.7, 154.2, 217.6. Anal. Calcd. for $C_{21}H_{21}NO_5$: C, 68.65; H, 5.76; N, 3.81. Found: C, 68.60; H, 6.00; N, 3.86.

4.6.17. (2R)-[(2R*,3R*,4S*)-6-Bromo-3-nitro-2-phenylchroman-4-yl]cyclopentan-1-one (ct-**9q**)*

Yield 0.35 g (84%), m.p. 164–165 °C. IR (ATR): 1741, 1550, 1480, 1333 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.68–2.56 (m, 7H, 3 CH_2, H-2′), 3.88 (br d, J = 6.2 Hz, 1H, H-4), 5.42 (d, J = 2.5 Hz, 1H, H-2), 5.58 (dd, J = 2.5, 1.7 Hz, 1H, H-3), 6.93 (d, J = 8.7 Hz, 1H, H-8), 7.15 (d, J = 2.3 Hz, 1H, H-5), 7.34 (dd, J = 8.7, 2.3 Hz, 1H, H-7), 7.36–7.47 (m, 5H, Ph); ^{13}C NMR (126 MHz, $CDCl_3$) δ 20.4, 28.3, 38.6, 38.7, 54.1, 73.4, 85.4, 113.8, 119.1, 121.1, 125.6, 128.8, 129.0, 131.5, 131.8, 135.3, 152.8, 217.2. Anal. Calcd. for $C_{20}H_{18}BrNO_4$: C, 57.71; H, 4.36; N, 3.36. Found: C, 57.73; H, 4.34; N, 3.34.

4.6.18. (2S)-[(2S*,3S*,4R*)-3-Nitro-2-(trifluoromethyl)chroman-4-yl]cyclopentan-1-one (tt-**9a**) and (2R*)-[(2S*,3S*,4R*)-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopentan-1-one (tt-**9'a**)*

Yield 0.26 g (80%), m.p. 75–76 °C. IR (ATR): 1738, 1566, 1490,

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1455, 1397, 1374 cm^{-1}. Ratio of diastereomers *tt*-**9a**:*tt*-**9'a** = 69:31.

*4.6.18.1. Compound tt-**9a**.* This compound was obtained in a pure state by recrystallisation of the diastereomeric mixture from hexane. Yield 0.11 g (64%), m.p. 89–90 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39–2.58 (m, 7H, 3 CH_2, H-2′), 4.04 (t, *J* = 5.8 Hz, 1H, H-4), 4.97 (dq, *J* = 7.2, 6.2 Hz, 1H, H-2), 5.60 (1H, dd, *J* = 7.2, 5.4 Hz, H-3), 6.98 (1H, dd, *J* = 7.6, 1.6 Hz, H-5), 7.04 (td, *J* = 7.5, 1.1 Hz, 1H, H-6), 7.06 (dd, *J* = 8.2, 1.1 Hz, 1H, H-8), 7.26 (td, *J* = 7.7, 1.6 Hz, 1H, H-7); ^{1}H NMR (400 MHz, C_6D_6) δ 0.73–2.06 (m, 7H, 3 CH_2, H-2′), 3.90 (t, *J* = 5.5 Hz, 1H, H-4), 4.37 (dq, *J* = 7.4, 6.2 Hz, 1H, H-2), 5.52 (dd, *J* = 7.4, 6.2 Hz, 1H, H-3), 6.64 (dd, *J* = 7.6, 1.4 Hz, 1H, H-5), 6.69 (td, *J* = 7.5, 1.0 Hz, 1H, H-6), 6.76 (dd, *J* = 8.2, 1.0 Hz, 1H, H-8), 6.81 (td, *J* = 7.7, 1.4 Hz, 1H, H-7); ^{19}F NMR (376 MHz, $CDCl_3$) δ 85.0 (d, *J* = 6.2 Hz, CF_3); ^{19}F NMR (376 MHz, C_6D_6) δ 86.1 (d, *J* = 6.2 Hz, CF_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 19.9, 26.3, 38.4, 40.7; 50.2, 75.2 (q, *J* = 33.1 Hz, C-2), 83.0, 118.0, 122.6 (q, *J* = 280.7 Hz, CF_3), 122.7, 124.1, 128.5, 129.4, 152.8, 217.5.

*4.6.18.2. Compound tt-**9'a**.* ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.67–2.80 (m, 7H, 3 CH_2, H-2′), 4.20 (dd, *J* = 8.3, 2.8 Hz, 1H, H-4), 4.85 (dq, *J* = 9.7, 5.5 Hz, 1H, H-2), 5.00 (1H, dd, *J* = 9.7, 8.3 Hz, H-3), 7.10 (td, *J* = 7.6, 1.1 Hz, 1H, H-6), 7.22 (d, *J* = 7.7 Hz, 1H, H-5) (signals of H-7 and H-8 are masked); ^{1}H NMR (400 MHz, C_6D_6) δ 0.69–2.11 (m, 7H, 3 CH_2, H-2′), 3.98 (dd, *J* = 8.5, 3.6 Hz, 1H, H-4), 4.20 (dq, *J* = 9.7, 5.5 Hz, 1H, H-2), 4.93 (t, *J* = 9.1 Hz, 1H, H-3), 6.74 (dd, *J* = 8.2, 1.1 Hz, 1H, H-8) (signals of H-5, H-7 and H-8 are masked); ^{19}F NMR (376 MHz, $CDCl_3$) δ 85.03 (d, *J* = 5.5 Hz, CF_3); ^{19}F NMR (376 MHz, C_6D_6) δ 86.3 (d, *J* = 5.6 Hz, CF_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 20.3, 24.7, 37.8, 38.6, 52.7, 74.7 (q, *J* = 32.6 Hz, C-2), 80.9, 117.7, 122.5 (q, *J* = 280.7 Hz, CF_3), 122.2, 123.9, 126.9, 129.0, 152.7, 215.4. Anal. Calcd. for $C_{15}H_{14}F_3NO_4$: C, 54.72; H, 4.29; N, 4.25. Found: C, 54.86; H, 4.27; N, 4.26.

4.6.19. (2S)-[(2S*,3S*,4R*)-6-Methoxy-3-nitro-2-(trifluoromethyl) chroman-4-yl]cyclopentan-1-one (tt-**9b**) and (2R*)-[(2S*,3S*,4R*)-6-methoxy-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopentan-1-one (tt-**9'b**)*

Yield 0.28 g (77%), m.p. 93–94 °C. IR (ATR): 1739, 1558, 1499, 1468, 1370 cm^{-1}. Ratio of diastereomers *tt*-**9b**:*tt*-**9'b** = 75:25.

*4.6.19.1. Compound tt-**9b**.* This compound was obtained in a pure state by recrystallisation of the diastereomeric mixture from hexane. Yield 0.18 g (86%), m.p. 104–105 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39–2.61 (m, 7H, 3 CH_2, H-2′), 3.74 (s, 3H, MeO), 3.97 (dd, *J* = 6.2, 4.7 Hz, 1H, H-4), 4.92 (quint, *J* = 6.6 Hz, 1H, H-2), 5.65 (dd, *J* = 7.0, 4.7 Hz, 1H, H-3), 6.53 (d, *J* = 2.9 Hz, 1H, H-5), 6.79 (dd, *J* = 8.8, 2.9 Hz, 1H, H-7), 7.00 (d, *J* = 8.8 Hz, 1H, H-8); ^{1}H NMR (400 MHz, C_6D_6) δ 0.73–2.12 (m, 7H, 3 CH_2, H-2′), 3.20 (s, 3H, MeO), 3.83 (t, *J* = 5.7 Hz, 1H, H-4), 4.48 (dq, *J* = 7.1, 6.3 Hz, 1H, H-2), 5.68 (dd, *J* = 7.1, 5.2 Hz, 1H, H-3), 6.42–6.48 (m, 2H, H-5, H-7), 6.67–6.74 (1H, m, H-8); ^{19}F NMR (376 MHz, $CDCl_3$) δ 85.0 (d, *J* = 6.2 Hz, CF_3); ^{19}F NMR (376 MHz, C_6D_6) δ 86.2 (d, *J* = 6.3 Hz, CF_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 19.9, 26.6, 38.5, 41.2, 50.2, 55.6, 75.5 (q, *J* = 32.9 Hz, C-2), 83.0, 113.5, 114.7, 118.8, 122.6 (q, *J* = 280.6 Hz, CF_3), 124.0, 146.6, 155.9, 217.9.

*4.6.19.2. Compound tt-**9'b**.* ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.67–2.74 (m, 7H, 3 CH_2, H-2′), 3.78 (s, 3H, MeO), 4.15 (dd, *J* = 7.8, 3.4 Hz, 1H, H-4), 4.77 (dq, *J* = 9.3, 5.6 Hz, 1H, H-2), 4.97 (dd, *J* = 9.3, 7.8 Hz, 1H, H-3), 6.72 (d, *J* = 2.9 Hz, 1H, H-5), 6.80 (dd, *J* = 8.7, 2.9 Hz, 1H, H-7), 6.98 (d, *J* = 8.7 Hz, 1H, H-8); ^{1}H NMR (400 MHz, C_6D_6) δ 0.73–2.12 (m, 7H, 3 CH_2, H-2′), 3.24 (s, 3H, MeO), 4.00 (dd, *J* = 7.7, 4.0 Hz, 1H, H-4), 4.27 (dq, *J* = 9.1, 5.7 Hz, 1H, H-2), 4.98 (dd, *J* = 9.1, 7.7 Hz, 1H, H-3), 6.40 (dd, *J* = 9.1, 2.8 Hz, 1H, H-7) (signals of H-5 and H-8 are masked); ^{19}F NMR (376 MHz, $CDCl_3$) δ 85.1 (d, *J* = 5.6 Hz, CF_3); ^{19}F NMR (376 MHz, C_6D_6) δ 86.4 (d, *J* = 5.7 Hz, CF_3). HRMS (ESI): calcd. for 382.0873 $[M+Na]^+$ $C_{16}H_{16}F_3NNaO_5$, found 382.0870.

4.6.20. (2S)-[(2S*,3S*,4R*)-8-Ethoxy-3-nitro-2-(trifluoromethyl) chroman-4-yl]cyclopentan-1-one (tt-**9c**) and (2R*)-[(2S*,3S*,4R*)-8-ethoxy-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopentan-1-one (tt-**9'c**)*

Yield 0.34 g (92%), m.p. 124–125 °C. IR (ATR): 1731, 1588, 1556, 1486, 1469, 1396, 1370, 1346, 1328 cm^{-1}. Ratio of diastereomers *tt*-**9c**:*tt*-**9'c** = 79:21.

*4.6.20.1. Compound tt-**9c**.* This compound was obtained in a pure state by recrystallisation of the diastereomeric mixture from hexane. Yield 0.23 g (87%), mp 131–132 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.42–2.61 (m, 7H, 3 CH_2, H-2′), 1.45 (t, *J* = 7.0 Hz, 3H, Me), 3.98 (dd, *J* = 6.8, 4.7 Hz, 1H, H-4), 4.08 (q, *J* = 7.0 Hz, 2H, OCH_2), 4.98 (quint, *J* = 6.5 Hz, 1H, H-2), 5.73 (dd, *J* = 6.8, 4.7 Hz, 1H, H-3), 6.58 (dd, *J* = 7.5, 1.1 Hz, 1H, H-5), 6.86 (dd, *J* = 8.4, 1.1 Hz, 1H, H-7), 6.96 (t, *J* = 8.0 Hz, 1H, H-6); ^{1}H NMR (400 MHz, C_6D_6) δ 0.78–2.13 (m, 7H, 3 CH_2, H-2′), 1.09 (t, *J* = 7.0 Hz, 3H, Me), 3.59 (dq, *J* = 9.4, 7.0 Hz, 1H, OC*H*H), 3.60 (dq, *J* = 9.4, 7.0 Hz, 1H, OCH*H*), 3.90 (t, *J* = 5.7 Hz, 1H, H-4), 4.53 (dq, *J* = 7.2, 6.3 Hz, 1H, H-2), 5.71 (dd, *J* = 7.2, 5.2 Hz, 1H, H-3), 6.42 (dd, *J* = 7.5, 1.1 Hz, 1H, H-5), 6.47 (dd, *J* = 8.4, 1.1 Hz, 1H, H-7), 6.68 (t, *J* = 8.0 Hz, 1H, H-6); ^{19}F NMR (376 MHz, $CDCl_3$) δ 85.2 (d, *J* = 6.3 Hz, CF_3); ^{13}C NMR (126 МГц, $CDCl_3$) δ 14.8, 19.9, 26.8, 38.5, 41.0, 49.8, 65.0, 75.5 (q, *J* = 33.2 Hz, C-2), 83.1, 113.7, 120.0, 122.6 (q, *J* = 280.5 Hz, CF_3), 124.1, 124.7, 142.4, 148.7, 218.0.

*4.6.20.2. Compound tt-**9'c**.* ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.44 (t, *J* = 6.8 Hz, 3H, Me), 1.65–2.76 (m, 7H, 3 CH_2, H-2′), 4.18 (dd, *J* = 7.8, 3.3 Hz, 1H, H-4), 4.85 (dq, *J* = 9.3, 5.6 Hz, 1H, H-2), 6.77 (br d, *J* = 7.5 Hz, 1H, H-5), 6.85 (br d, *J* = 8.4 Hz, 1H, H-7), 7.01 (1H, t, *J* = 8.0 Hz, H-6) (signals of H-3 and OCH_2 are masked); ^{1}H NMR (400 MHz, C_6D_6) δ 0.74–2.16 (m, 7H, 3 CH_2, H-2′), 1.10 (t, *J* = 7.0 Hz, 3H, Me), 4.05 (dd, *J* = 7.9, 3.5 Hz, 1H, H-4), 4.27 (dq, *J* = 9.3, 5.8 Hz, 1H, H-2), 4.99 (dd, *J* = 9.3, 7.9 Hz, 1H, H-3), 6.36 (br d, *J* = 7.8 Hz, 1H, H-5), 6.73 (t, *J* = 8.1 Hz, 1H, H-6) (signals of H-7 and OCH_2 are masked); ^{19}F NMR (376 MHz, $CDCl_3$) δ 85.2 (d, *J* = 5.6 Hz, CF_3). Anal. Calcd. for $C_{17}H_{18}F_3NO_5$: C, 54.69; H, 4.86; N, 3.75. Found: C, 54.55; H, 4.59; N, 3.75.

4.6.21. (2S)-[(2S*,3S*,4R*)-6-Chloro-3-nitro-2-(trifluoromethyl) chroman-4-yl]cyclopentan-1-one (tt-**9d**) and (2R*)-[(2S*,3S*,4R*)-6-chloro-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopentan-1-one (tt-**9'd**)*

Yield 0.27 g (73%), m.p. 82–83 °C. IR (ATR): 1745, 1561, 1484, 1420, 1352, 1328 cm^{-1}. Ratio of diastereomers *tt*-**9d**:*tt*-**9'd** = 74:26.

*4.6.21.1. Compound tt-**9d**.* This compound was obtained in a pure state by recrystallisation of the diastereomeric mixture from hexane. Yield 0.13 g (65%), m.p. 89–90°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41–2.57 (m, 7H, 3 CH_2, H-2′), 3.95 (dd, *J* = 6.9, 4.7 Hz, 1H, H-4), 4.98 (quint, *J* = 6.4 Hz, 1H, H-2), 5.73 (dd, *J* = 6.6, 4.7 Hz, 1H, H-3), 7.00 (d, *J* = 2.4 Hz, 1H, H-5), 7.02 (d, *J* = 8.7 Hz, 1H, H-8), 7.24 (dd, *J* = 8.7, 2.4 Hz, 1H, H-7); ^{19}F NMR (376 MHz, $CDCl_3$) δ 85.1 (d, *J* = 6.2 Hz, CF_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 19.9, 26.9, 38.4, 40.6, 49.6, 75.4 (q, *J* = 33.4 Hz, C-2), 82.3, 119.5, 122.4 (q, *J* = 280.7 Hz, CF_3), 124.7, 126.9, 128.3, 129.5, 151.2, 217.4.

*4.6.21.2. Compound tt-**9'd**.* ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.69–2.75 (m, 7H, 3 CH_2, H-2′), 4.15 (dd, *J* = 8.2, 3.8 Hz, 1H, H-4), 4.84 (dq, *J* = 9.1, 5.5 Hz, 1H, H-2), 5.00 (dd, *J* = 9.1, 8.2 Hz, 1H, H-3), 6.91 (d, *J* = 2.4 Hz, 1H, H-5), 6.95 (d, *J* = 8.7 Hz, 1H, H-8), 7.19 (dd, *J* = 8.7, 2.4 Hz, 1H, H-7); ^{19}F NMR (376 MHz, $CDCl_3$) δ 85.0 (d, *J* = 5.5 Hz,

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CF_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 20.3, 24.7, 37.6, 38.3, 52.6, 74.7 (q, J = 33.1 Hz, C-2), 80.4, 119.2, 122.4 (q, J = 281.9 Hz, CF_3), 124.0, 129.1, 129.2, 129.3, 151.1, 215.2. Anal. Calcd. for $C_{15}H_{13}ClF_3NO_4$: C, 49.53; H, 3.60; N, 3.85. Found: C, 49.64; H, 3.40; N, 3.81.

4.6.22. (2S)-[(2S*,3S*,4R*)-6-Bromo-3-nitro-2-(trifluoromethyl) chroman-4-yl]cyclopentan-1-one (tt-**9e**) and (2R*)-[(2S*,3S*,4R*)-6-bromo-3-nitro-2-(trifluoromethyl)chroman-4-yl]cyclopentan-1-one (tt-**9'e**)*

Yield 0.34 g 84%, m.p. 78–79 °C. IR (ATR): 1727, 1561, 1480, 1408, 1351, 1320 cm^{-1}. Ratio of diastereomers *tt*-**9e**:*tt*-**9'e** = 71:29.

*4.6.22.1. Compound tt-**9e**.* ^1H NMR (400 MHz, $CDCl_3$) δ 1.39–2.58 (m, 7H, 3 CH_2, H-2′), 3.95 (dd, J = 6.4, 4.8 Hz, 1H, H-4), 4.99 (quint, J = 6.4 Hz, 1H, H-2), 5.73 (dd, J = 6.4, 4.8 Hz, 1H, H-3), 6.97 (d, J = 8.6 Hz, 1H, H-8), 7.15 (d, J = 2.2 Hz, 1H, H-5), 7.38 (dd, J = 8.6, 2.2 Hz, 1H, H-7); ^1H NMR (400 MHz, C_6D_6) δ 0.54–1.99 (m, 7H, 3 CH_2, H-2′), 3.58 (dd, J = 6.8, 5.0 Hz, 1H, H-4), 4.39 (quint, J = 6.6 Hz, 1H, H-2), 5.73 (dd, J = 6.7, 5.0 Hz, 1H, H-3), 6.39 (d, J = 8.6 Hz, 1H, H-8), 6.88–6.93 (m, 2H, H-5, H-7); ^{19}F NMR (376 MHz, $CDCl_3$) δ 85.1 (d, J = 6.3 Hz, CF_3); ^{19}F NMR (376 MHz, C_6D_6) δ 86.2 (d, J = 6.4 Hz, CF_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 19.9, 26.9, 38.4, 40.5, 49.6, 75.3 (q, J = 33.4 Hz, C-2), 82.3, 111.6, 119.9, 122.4 (q, J = 280.6 Hz, CF_3), 125.2, 129.8, 132.5, 151.7, 217.4.

*4.6.22.2. Compound tt-**9'e**.* ^1H NMR (400 MHz, $CDCl_3$) δ 1.68–2.74 (m, 7H, 3 CH_2, H-2′), 4.16 (dd, J = 8.2, 3.4 Hz, 1H, H-4), 4.84 (dq, J = 9.2, 5.6 Hz, 1H, H-2), 4.97 (dd, J = 9.2, 8.2 Hz, 1H, H-3), 6.95 (d, J = 8.6 Hz, 1H, H-8), 7.33–7.38 (m, 2H, H-5, H-7); ^1H NMR (400 MHz, C_6D_6) δ 0.64–1.84 (m, 7H, 3 CH_2, H-2′), 3.83 (dd, J = 8.4, 3.4 Hz, 1H, H-4), 4.12 (dd, J = 9.3, 5.6 Hz, 1H, H-2), 4.79 (dd, J = 9.3, 8.4 Hz, 1H, H-3), 6.35 (d, J = 8.6 Hz, 1H, H-8), 6.86–6,93 (m, 2H, H-5, H-7); ^{19}F NMR (376 MHz, $CDCl_3$) δ 85.0 (d, J = 5.6 Hz, CF_3); ^{19}F NMR (376 MHz, C_6D_6) δ 86.3 (d, J = 5.6 Hz, CF_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 20.3, 24.6, 37.6, 38.2, 52.6, 74.6 (q, J = 32.9 Hz, C-2), 80.4, 116.5, 119.5, 122.3 (q, J = 282.2 Hz, CF_3), 124.4, 129.8, 132.2, 151.6, 215.2. Anal. Calcd. for $C_{15}H_{13}BrF_3NO_4 \cdot 0.5H_2O$: C, 43.19; H, 3.38; N, 3.36. Found: C, 43.10; H, 3.27; N, 3.36.

4.6.23. (2S)-[(2S*,3S*,4R*)-3-Nitro-2-(trichloromethyl)chroman-4-yl]cyclopentan-1-one (tt-**9h**)*

This compound was obtained by hydrolysis of the mixture *tt*-**8h**:*ct*-**8h** = 64:36 and purified by column chromatography over silica gel (eluent – $CHCl_3$). Yield 0.19 g (51%), m.p. 162–163 °C. IR (ATR): 1731, 1554, 1487, 1462, 1419, 1363 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 1.40–2.74 (m, 7H, 3 CH_2, H-2′), 3.70 (dd, J = 7.6, 3.0 Hz, 1H, H-4), 5.21 (d, J = 6.8 Hz, 1H, H-2), 6.03 (dd, J = 6.8, 3.0 Hz, 1H, H-3), 7.02 (dd, J = 7.5, 1.2 Hz, 1H, H-5), 7.08 (td, J = 7.5, 0.8 Hz, 1H, H-6), 7.16 (br d, J = 7.7 Hz, 1H, H-8), 7.31 (td, J = 7.9, 1.2 Hz, 1H, H-7); ^{13}C NMR (126 MHz, $CDCl_3$) δ 19.8, 27.4, 38.4, 43.2, 50.2, 86.6, 87.2, 97.2, 118.3, 124.5, 124.9, 128.4, 129.5, 154.0, 217.5. Anal. Calcd. for $C_{15}H_{14}Cl_3NO_4$: C, 47.58; H, 3.73; N, 3.70. Found: C, 47.54; H, 3.50; N, 3.64.

4.6.24. (2S)-[(2S*,3S*,4R*)-6-Chloro-3-nitro-2-(trichloromethyl) chroman-4-yl]cyclopentan-1-one (tt-**9k**) and (2R*)-[(2S*,3S*,4R*)-6-chloro-3-nitro-2-(trichloromethyl)chroman-4-yl]cyclopentan-1-one (tt-**9'k**)*

Yield 0.39 g (94%), m.p. 156–157 °C. IR (ATR): 1731, 1555, 1481, 1453, 1404, 1374, 1359 cm^{-1}. Ratio of diastereomers *tt*-**9k**:*tt*-**9'k** = 71:29.

*4.6.24.1. Compound tt-**9k**.* ^1H NMR (400 MHz, $CDCl_3$) δ 1.44–2.77 (m, 7H, 3 CH_2, H-2′), 3.64 (dd, J = 8.0, 2.7 Hz, 1H, H-4), 5.19 (d, J = 6.6 Hz, 1H, H-2), 6.08 (dd, J = 6.6, 2.7 Hz, 1H, H-3), 7.02 (d, J = 2.3 Hz, 1H, H-5), 7.11 (d, J = 8.6 Hz, 1H, H-8), 7.28 (dd, J = 8.6, 2.3 Hz, 1H, H-7); ^{13}C NMR (101 MHz, $CDCl_3$) δ 19.7, 27.7, 38.3, 43.1, 49.7, 86.1, 87.4, 96.9, 119.7, 126.9, 128.3, 129.5, 129.6, 152.5, 217.0.

*4.6.24.2. Compound tt-**9'k**.* ^1H NMR (400 MHz, $CDCl_3$) δ 1.51–2.77 (m, 7H, 3 CH_2, H-2′), 3.95 (dd, J = 8.4, 3.6 Hz, 1H, H-4), 5.10 (dd, J = 8.4, 7.1 Hz, 1H, H-3), 5.42 (d, J = 7.1 Hz, 1H, H-2), 7.06 (d, J = 8.6 Hz, 1H, H-8), 7.13 (br d, J = 2.3 Hz, 1H, H-5), 7.27 (dd, J = 8.6, 2.3 Hz, 1H, H-7); ^{13}C NMR (101 MHz, $CDCl_3$) δ 20.3, 24.7, 37.4, 39.3, 50.1, 84.8, 86.6, 100.0, 119.6, 125.2, 126.5, 129.1, 129.3, 152.6, 214.9. Anal. Calcd. for $C_{15}H_{13}Cl_4NO_4$: C, 43.62; H, 3.17; N, 3.39. Found: C, 44.07; H, 3.08; N, 3.28.

4.6.25. (2S)-[(2S*,3S*,4R*)-6-Bromo-3-nitro-2-(trichloromethyl) chroman-4-yl]cyclopentan-1-one (tt-**9l**) and (2R*)-[(2S*,3S*,4R*)-6-bromo-3-nitro-2-(trichloromethyl)chroman-4-yl]cyclopentan-1-one (tt-**9'l**)*

Yield 0.44 g (96%), m.p. 140–141 °C. IR (ATR): 1732, 1553, 1478, 1451, 1405, 1374, 1358 cm^{-1}. Ratio of diastereomers *tt*-**9l**: *tt*-**9'l** = 63:37.

*4.6.25.1. Compound tt-**9l**.* ^1H NMR (400 MHz, $CDCl_3$) δ 1.44–2.78 (m, 7H, 3 CH_2, H-2′), 3.63 (dd, J = 8.0, 2.7 Hz, 1H, H-4), 5.19 (d, J = 6.6 Hz, 1H, H-2), 6.08 (dd, J = 6.6, 2.7 Hz, 1H, H-3), 7.06 (d, J = 8.6 Hz, 1H, H-8), 7.17 (d, J = 2.3 Hz, 1H, H-5), 7.43 (dd, J = 8.6, 2.3 Hz, 1H, H-7); ^{13}C NMR (101 MHz, $CDCl_3$) δ 19.7, 27.7, 38.3, 43.1, 49.7, 86.0, 87.4, 96.9, 117.0, 120.1, 127.3, 131.1, 132.5, 153.0, 217.0.

*4.6.25.2. Compound tt-**9'l**.* ^1H NMR (400 MHz, $CDCl_3$) δ 1.51–2.78 (m, 7H, 3 CH_2, H-2′), 3.96 (dd, J = 8.3, 4.0 Hz, 1H, H-4), 5.10 (dd, J = 8.3, 7.1 Hz, 1H, H-3), 5.41 (д, J = 7.1 Hz, 1H, H-2), 7.01 (d, J = 8.6 Hz, 1H, H-8), 7.28 (dd, J = 2.3, 1.0 Hz, 1H, H-5), 7.41 (dd, J = 8.6, 2.3 Hz, 1H, 1H, H-7); ^{13}C NMR (101 MHz, $CDCl_3$) δ 20.3, 24.6, 37.4, 39.1, 50.1, 84.7, 86.5, 98.1, 116.5, 120.0, 125.6, 129.3, 132.3, 153.1, 215.0. Anal. Calcd. for $C_{15}H_{13}BrCl_3NO_4$: C, 39.38; H, 2.86; N, 3.06. Found: C, 39.53; H, 2.93; N, 3.28.

4.6.26. (2S)-[(2R*,3S*,4R*)-3-Nitro-2-phenylchroman-4-yl] cyclopentan-1-one (tt-**9o**) and (2R*)-[(2R*,3S*,4R*)-3-nitro-2-phenylchroman-4-yl]cyclopentan-1-one (tt-**9'o**)*

Yield 0.29 g (87%), m.p. 180–182 °C. IR (ATR): 1732, 1552, 1468, 1452, 1362 cm^{-1}. Ratio of diastereomers *tt*-**9o**:*tt*-**9'o** = 76:24.

*4.6.26.1. Compound tt-**9o**.* ^1H NMR (400 MHz, $CDCl_3$) δ 1.44–2.51 (m, 7H, 3 CH_2, H-2′), 4.50 (dd, J = 9.8, 2.4 Hz, 1H, H-4), 4.95 (t, J = 9.7 Hz, 1H, H-3), 5.18 (d, J = 9.6 Hz, 1H, H-2), 6.90 (d, J = 7.6 Hz, 1H, H-8), 6.93–6.99 (m, 2H, H-5, H-6), 7.19 (t, J = 7.5 Hz, 1H, H-7), 7.36–7.46 (m, 5H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 20.3, 23.8, 38.6, 40.3, 52.2, 78.9, 90.2, 117.9, 120.5, 218.2, 122.5, 127.2, 128.1, 128.6, 128.9, 129.8, 135.1, 154.9.

*4.6.26.2. Compound tt-**9'o**.* ^1H NMR (400 MHz, $CDCl_3$) δ 1.70–2.88 (m, 7H, 3 CH_2, H-2′), 4.46 (dd, J = 9.6, 2.4 Hz, 1H, H-4), 4.99 (t, J = 9.7 Hz, 1H, H-3), 5.12 (d, J = 9.8 Hz, 1H, H-2), 6.93–7.30 (m, 4H, H-5, H-6, H-7, H-8), 7.36–7.46 (m, 5H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 20.5; 24.4, 38.0, 39.2, 53.4, 79.0, 90.2, 117.8, 121.9, 122.7, 126.9, 127.4, 128.4, 128.9, 129.8, 135.0; 154.8, 216.4. Anal. Calcd. for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.68; N, 4.15. Found: C, 71.16; H, 5.49; N, 4.18.

4.7. X-ray diffraction study of compounds ct-7h, tt-8a, ct-9l, tt-9c and tt-9h

Intensity data for the compounds *ct*-**7h**, *tt*-**8a** and *ct*-**9l**, *tt*-**9c**, *tt*-**9h**, were collected on a “Xcalibur S” or “Xcalibur Eos”

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diffractometer, corresponding at 295 (2) K (Mo-Kα or Cu-Kα (compound *tt*-**8a**) radiation, graphite monochromator, ω-scan). The structures were solved by direct methods and refined by full-matrix least-squares method using the SHELX-97 program package.[12] All non-hydrogen atoms were refined with anisotropic atomic displacement and hydrogen atoms were included at calculated position using a riding model.

4.7.1. Crystal data for ct-7h

$C_{19}H_{21}Cl_3N_2O_4$, $M = 447.74$. Monoclinic crystals space group $C2/c$, $a = 29.367$ (4), $b = 8.5321$ (8), $c = 18.145$ (3) Å, $\alpha = \gamma = 90.00$, $\beta = 116.269$ (5)°, $V = 4077.0$ (10) Å^3, $D_c = 1.459$ g/cm^3, absorption coefficient $\mu = 0.478$ mm^{-1}, $Z = 8$. The intensities of 4995 independent reflections ($R_{int} = 0.0287$) were measured. The final discrepancy factors $R_1 = 0.0382$, w$R_2 = 0.0848$, GooF = 1.003 for 2452 reflections with $I > 2\sigma(I)$; $R_1 = 0.0869$, w$R_2 = 0.0910$ (all data). Largest different peak and hole: 0.345 and −0.359 eÅ^{-3}. Completeness to $\theta = 28.3°$ (98.6%). Deposition number CCDC 1541656.

4.7.2. Crystal data for tt-8a

$C_{19}H_{21}F_3N_2O_4$, $M = 398.38$. Triclinic crystals space group P-1, $a = 9.171$ (9), $b = 10.247$ (10), $c = 11.403$ (13) Å, $\alpha = 86.08$ (9), $\beta = 67.90$ (10), $\gamma = 69.73$ (9)°, $V = 929.0$ (17) Å^3, $D_c = 1.424$ g/cm^3, absorption coefficient $\mu = 1.029$ mm^{-1}, $Z = 2$. The intensities of 3103 independent reflections ($R_{int} = 0.0381$) were measured. The final discrepancy factors $R_1 = 0.0514$, w$R_2 = 0.1579$, GooF = 1.015 for 2502 reflections with $I > 2\sigma(I)$; $R_1 = 0.0593$, w$R_2 = 0.1655$ (all data). Largest different peak and hole: 0.274 and −0.245 eÅ^{-3}. Completeness to $\theta = 65.5°$ (94.4%). Deposition number CCDC 1541653.

4.7.3. Crystal data for ct-9l

$C_{15}H_{13}BrCl_3NO_4$, $M = 457.53$. Ortorombic crystals space group $P2_12_12_1$, $a = 10.9805$ (7), $b = 10.9040$ (6), $c = 30.9588$ (15) Å, $\alpha = \beta = \gamma = 90.00°$, $V = 3538.6$ (4) Å^3, $D_c = 1.718$ g/cm^3, absorption coefficient $\mu = 2.795$ mm^{-1}, $Z = 8$. The intensities of 8302 independent reflections ($R_{int} = 0.0321$) were measured. The final discrepancy factors $R_1 = 0.0506$, w$R_2 = 0.0882$, GooF = 1.005 for 5463 reflections with $I > 2\sigma(I)$; $R_1 = 0.0967$, w$R_2 = 0.1071$ (all data). Largest different peak and hole: 0.561 and −0.695 eÅ^{-3}. Completeness to $\theta = 28.22°$ (99.82%). Deposition number CCDC 1541657.

4.7.4. Crystal data for tt-9c

$C_{17}H_{18}F_3NO_5$, $M = 373.11$. Triclinic crystals space group P-1, $a = 9.1032$ (7), $b = 9.3424$ (8), $c = 10.6210$ (9) Å, $\alpha = 69.803$ (8), $\beta = 81.215$ (7), $\gamma = 81.790$ (7)°, $V = 833.83$ (12) Å^3, $D_c = 1.487$ g/cm^3, absorption coefficient $\mu = 0.130$ mm^{-1}, $Z = 2$. The intensities of 4525 independent reflections ($R_{int} = 0.0188$) were measured. The final discrepancy factors $R_1 = 0.0492$, w$R_2 = 0.1363$, GooF = 1.008 for 3106 reflections with $I > 2\sigma(I)$; $R_1 = 0.0803$, w$R_2 = 0.1606$ (all data). Largest different peak and hole: 0.212 and −0.251 eÅ^{-3}. Completeness to $\theta = 28.22°$ (99.98%). Deposition number CCDC 1541655.

4.7.5. Crystal data for tt-9h

$C_{15}H_{14}Cl_3NO_4$, $M = 378.63$. Triclinic crystals space group P-1, $a = 9.4893$ (6), $b = 9.5851$ (6), $c = 10.6764$ (7) Å, $\alpha = 79.477$ (6), $\beta = 73.457$ (6), $\gamma = 61.813$ (6)°, $V = 819.15$ (9) Å^3, $D_c = 1.535$ g/cm^3, absorption coefficient $\mu = 0.577$ mm^{-1}, $Z = 2$. The intensities of 4498 independent reflections ($R_{int} = 0.0218$) were measured. The final discrepancy factors $R_1 = 0.0495$, w$R_2 = 0.1423$, GooF = 1.01 for 3261 reflections with $I > 2\sigma(I)$; $R_1 = 0.0729$, w$R_2 = 0.1697$ (all data). Largest different peak and hole: 0.510 and −0.459 eÅ^{-3}. Completeness to $\theta = 28.22°$ (100.00%). Deposition number CCDC 1541654.

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