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Access to 2,3-diaryl-4-nitrothiochroman *S*,*S*-dioxides from 3-nitrobenzo[*b*]thiophene

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ABSTRACT

The base-induced cyclization of (*E*)-2-aryl-1-[2-(benzylsulfonyl)phenyl]-1-nitroethenes to polysubstituted thiochroman *S*,*S*-dioxides exhibits a diastereoselectivity that can be oriented towards a selected isomer by means of appropriate adjustments of the experimental conditions. The interest of such a result also rests on the promising pharmacological activity of the products, whose structure encompasses different well-acknowledged pharmacophores. A conformational ^{1}H NMR investigation, backed by molecular-mechanics calculations, has also been accomplished.

1. Introduction

Within the framework of our long-standing project on the synthetic exploitation of the ring-opening of nitrothiophenes[1–6] we have reported a novel approach to 3,4-disubstituted thiochroman *S*,*S*-dioxides (**6**, Scheme 1).[4] The pivotal step is represented by an intramolecular Michael-type addition onto a nitrovinyl moiety (Scheme 1, step v) and the overall procedure from 3-nitrobenzo[*b*]thiophene (**1**) can be envisaged as a 5 to 6 enlargement of the sulfur heterocycle, with the carbon atom at position 2 as the new entry, provided by MeI (step ii).

The cyclization step of **5** to **6** proved very efficient, always proceeding with high practical yields, thus allowing a more than satisfactory completion of the ring-opening/ring-closure protocol. The resulting nitrothiochroman *S*,*S*-dioxides **6** are polyfunctionalized molecules of undeniable interest. As a matter of fact, some structural features make such sulfur heterocycles suitable candidates for pharmacological/biological evaluation: this is because they contain, within a relatively simple molecular array, well-known pharmacophores, such as the sulfonyl and the nitro groups, while the electronic properties of the Ar moiety could be modulated by means of suitable substituents.

In the light of the possible biological interest attached to **6**, a drawback of the synthetic procedure is represented by the low diastereoselectivity shown by the cyclization step in the conditions described (see footnotes of Scheme 1): actually, mixtures of the *cis* and *trans* isomers of **6** were generally formed, with a very small preference for the cis isomer.[3] A somehow more significant diastereoselection was observed only when Ar=1-naphthyl and *o*-tolyl (cis to trans ratio=3 and 2.2, respectively), so demonstrating some dependence on steric hindrance.

On these grounds, in order to widen the applicability range of the ring-enlargement procedure and also with the aim of improving the diastereoselection of the cyclization step, we have increased the structural complexity of our system allowing a substituent also on the incoming carbon atom (e.g., at position 2 of the final heteroring): relevant synthetic results are presented and discussed herein, with particular attention to the stereochemical aspects of the process.

2. Results and discussion

2.1. Synthetic and diastereoselective aspects

The synthesis of the trisubstituted thiochroman *S*,*S*-dioxides **10**, bearing a phenyl substituent at C(2) of the heteroring, was accomplished following the procedure already described for the

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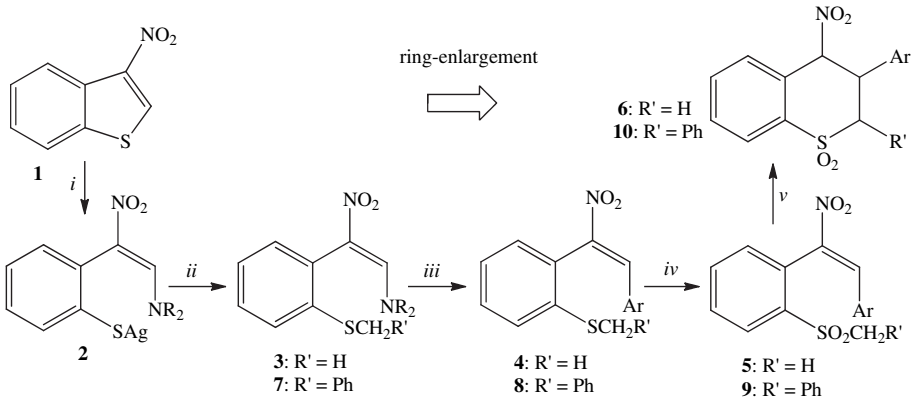


Scheme 1. (i) Pyrrolidine (R_2NH, 2 mol equiv)/$AgNO_3$ (2 mol equiv), abs. EtOH, rt, overnight; (ii) excess MeI or $PhCH_2Cl$, 0 °C to rt, 2 h; (iii) ArMgX or ArLi (1.1 mol equiv), THF, −78 °C, 15–45 min, followed by acidic quenching; (iv) MCPBA (2 mol equiv), CH_2Cl_2, rt; (v) LHMDS (1.1 mol equiv), THF, rt, 4 h, followed by NH_4Cl quenching, 15 min.

parent compounds **6**, as summarized in Scheme 1. The phenyl moiety can be easily introduced during step ii, employing benzyl chloride instead of methyl iodide as the alkylating agent for the trapping of the thiolate intermediate **2**, in otherwise similar experimental conditions.

Replacement of the NR_2 group with an aryl moiety by treatment of nitroenamine **7** with Grignard reagents experienced the same stereoselectivity as previously observed for the synthesis of **4**.

According to a well established procedure,[4,7,8] sulfides **8a–j** were then treated with MCPBA to give the corresponding sulfones **9a–j** in very high yield throughout (see Table 1).

Treatment of sulfones **9a–j** with lithium bis(trimethylsilyl)amide (LHMDS, 1.1 mol equiv) in THF (a solvent capable to solvate lithium cations) in standard conditions (see footnotes of Scheme 1), followed by acidic quenching, allowed the isolation of the corresponding cyclized products **10a–j** (Scheme 1) in more than satisfactory yields (Table 1).

Table 1
Yields for the synthesis of sulfides **8a–j**, sulfones **9a–j** and thiochromans **10a–j** according to Scheme 1.[a] Diastereomeric ratios obtained from ^{1}H NMR spectroscopic analysis for compounds **10a–j** are also reported

Entry	Ar in ArMgX	**8**: Yield %[b]	**9**: Yield %[b]	**10**:		
				Yield %[c]	**A**:**B**:**C**[d]	**A**:(**B**+**C**)[e]
1	Ph	**8a**: 97	**9a**: 99	**10a**: 83	10.8:2.1:1	3.5
2	2-MeC_6H_4	**8b**: 99	**9b**: 92	**10b**: 82	26.6:2.1:1	8.6
3	3-MeC_6H_4	**8c**: 93	**9c**: 97	**10c**: 88	9.9:2.0:1	3.3
4	4-MeC_6H_4	**8d**: 96	**9d**: 99	**10d**: 98	9.9:1.8:1	3.5
5	4-MeOC_6H_4	**8e**: 99	**9e**: 99	**10e**: 82	4.6:2.9:1	1.2
6	4-ClC_6H_4	**8f**: 99	**9f**: 97	**10f**: 90	3.3:1.0:1	1.6
7	4-BrC_6H_4	**8g**: 77	**9g**: 99	**10g**: 97	2.2:0.7:1	1.3
8	1-Naphthyl	**8h**: 89	**9h**: 99	**10h**: 94	18.8:2.9:1	4.8
9	2-Thienyl	**8i**: 96	**9i**: 97	**10i**: 93	0.2:0.8:1	0.1
10	3-Thienyl	**8j**: 99	**9j**: 99	**10j**: 82	4.0:1.1:1	1.9

[a] For the reaction conditions, see footnotes of Scheme 1, steps iii, iv and v, respectively.
[b] Yields of chromatographically isolated compounds.
[c] Yields of solid crude residues, showing three series of signals by ^{1}H NMR spectroscopic analysis.
[d] Isomer **D** was never observed (see text).
[e] The significance of the **A**:(**B**+**C**) ratio will be enlightened in the text.

In each case investigated, the ^{1}H NMR spectroscopic analysis of the crude reaction product showed the presence of three series of similar signals with different relative intensities, which, on the grounds of the structure of the expected thiochroman, could straightforwardly be attributed to three different diastereomers, named **A**, **B** and **C**. Actually, the cyclization process generates three stereogenic centres and should theoretically give four different diastereomeric products: thus, the absence of one of them (i.e., **D**) immediately appeared somehow intriguing.

From the observed relative ratios, reported in Table 1, calculated versus the signal for the **C** isomer (usually the lowest), a sizeable prevalence of **A** in all cases but for entry 9 (Ar=2-thienyl) clearly emerges.

The structures of **A**, **B** and **C** were later identified as depicted in Fig. 1 by a combined molecular-mechanics and ^{1}H NMR spectroscopic investigation (see details in Section 2.2 below); the **D** structure was deduced subsequently.

Before considering the stereochemical results shown in the last two columns of Table 1, it is necessary to analyze the process in detail. The base-induced cyclization under investigation (i.e., step v of Scheme 1) is composed of four different, consecutive events (Scheme 2), namely: (a) proton extraction from **9** to give the delocalized carbanion $\mathbf{9}^-$; (b) intramolecular conjugated Michael-type addition of the anion onto the nitrovinylic moiety, to give the nitronate anion intermediate $\mathbf{11}^-$; (c) protonation of the nitronate, most likely to initially give the corresponding nitronic acid **11**, and then (d) nitronic acid/nitroalkane tautomeric equilibration to the observed final product **10**.[9]

It should be remarked that the relative position of the substituents at C(2) and C(3) is determined during the second event, while the stereochemistry at C(4) is established after acidic quenching.

The stereochemical aspect is thus set-up along with step **b**, whereby two diastereomeric nitronates (*cis*-$\mathbf{11}^-$ and *trans*-$\mathbf{11}^-$) are generated, which would in turn eventually lead to the **A**/**D** (**D** being never observed throughout in the conditions employed) and the **B**/**C** products, respectively. The *cis*-nitronate/*trans*-nitronate ratios can be deduced from the **A**:**B**:**C** ratios as **A**:(**B**+**C**) and relevant values are reported in the last column of Table 1.

Such data show that, in the conditions employed, the cyclization step generally favours the *cis*-nitronate, the diastereoselectivity being good for Aryl=*o*-tolyl (entry 2, *cis*/*trans*=8.6) and 1-naphthyl (entry 8, *cis*/*trans*=4.8) but moderate to low in all of the other cases. For Ar=2-thienyl, the diastereoselectivity is appreciable but inverted (entry 9, *cis*/*trans*=0.1): this outcome, which is rather surprising but definitely confirmed by replicate experiments, could be ascribed to some steric and/or stereoelectronic effects selectively played by the 2-thienyl moiety; on the other hand, under kinetic control (see below in the text) the same derivative lines up nicely with all of the others (see Table 3).

On the grounds of the just described outcomes, in order to better understand which parameters might influence the diastereomeric ratios, some targeted experiments on the model compounds **9d** and **10d** were devised and relevant selected results are reported in Table 2.

Two main outcomes clearly emerge from the data collected: (a) comparison of entries 1 and 2 as well as of entries 3 and 4

Table 2
Diastereoselectivity tests for the model **9d** to **10d** transformation: relative percentages of **A**, **B**, **C** by varying the time of permanence of **9d** or **10d** in basic and/or acidic medium

Entry	Substrate	LHMDS mol equiv	Time elapsed in basic medium	Time elapsed in acidic medium[a]	**A**%[b]	**B**%[b]	**C**%[b]	*cis*-**11**/*trans*-**11** [**A**:(**B**+**C**)]	**B**:**C**
1	**9d**	1.1	4 h	15′	75	15	10	3	1.5
2	**9d**	1.1	24 h	15′	66	21	13	1.9	1.6
3	**9d**	1.1	4 h	Prolonged	77	5	18	3.3	0.3
4	**9d**	1.1	24 h	Prolonged	65	8	27	1.9	0.3
5	**9d**	2.5	4 h	15′	—	60	40	0	1.5
6	**10d-A**	1.1	4 h	15′	48	31	21	0.9	1.5
7	**10d-A**	1.1	4 h	Prolonged	42	16	42	0.7	0.4

[a] Quenching: NH_4Cl aqueous solution (excess).
[b] Normalized percentage, calculated by ^1H NMR spectroscopic analysis.

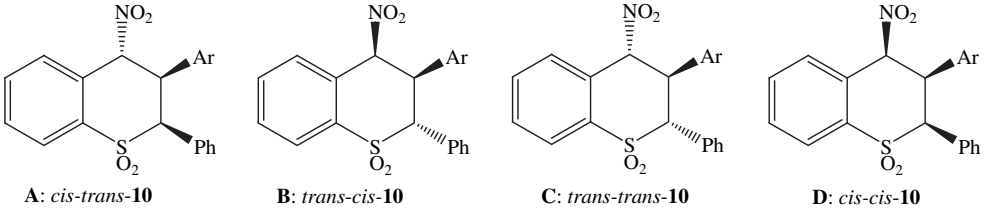
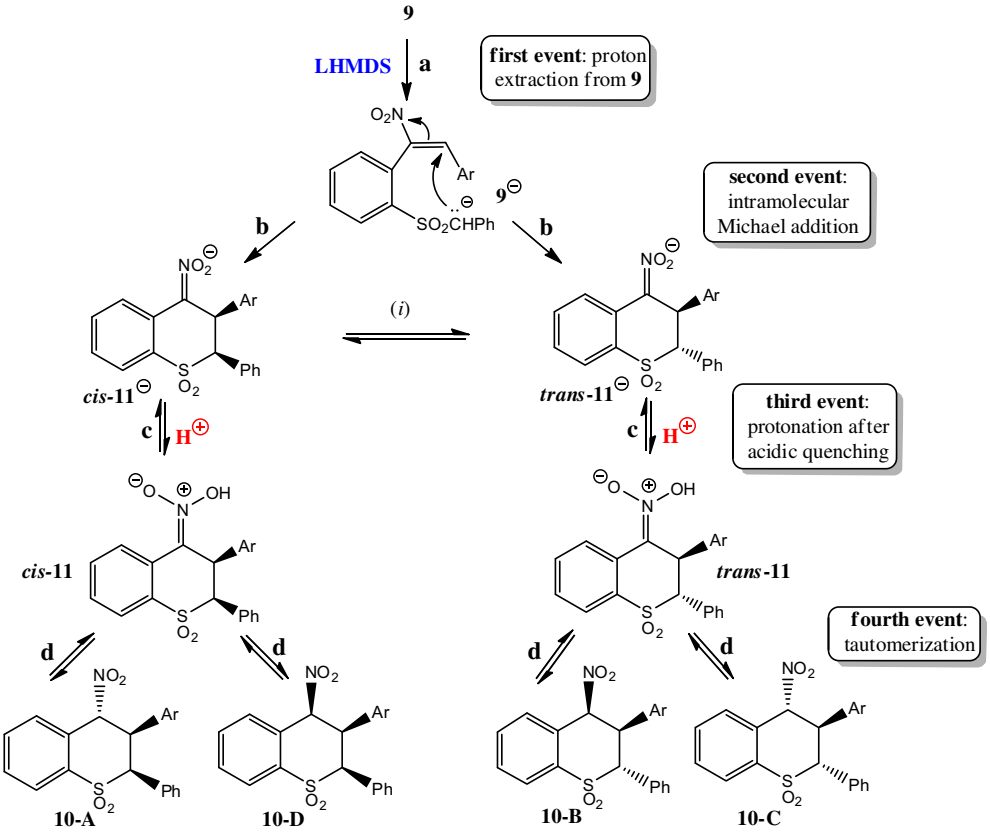


Fig. 1. Structure of the four possible diastereomeric racemic couples for compounds **10**.



Scheme 2. (i) Represents racemization at C(2) via a dianion in the presence of excess base (see text and Scheme 3 below).

establishes that the *cis*-nitronate/*trans*-nitronate [**A**:(**B**+**C**)] ratio is affected by the time elapsed in basic medium, the *cis*-nitronate being significantly favoured at shorter times, and (b) on the other hand, comparison of entries 1 and 3 as well as of entries 2 and 4 states that the time elapsed after acidic quenching, while uninfluent upon the **A**:(**B**+**C**) ratio, strongly affects the **B**:**C** ratio, the latter prevailing at longer times.

The first outcome above implicitly suggests that the attack of the anion upon the nitrovinyl moiety could be per se even more diastereoselective: a selectivity which is partly lost because of an equilibration between the two nitronates prior to acidic quenching.

A rationalization could be offered, at least in principle, by the reversibility of the Michael addition; actually, besides being in general quite controversial,[10] herein such an occurrence appears a most unlikely one, when considering that it would lead to a less stabilized anion[11] through a thermodynamically unfavourable ring-opening.

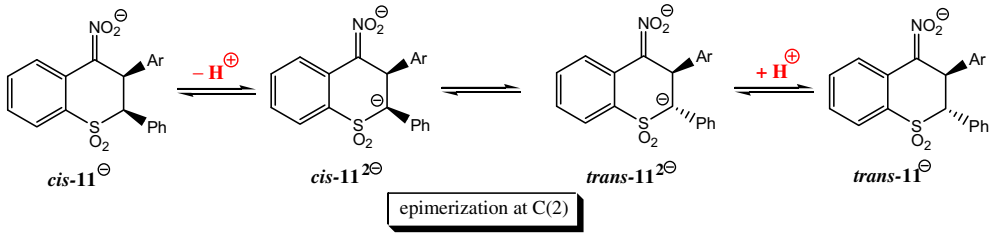
On the other hand, direct equilibration between *cis*-**11**$^-$ and *trans*-**11**$^-$, as depicted in Scheme 2, cannot occur and a dianion (e.g., *cis*-

Table 3
Yields and diastereomeric ratios for the **9** to **10** intramolecular process at −78 °C[a]

Entry	Ar	**10**: Yield %[b]	A:B:C[c]	A:(B+C)	Ratio between the A:(B+C) values at −78 °C and 22 °C[d]
1	Phenyl	**10a**: 84	32.1:1.3:1	14.0	4
2	2-MeC_6H_4	**10b**: 88	49.9:2.4:1	14.7	1.7
3	3-MeC_6H_4	**10c**: 81	24.6:1.6:1	9.5	2.9
4	4-MeC_6H_4	**10d**: 97	217.8:3.9:1	44.4	12.7
5	4-$MeOC_6H_4$	**10e**: 85	28.8:0.7:1	16.9	14.1
6	4-ClC_6H_4	**10f**: 90	17.5:1.0:1	8.8	5.5
7	4-BrC_6H_4	**10g**: 90	32.8:1.0:1	16.4	12.6
8	1-Naphthyl	**10h**: 90	20.7:1.6:1	8.0	1.7
9	2-Thienyl	**10i**: 95	17.6:0.9:1	9.3	93
10	3-Thienyl	**10j**: 90	28.0:1.0:1	14.0	7.4

[a] Experimental conditions otherwise identical to those for the reactions in Table 1.
[b] Yields of solid crude residues, showing three series of signals by ^1H NMR spectroscopic analysis.
[c] Isomer **D** was never observed.
[d] Data from Table 1.

11^{2-}, Scheme 3) must be necessarily postulated in the experimental conditions adopted. As a matter of fact, when considering the structure of the final thiochroman derivative, not only H(4) (a nitro-activated hydrogen) but also H(2) (a benzylic hydrogen adjacent to a sulfonyl group) should conceivably display some acidic character: on these grounds, the participation of a carbanion as **11**$^{2-}$ in the presence of excess base could reasonably be hypothesized, which would justify equilibration between *cis*-**11**$^-$ and *trans*-**11**$^-$ when admitting some resonance charge delocalization onto the sulfonyl and/or the phenyl group and hence epimerization at C(2) (Scheme 3).



Scheme 3.

The role of excess base (ca. 10% in the experimental conditions generally applied: see Tables 1 and 2) seems clearly testified by the results of expt 5 of Table 2, whereby the employment of 2.5 equiv of base in conditions otherwise similar to those of expt 1 leads, after comparable reaction times, to the complete disappearance of **A** in the final mixture, which only contains **B** and **C** in a 1.5 to 1 approximate ratio. While the absence of any detectable **A** (besides to the lack of **D**) clearly mirrors a high degree of stereoselectivity favouring the *trans*-nitronate **11**$^-$, which should be of thermodynamic origin (see below), interestingly enough, the **B**:**C** ratio well matches the values reported in Table 1 (entry 4, **B**:**C**=1.8) and 2 (entries 1, 2 and 6; **B**:**C**=1.5, 1.6 and 1.5, respectively), firmly stating that such a ratio is not affected by base concentration/excess and/or time of permanence in basic medium (see below in the discussion). Actually, as already mentioned above, all of the data collected strongly suggest the dependence of the **B**:**C** ratio (Table 2, last column) on the time of permanence in acidic medium after quenching, moving from the initial 1.5 figure (entries 1 and 2) to a possibly definitive 0.3 value (entries 3 and 4) obtained after an overnight permanence. It should be noted that the same initial and final values for the **B**:**C** ratio are obtained when the isolated **A** isomer of **10d** is subjected to the same experimental procedure as applied for the cyclization of **9d** (entries 6 and 7).

At this stage of our study, at least as far as the model **9d**/**10d** system is concerned, but presumably in a more general way, we can assess that the *cis*-nitronate (*cis*-**11**$^-$) is the 'kinetic' intermediate, while the *trans*-nitronate is the 'thermodynamic' one, becoming prevalent at longer times in basic medium; in addition, the protonation after acidic quenching [step (c) of Scheme 2] kinetically favours the *trans*–*cis* isomer **B**, while the *trans*–*trans* isomer **C**, eventually prevails if enough time is allowed for equilibration (most likely through the nitronic acid **11**, by means of an acid catalyzed aci/nitro tautomerism: step **d** of Scheme 2). Within the **A**/**D** pair, the first is probably favoured both from a kinetic and a thermodynamic point of view, an outcome which justifies the total absence of **D**.

On the grounds of the considerations above, with the aim of improving the diastereoselectivity according to a kinetic control, the same series of reactions as reported in Table 1 was repeated at −78 °C, in otherwise unchanged experimental conditions. Besides to yields (reported in Table 3, column 3) always comparable to those obtained at room temperature, the noteworthy enhancement in diastereoselectivity in favour of **A** (which becomes the major product even in the case of Ar=2-Th: entry 9) is evident from the data in columns 4, 5 and 6: in the latter the ratios **A**:(**B**+**C**) values, representative of *cis*-nitronate/*trans*-nitronate ratios, are compared at the two temperatures employed.

Finally, we anticipated that an even higher diastereoselectivity in favour of **A** could be obtained when avoiding excess base and/or at shorter reaction times. Accordingly, the experiment of entry 6 of Table 1 (Ar=4-ClC_6H_4: the substrate was purposely chosen as it displayed one of the lowest stereoselectivities) was repeated employing exactly 1 equiv of LHMDS and quenching aliquots after 2 and 4 h. In both cases, the *cis*-nitronate/*trans*-nitronate ratio raised from 8.8 (see Table 3) to 14, thus testifying that if no excess free base is present in the reaction medium, the preference for *cis*-**11**$^-$ (and hence for **A** in the final mixture) is further improved; moreover, in such conditions time elapsing before acidic quenching loses its significance, as any equilibration between *cis*-**11**$^-$ and *trans*-**11**$^-$ through a dianion is practically precluded.

Nitronate *cis*-**11**$^-$ was thus confirmed as the kinetically-favoured intermediate with respect to the presumably more stable *trans*-**11**$^-$. Searching for a possible explanation, we speculate that the conversion of the carbanion **9**$^-$ into the more stable nitronate **11**$^-$ should exhibit an early transition state, so that the lower-energy transition state could not correspond to the more stable reaction product. It seems reasonable to advance the hypothesis that the reactive sites of **9**$^-$ approach each other as described in **I** (Fig. 2), a disposition that preludes to the *cis*-nitronate. As a matter of fact, the approach depicted in **II**, precursor of the *trans*-nitronate, would be less energetically advantageous because of the developing unfavourable 1,3-diaxial-like interaction between the phenyl and the nitro group.

2.2. Assignment of the stereostructures to A–D isomers

The stereostructures of the three observed (**A**, **B** and **C**) enantiomeric pairs have been determined by a careful analysis of the ^1H

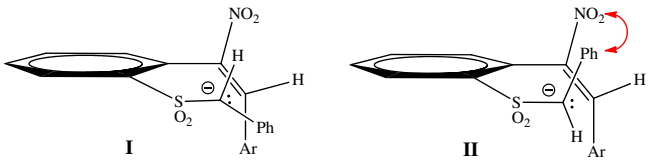


Fig. 2. Alternative spatial approaches for the intramolecular Michael addition of Scheme 2.

NMR spectroscopic data (reported in Table 4), coupled with a conformational analysis based on molecular-mechanics calculations (results in Table 5).

Table 4
^{1}H NMR spectroscopic data[a] for the non-aromatic protons of the enantiomeric pairs **10A–C**

10	Ar	Stereoisomer	δ (4-H)[b]	δ (3-H)[c]	δ (2-H)[b]	J (3-H, 4-H)	J (2-H, 3-H)
a	Phenyl	A	6.34	5.19	4.65	11.7	3.9
		B	6.13	4.84	5.98	4.8	12.9
		C	6.19	5.00	4.70	9.3	11.7
b	2-MeC$_6$H$_4$	A	6.34	5.56	4.49	12.0	3.6
		B	6.04	5.04	5.96	4.8	12.6
		C	6.15	5.32	4.56	8.0	10.5
c	3-MeC$_6$H$_4$	A	6.32	5.16	4.63	12.0	3.6
		B	6.12	4.79	5.96	4.8	12.6
		C	6.18	4.94	4.68	9.3	11.4
d	4-MeC$_6$H$_4$	A	6.30	5.15	4.64	11.6	3.8
		B	6.10	4.80	5.96	5.2	12.8
		C	6.17	4.94	4.73	9.3	11.7
e	4-MeOC$_6$H$_4$	A	6.27	5.13	4.63	11.4	3.9
		B	6.10	4.78	5.93	4.5	12.6
		C	6.16	4.93	4.67	9.3	11.7
f	4-ClC$_6$H$_4$	A	6.28	5.16	4.62	11.4	3.6
		B	6.10	4.83	5.92	4.5	12.9
		C	6.15	4.98	4.67	9.6	11.7
g	4-BrC$_6$H$_4$	A	6.27	5.15	4.62	11.5	3.6
		B	6.11	4.82	5.91	4.7	12.8
		C	6.15	4.96	4.70	9.5	11.5
h	1-Naphthyl	A	6.49	6.23	4.80	12.3	3.0
		B	6.27	5.74	6.14	4.2	12.3
		C	6.29	6.06	4.78	8.4	10.3
i	2-Thienyl	A	6.25	5.53	4.74	11.1	4.2
		B	6.19	5.09	5.96	4.8	12.6
		C	6.20	5.38	4.64	9.0	11.7
j	3-Thienyl	A	6.20	5.32	4.71	11.1	3.9
		B	6.14	4.99	5.93	4.8	12.6
		C	6.16	5.17	4.66	9.6	11.4

[a] Chemical shifts δ in ppm from internal TMS, coupling constants J in Hz, solvent $CDCl_3$ no long-range coupling was detected at 300 MHz.
[b] Doublet.
[c] Doublet of doublets.

side (generating two non-equivalent boats): in the latter case, though, severe eclipsing at the C(2)–C(3) bond should be expected. Another possibility is represented by sofa conformations, exhibiting just one carbon out of the plane and thus partially avoiding eclipsing. For this reason sofa conformations received much attention as possible competitors to half chairs in related systems.[12–15]

We have approached the problem by means of MMX3 calculations (PCMODEL[16]) on **10a** as the model compound. The results obtained (in the absence of solvent) are in perfect agreement with what previously observed for the C(2) unsubstituted thiochromans **6**, showing that for each diastereomer the most stable conformations are the two possible half chairs showed in Fig. 3.

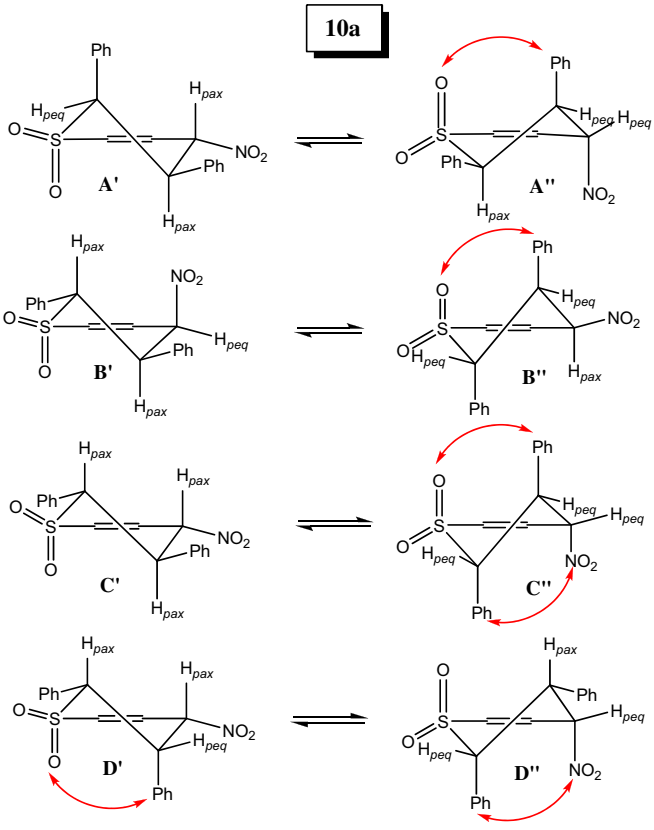


Fig. 3. Most stable, half-chair conformations for stereoisomers **A**–**D**.

Table 5
Optimization of stereostructures **A**, **B**, **C**, **D** when Ar=Ph (**10a**) according to PCModel (in the absence of solvent)[a]

10a	E[b] (kcal/mol)	μ (Debye)	Dihedral (degrees)						
			C(4a)–C(8a)–S(1)–C(2)	C(8a)–C(4a)–C(4)–C(3)	H(2)–C(2)–C(3)–H(3)	H(3)–C(3)–C(4)–H(4)	2-Ph rot[c]	3-Ph rot[d]	NO_2 rot[e]
A′	43.4	2.9	8.1	20.0	57.5	179.5	45.8	47.5	62.7
B′	41.7	4.5	7.0	22.4	173.2	53.1	80.2	87.9	53.3
C′	41.4	2.6	5.2	24.1	173.4	177.8	77.1	66.0	63.7
D′	46.6	2.8	9.1	18.8	59.7	51.2	55.1	48.3	48.3

[a] MMX3 program.
[b] Steric energy.
[c] S(1)–C(2)–C(1′)–C(2′).
[d] C(4)–C(3)–C(1″)–C(2″).
[e] C(4a)–C(4)–N–O.

As a matter of fact, as far as thiochromans **10** are concerned, while the sulfur atom and C(4) are coplanar with the condensed benzene moiety, C(2) and C(3) can be either on opposite sides with respect to the plane (generating two non-equivalent half chairs) or on the same

In particular **A′**, **B′** and **C′** result to be the most stable because all of the others (**D′**, **A″**, **B″**, **C″**, **D″**) exhibit unfavourable 1,3-pseudodiaxial interactions between substituents (as indicated in Fig. 3); it is actually well-known that the stability of six-membered

rings is ruled by 1,3-diaxial interactions, which usually destabilize conformations with axial substituents with respect to those with the same substituents in an equatorial position.

In Table 5 we report details of this study relevant to the optimized structures. It should be underlined that isomer **D** shows the highest value of steric energy, in agreement with its absence in the crude product. As far as dihedral angles are concerned, the four lower-energy conformations do present different values for H(2)–C(2)–C(3)–H(3) and H(3)–C(3)–C(4)–H(4), but in any case the calculated values are not far away from the standard values of 180° and 60° expected for *trans*-diaxial and *cis* geometries, respectively.

The results obtained from the molecular-mechanics calculations allowed the interpretation of ^{1}H NMR spectra, on the basis of the Karplus–Conroy rule:[17,18] *quasi-trans* 1,2-pseudodiaxial interactions need large vicinal J_{H-H} coupling constants (10–15 Hz) while 1,2-pseudoaxial-pseudoequatorial interactions need small ones (2–5 Hz). Thus, the non-aromatic signals of **A**, **B** and **C** in the ^{1}H NMR spectra of the crude products could be assigned without uncertainty.

It is convenient to start our analysis from stereostructures **C**, as they exhibit two large (9.0–11.7 Hz) vicinal coupling constants, unequivocally showing that the main conformation exhibits three pseudoaxial protons and therefore all of the three substituents are pseudoequatorial. In this kind of stereostructure, the observed chemical shift difference between 4-H and 2-H is always 1.44–1.56 ppm, in excellent agreement with the observed difference between CH_3NO_2 (δ_H=4.3 ppm) and CH_3SO_2R (δ_H=2.8 ppm).

Either **A** or **B** exhibit both a large and a small vicinal coupling constant. Therefore 3-H has to be pseudo-axial again, while either 2-H or 4-H are pseudo-equatorial in turn. We can observe that **A** and **C** exhibit similar chemical shifts values, while in **B** some perturbing effect strongly deshields 2-H, very likely as a consequence of the effect of a pseudo-axial 4-nitro group on a pseudo-axial 2-H.

Accordingly, in most *trans*-4-nitro-3-arylthiochroman *S*,*S*-dioxides **6** [see Ref. 3, Table 3], 2-H_{pax} and 2-H_{peq} exhibited very similar chemical shifts as the nitro group was pseudo-equatorial, while in the *cis* forms, where the nitro group was pseudo-axial, 2-H_{pax} exhibited a further deshielding of 1 ppm.

On the basis of such considerations, the stereostructures **A**–**C** were assigned to the obtained compounds, as reported in Fig. 1.

3. Conclusions

The intramolecular base-induced Michael addition discussed in the present report represents a convenient approach to the substituted thiochroman *S*,*S*-dioxides **10**, obtained in high yields generally as mixtures of diastereomers.

The renewed interest for the thiochroman ring-system, especially when densely functionalized, is testified by a number of publications in the recent literature[19–25] and is strictly connected to a noteworthy biological and pharmacological activity.[26–31]

On these grounds, the concurrence of different well-acknowledged pharmacophores makes compounds **10** appealing for pharmacological tests: it is surely worth mentioning that, in particular, a promising activity as calcium-channel modulators is emerging from preliminary tests.[32] Thus, the stereochemical aspects displayed by the cyclization process herein seem particularly rewarding: as a matter of facts, while one (namely, **D**) out of the four expected racemic pairs is never observed, as far as **A**, **B**, and **C** are concerned, a remarkable diastereoselectivity, adjustable in dependence of the experimental conditions, allows the obtainment on one side of mixtures highly enriched in **A** (reactions carried out at low temperature and/or avoiding excess of base), from which **A** (as a racemic mixture) can be easily isolated in a pure form by crystallization, or, on the other side, of mixtures of **B** and **C** (reactions carried out at room temperature, in the presence of excess base and/or prolonging the time of permanence in the basic medium prior to acidic quenching), whose molar ratio can be in turn modulated thanks to equilibration in acidic medium.

It should be finally mentioned that the introduction on the thiochroman ring-system of an additional substituent at C(2), besides to the impact on the stereochemical aspects of the cyclization process represents, with respect to the C(2)-unsubstituted analogues **6** of Scheme 1, a means for further diversification, with possible effects also on the hydrophilic/hydrophobic character of the molecule and hence, e.g., on its polar/non polar interactions with biological sites.

4. Experimental section

4.1. General

^{1}H NMR and ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz, respectively, chemical shifts (TMS as internal reference) are reported as δ values (ppm). IR spectra were recorded on a Perkin–Elmer 881 Infrared Spectrophotometer. MS(ESI) analyses were recorded on a Micromass ZMD Waters instrument (30 V, 3.2 kV, isotopes observed ^{35}Cl and ^{79}Br). HRMS were recorded on a THERMO FINNIGAN MAT95XP apparatus (isotopes observed ^{35}Cl and ^{79}Br). Melting points were determined with a Büchi 535 apparatus. Petroleum ether and light petroleum refer to the fractions with bp 40–60 °C and 80–100 °C, respectively. Silica gel 230–400 mesh was used for column chromatography, all solvents being distilled before use. Tetrahydrofuran (THF) was purified by standard methods and distilled over potassium benzophenone ketyl before use. Pyrrolidine was dried and distilled over potassium hydroxide before use. Lithium bis(trimethylsilyl)amide (LHMDS, 1 M in THF) and all of the other commercially available reagents were used as received.

Organometallic reagents. All the reagents were THF or Et_2O solutions titrated just before use. Phenyl-, 4-methoxyphenyl-, 4-methylphenyl-, 1-naphthyl-magnesium bromides, 2-methylphenyl-, 3-methylphenyl-magnesium chlorides, 3-thienylmagnesium iodide were commercial solutions in THF; 4-chlorophenylmagnesium bromide and 2-thienyllithium were commercial solutions in Et_2O. 4-Bromophenylmagnesium bromide was prepared from the corresponding commercial 1,4-dibromobenzene using standard procedures.

4.2. Ring-opening of 3-nitrobenzo[*b*]thiophene

The ring-opening reaction was performed on 2 g of substrate, according to conditions previously reported;[33] the alkylation of the obtained silver thiolate was realized with an excess of benzyl chloride.

*4.2.1. (E)-1-[2-(2-Benzylsulfanylphenyl)-2-nitrovinyl]pyrrolidine (**7**).* Yield (2.3 g, 62%). Yellow solid, mp 124–125 °C (toluene); ν_{max} (Nujol) 1610, 1345, 1258, 1140, 1070, 1019 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.75 (4H, m), 2.52 (2H, m), 3.60 (2H, m), 4.06 (1H, d, *J* 12.8 Hz), 4.15 (1H, d, *J* 12.8 Hz), 7.11–7.36 (9H, m), 8.63 (1H, s); ^{13}C NMR ($CDCl_3$) δ 24.2, 25.9, 37.3, 48.0, 55.1, 122.5, 125.0, 127.0, 127.2, 128.4, 128.9, 129.5, 131.3, 133.4, 136.9, 140.3, 145.7. MS(ESI): *m*/*z* 363 [M+Na]$^+$, 379 [M+K]$^+$. MS(EI) *m*/*z* 340 (M$^+$, 4), 294 (100), 223 (56), 203 (37), 134 (46), 91 (55), 84 (51). HRMS calcd for $C_{19}H_{20}N_2O_2S$, 340.1246; found 340.1245.

4.3. Reactions of 7 with aromatic organometallic reagents

The reactions were performed on 1 g of compound **7** (2.94 mmol) following the procedure previously reported for the

related methylthio derivatives.[4] Yields of compounds **8a–j** are collected in Table 1.

*4.3.1. (E)-1-[2-(Benzylsulfanyl)phenyl]-1-nitro-2-phenylethene (**8a**).* Yield (0.99 g, 97%). Yellow solid, mp 75–76 °C (light petroleum); ν_{max} (Nujol) 1646, 1584, 1512, 1493, 1322, 1294, 1211, 1161, 1073, 1031 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.02 (1H, d, *J* 12.9 Hz), 4.07 (1H, d, *J* 12.9 Hz), 7.03 (2H, d, *J* 7.5 Hz), 7.18–7.34 (10H, m), 7.41–7.43 (2H, m), 8.28 (1H, s); ^{13}C NMR (CD_3COCD_3) δ 38.2, 127.7, 128.1, 129.3, 129.7, 129.8, 130.6, 131.6, 131.8, 131.9, 132.2, 132.4, 132.4, 136.4, 137.8, 139.1, 149.4. MS(ESI): *m/z* 370 $[M+Na]^+$, 386 $[M+K]^+$. MS(EI) *m/z* 347 (M^+, 9), 301 (9), 210 (84), 165 (12), 91 (100). HRMS calcd for $C_{21}H_{17}NO_2S$, 347.0980; found 347.0980.

*4.3.2. (E)-1-[2-(Benzylsulfanyl)phenyl]-1-nitro-2-(o-tolyl)ethene (**8b**).* Yield (1.05 g, 99%). Yellow solid, mp 72–73 °C (light petroleum); ν_{max} (Nujol) 1643, 1599, 1581, 1523, 1326, 1240, 1227, 1158, 1069, 1028 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.46 (3H, s), 4.05 (2H, app d, *J* 2.9 Hz), 6.61 (1H, d, *J* 7.8 Hz), 6.82 (1H, td, *J* 7.8, 2.1 Hz), 7.10–7.24 (9H, m), 7.31–7.38 (2H, m), 8.48 (1H, s); ^{13}C NMR (CD_3COCD_3) δ 20.1, 38.2, 126.6, 127.2, 128.1, 129.3, 129.8, 129.9, 130.2, 131.1, 131.2, 131.3, 131.4, 132.1, 132.8, 134.7, 137.8, 139.2, 139.9, 150.4. MS(ESI): *m/z* 384 $[M+Na]^+$, 400 $[M+K]^+$. MS(EI) *m/z* 361 (M^+, 10), 315 (8), 224 (80), 91 (100). HRMS calcd for $C_{22}H_{19}NO_2S$, 361.1137; found 361.1135.

*4.3.3. (E)-1-[2-(Benzylsulfanyl)phenyl]-1-nitro-2-(m-tolyl)ethene (**8c**).* Yield (0.99 g, 93%). Yellow oil, ν_{max} (Neat) 3057, 3027, 2920, 1950, 1701, 1647, 1602, 1583, 1512, 1494, 1453, 1435, 1366, 1327, 1247, 1179, 1129, 1096, 1069, 1043, 1030, 1000 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.19 (3H, s), 4.00 (1H, d, *J* 12.9 Hz), 4.05 (1H, d, *J* 12.6 Hz), 6.78 (1H, d, *J* 7.5 Hz), 6.88 (1H, s), 7.07 (1H, t, *J* 7.5 Hz), 7.13 (1H, d, *J* 7.8 Hz), 7.18–7.31 (7H, m), 7.41 (2H, app d, *J* 3.7 Hz), 8.25 (1H, s); ^{13}C NMR ($CDCl_3$) δ 21.3, 38.6, 127.2, 127.3, 128.0, 128.5, 128.7, 128.9, 130.6, 130.6, 130.6, 131.0, 131.4, 131.8, 132.1, 136.2, 136.6, 137.9, 138.4, 148.1. MS(ESI): *m/z* 384 $[M+Na]^+$, 400 $[M+K]^+$. MS(EI) *m/z* 361 (M^+, 2), 312 (12), 224 (22), 119 (21), 91 (100). HRMS calcd for $C_{22}H_{19}NO_2S$, 361.1137; found 361.1134.

*4.3.4. (E)-1-[2-(Benzylsulfanyl)phenyl]-1-nitro-2-(p-tolyl)ethene (**8d**).* Yield (1.02 g, 96%). Yellow solid, mp 121–122 °C (light petroleum). ν_{max} (Nujol) 1639, 1608, 1502, 1367, 1323, 1186, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.31 (3H, s), 4.02 (1H, d, *J* 12.9 Hz), 4.07 (1H, d, *J* 12.9 Hz), 6.93 (2H, d, *J* 8.4 Hz), 7.02 (2H, d, *J* 8.1 Hz), 7.19–7.33 (7H, m), 7.41–7.43 (2H, m), 8.28 (1H, s); ^{13}C NMR ($CDCl_3$) δ 21.5, 38.5, 127.2, 127.3, 128.2, 128.5, 128.9, 129.6, 130.5, 130.6, 131.1, 131.4, 132.1, 136.2, 136.6, 138.0, 141.8, 147.4. MS(ESI): *m/z* 384 $[M+Na]^+$, 400 $[M+K]^+$. MS(EI) *m/z* 361 (M^+, 8), 315 (9), 224 (100), 91 (85). HRMS calcd for $C_{22}H_{19}NO_2S$, 361.1137; found 361.1136.

*4.3.5. (E)-1-[2-(Benzylsulfanyl)phenyl]-2-(p-methoxyphenyl)-1-nitroethene (**8e**).* Yield (1.10 g, 99%). Yellow solid, mp 107–108 °C (light petroleum); ν_{max} (Nujol) 1633, 1599, 1302, 1258, 1171, 1071, 1029 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.77 (3H, s), 4.01 (1H, d, *J* 13.1 Hz), 4.07 (1H, d, *J* 13.1 Hz), 6.72 (2H, d, *J* 9.0 Hz), 6.97 (2H, d, *J* 9.0 Hz), 7.18–7.31 (7H, m), 7.41–7.43 (2H, m), 8.28 (1H, s); ^{13}C NMR ($CDCl_3$) δ 38.3, 55.3, 114.4, 123.5, 127.1, 127.3, 128.5, 128.9, 130.3, 130.5, 131.4, 132.1, 133.1, 136.0, 136.6, 138.1, 145.9, 161.9. MS(ESI): *m/z* 400 $[M+Na]^+$, 416 $[M+K]^+$. MS(EI) *m/z* 377 (M^+, 5), 330 (14), 240 (100), 225 (25), 197 (24), 91 (81). HRMS calcd for $C_{22}H_{19}NO_3S$, 377.1086; found 377.1083.

*4.3.6. (E)-1-[2-(Benzylsulfanyl)phenyl]-2-(4-chlorophenyl)-1-nitroethene (**8f**).* Yield (1.11 g, 99%). Yellow solid, mp 125–126 °C (light petroleum); ν_{max} (Nujol) 1642, 1590, 1512, 1405, 1325, 1302, 1210, 1181, 1092, 1068, 1013 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.03 (1H, d, *J* 12.9 Hz), 4.09 (1H, d, *J* 13.2 Hz), 6.93 (2H, d, *J* 8.4 Hz), 7.15–7.31 (9H, m), 7.44 (2H, app d, *J* 3.7 Hz), 8.22 (1H, s); ^{13}C NMR (CD_3COCD_3) δ 38.1, 127.7, 128.1, 129.3, 129.8, 129.8, 130.5, 131.0, 131.7, 131.9, 132.4, 133.3, 135.1, 137.2, 137.8, 139.0, 149.8. MS(ESI): *m/z* 404 $[M+Na]^+$, 420 $[M+K]^+$. MS(EI) *m/z* 381 (M^+, 5), 244 (34), 91 (100). HRMS calcd for $C_{21}H_{16}ClNO_2S$, 381.0590; found 381.0590.

*4.3.7. (E)-1-[2-(Benzylsulfanyl)phenyl]-2-(4-bromophenyl)-1-nitroethene (**8g**).* Yield (0.96 g, 77%). Yellow solid, mp 123–124 °C (toluene/light petroleum); ν_{max} (Nujol) 1643, 1582, 1514, 1403, 1322, 1184, 1069, 1010 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.03 (1H, d, *J* 12.9 Hz), 4.09 (1H, d, *J* 12.9 Hz), 6.85 (2H, d, *J* 8.4 Hz), 7.16–7.19 (1H, m), 7.20–7.30 (6H, m), 7.32 (2H, d, *J* 8.4 Hz), 7.42–7.44 (2H, m), 8.20 (1H, s); ^{13}C NMR ($CDCl_3$) δ 38.3, 125.6, 127.1, 127.4, 128.5, 128.9, 129.9, 130.1, 130.8, 131.1, 131.2, 132.1, 132.2, 134.7, 136.4, 138.1, 148.6; MS(ESI): *m/z* 448 $[M+Na]^+$, 464 $[M+K]^+$. MS(EI) *m/z* 425 (M^+, 3), 290 (19), 208 (7), 165 (10), 91 (100). HRMS calcd for $C_{21}H_{16}BrNO_2S$, 425.0085; found 425.0083.

*4.3.8. (E)-1-[2-(Benzylsulfanyl)phenyl]-2-(1-naphthyl)-1-nitroethene (**8h**).* Yield (1.04 g, 89%). Yellow solid, mp 141–142 °C (toluene/light petroleum); ν_{max} (Nujol) 1646, 1581, 1504, 1317, 1246, 1067 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.06 (2H, s), 6.90 (1H, d, *J* 7.2 Hz), 7.07–7.15 (3H, m), 7.21–7.27 (5H, m), 7.33 (1H, app t, *J* 6.7 Hz), 7.39 (1H, d, *J* 7.5 Hz), 7.56 (1H, app t, *J* 6.9 Hz), 7.63 (1H, app t, *J* 7.0 Hz), 7.79 (1H, d, *J* 8.4 Hz), 7.86 (1H, d, *J* 7.5 Hz), 8.14 (1H, d, *J* 8.1 Hz), 8.98 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 36.1, 123.9, 125.0, 126.0, 126.5, 127.1, 127.3, 127.6, 128.1, 128.3, 128.4, 128.6, 128.7, 130.0, 130.3, 130.5, 131.2, 131.7, 132.8, 133.8, 136.7, 137.7, 150.1. MS(ESI): *m/z* 420 $[M+Na]^+$, 436 $[M+K]^+$. MS(EI) *m/z* 397 (M^+, 10), 351 (10), 260 (89), 91 (100). HRMS calcd for $C_{25}H_{19}NO_2S$, 397.1137; found 397.1133.

*4.3.9. (E)-1-[2-(Benzylsulfanyl)phenyl]-1-nitro-2-(2-thienyl)ethene (**8i**).* Yield (1.00 g, 96%). Yellow solid, mp 123–124 °C (light petroleum); ν_{max} (Nujol) 1627, 1580, 1514, 1501, 1331, 1311, 1288, 1246, 1157, 1068, 1052 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.02 (1H, d, *J* 13.2 Hz), 4.06 (1H, d, *J* 13.5 Hz), 7.03 (1H, dd, *J* 5.4, 3.9 Hz), 7.18–7.25 (5H, m), 7.28–7.40 (4H, m), 7.43–7.51 (2H, m), 8.53 (1H, s); ^{13}C NMR ($CDCl_3$) δ 38.6, 127.3, 127.5, 127.6, 128.5, 129.0, 130.1, 130.8, 130.8, 131.2, 131.9, 133.5, 135.0, 136.2, 136.6, 138.7, 145.3. MS(ESI): *m/z* 376 $[M+Na]^+$, 392 $[M+K]^+$. MS(EI) *m/z* 353 (M^+, 3), 306 (21), 216 (53), 91 (100). HRMS calcd for $C_{19}H_{15}NO_2S_2$, 353.0544; found 353.0546.

*4.3.10. (E)-1-[2-(Benzylsulfanyl)phenyl]-1-nitro-2-(3-thienyl)ethene (**8j**).* Yield (1.03 g, 99%). Yellow solid, mp 105–106 °C (light petroleum); ν_{max} (Nujol) 1633, 1581, 1313, 1248, 1174, 1067 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.00 (1H, d, *J* 13.2 Hz), 4.05 (1H, d, *J* 13.2 Hz), 6.41 (1H, dd, *J* 5.1, 1.2 Hz), 7.12 (1H, dd, *J* 5.1, 3.0 Hz), 7.17–7.35 (8H, m), 7.43 (2H, app d, *J* 3.4 Hz), 8.32 (1H, s); ^{13}C NMR ($CDCl_3$) δ 38.5, 126.7, 127.1, 127.3, 127.7, 128.4, 128.9, 129.9, 130.5, 130.7, 131.4, 131.9, 132.5, 133.1, 136.5, 138.0, 146.8. MS(ESI): *m/z* 376 $[M+Na]^+$, 392 $[M+K]^+$. MS(EI) *m/z* 353 (M^+, 6), 307 (11), 216 (65), 91 (100). HRMS calcd for $C_{19}H_{15}NO_2S_2$, 353.0544; found 353.0547.

4.4. Oxidation of sulfides 8a–j to sulfones 9a–j

Reactions were performed on 2 mmol of the appropriate **8**, according to the conditions described in Ref. 3. Yields are reported in Table 1.

*4.4.1. (E)-1-[2-(Benzylsulfonyl)phenyl]-1-nitro-2-phenylethene (**9a**).* Yield (750 mg, 99%). Yellow solid, mp 139–140 °C (ethanol); ν_{max} (Nujol) 1642, 1514, 1310, 1203, 1155, 1116, 1068 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.21 (1H, d, *J* 13.5 Hz), 4.34 (1H, d, *J* 13.5 Hz), 7.03 (2H, d, *J* 7.5 Hz), 7.19–7.37 (9H, m), 7.45–7.52 (2H, m), 7.62–7.67 (1H, m),

8.39 (1H, s); ^{13}C NMR (CD_3COCD_3) δ 61.8, 128.7, 129.2, 129.5, 129.9, 131.5, 131.8, 131.9, 131.9, 132.0, 132.1, 132.7, 134.9, 135.5, 135.8, 139.5, 148.3. MS(ESI): *m/z* 402 $[M+Na]^+$, 418 $[M+K]^+$. MS(EI) *m/z* 333 (M−46, 20), 178 (11), 91 (100). Anal. Calcd for $C_{21}H_{17}NO_4S$ (MW 379.43): C, 66.5; H, 4.5; N, 3.7%. Found: C, 66.4; H, 4.6; N, 3.6%.

*4.4.2. (E)-1-[2-(Benzylsulfonyl)phenyl]-1-nitro-2-(o-tolyl)ethene (**9b**).* Yield (723 mg, 92%). Yellow solid, mp 171–172 °C (ethanol); ν_{max} (Nujol) 1599, 1309, 1201, 1152, 1115, 1067 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.50 (3H, s), 4.24 (1H, d, *J* 13.5 Hz), 4.38 (1H, d, *J* 13.8 Hz), 6.69 (1H, d, *J* 8.1 Hz), 6.87 (1H, td, *J* 8.1, 2.1 Hz), 7.14–7.23 (4H, m), 7.27–7.41 (6H, m), 7.49–7.57 (1H, m), 8.58 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 20.3, 60.9, 126.6, 128.3, 129.1, 129.4, 129.5, 130.1, 130.7, 131.1, 131.4, 131.6, 131.7, 131.8, 134.1, 135.0, 135.2, 138.7, 139.8, 148.7. MS(ESI): *m/z* 416 $[M+Na]^+$, 432 $[M+K]^+$. MS(EI) *m/z* 347 (M−46, 30), 191 (11), 91 (100). Anal. Calcd for $C_{22}H_{19}NO_4S$ (MW 393.46): C, 67.2; H, 4.9; N, 3.6%. Found: C, 67.1; H, 4.7; N, 3.6%.

*4.4.3. (E)-1-[2-(Benzylsulfonyl)phenyl]-1-nitro-2-(m-tolyl)ethene (**9c**).* Yield (762 mg, 97%). Yellow solid, mp 148–149 °C (ethanol); ν_{max} (Nujol) 1644, 1565, 1516, 1327, 1311, 1249, 1202, 1151, 1130, 1116, 1068 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.21 (3H, s), 4.19 (1H, d, *J* 13.5 Hz), 4.33 (1H, d, *J* 13.2 Hz), 6.76 (1H, d, *J* 7.5 Hz), 6.90 (1H, s), 7.09 (1H, t, *J* 7.5 Hz), 7.14 (1H, d, *J* 7.8 Hz), 7.19 (2H, app d, *J* 7.8 Hz), 7.27–7.39 (4H, m), 7.48–7.51 (2H, m), 7.63–7.69 (1H, m), 8.34 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 20.7, 60.2, 127.3, 127.8, 128.3, 128.6, 128.8, 129.8, 130.4, 130.9, 131.1, 131.2, 131.8, 131.8, 134.0, 134.7, 135.1, 137.7, 138.2, 146.4. MS(ESI): *m/z* 416 $[M+Na]^+$, 432 $[M+K]^+$. MS(EI) *m/z* 347 (M−46, 16), 91 (100), 69 (11). Anal. Calcd for $C_{22}H_{19}NO_4S$ (MW 393.46): C, 67.2; H, 4.9; N, 3.6%. Found: C, 67.0; H, 5.0; N, 3.7%.

*4.4.4. (E)-1-[2-(Benzylsulfonyl)phenyl]-1-nitro-2-(p-tolyl)ethene (**9d**).* Yield (778 mg, 99%). Yellow solid, mp 143–144 °C (ethanol); ν_{max} (Nujol) 1647, 1603, 1515, 1319, 1307, 1214, 1184, 1160, 1117 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.28 (3H, s), 4.19 (1H, d, *J* 13.6 Hz), 4.34 (1H, d, *J* 13.8 Hz), 6.91 (2H, d, *J* 8.4 Hz), 7.03 (2H, d, *J* 8.0 Hz), 7.18–7.39 (6H, m), 7.44–7.54 (2H, m), 7.61–7.69 (1H, m), 8.37 (1H, s); ^{13}C NMR ($CDCl_3$) δ 21.5, 61.6, 127.7, 127.9, 128.6, 128.9, 129.8, 130.3, 131.1, 131.2, 131.4, 132.5, 133.5, 134.5, 136.3, 137.9, 142.1, 146.1. MS(ESI): *m/z* 416 $[M+Na]^+$, 432 $[M+K]^+$. MS(EI) *m/z* 347 (M−46, 24), 192 (11), 91 (100). Anal. Calcd for $C_{22}H_{19}NO_4S$ (MW 393.46): C, 67.2; H, 4.9; N, 3.6%. Found: C, 67.2; H, 4.8; N, 3.5%.

*4.4.5. (E)-1-[2-(Benzylsulfonyl)phenyl]-2-(p-methoxyphenyl)-1-nitroethene (**9e**).* Yield (810 mg, 99%). Yellow solid, mp 129–130 °C (ethanol); ν_{max} (Nujol) 1649, 1595, 1505, 1318, 1303, 1254, 1212, 1198, 1172, 1157, 1115, 1026 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.76 (3H, s), 4.22 (1H, d, *J* 13.5 Hz), 4.35 (1H, d, *J* 13.5 Hz), 6.75 (2H, d, *J* 8.7 Hz), 6.96 (2H, d, *J* 9.3 Hz), 7.20–7.40 (6H, m), 7.46–7.55 (2H, m), 7.64–7.70 (1H, m), 8.38 (1H, s); ^{13}C NMR ($CDCl_3$) δ 55.4, 61.6, 114.6, 123.2, 127.8, 128.6, 128.9, 130.2, 131.3, 131.3, 132.6, 133.4, 133.5, 134.6, 136.4, 138.0, 144.7, 162.1. MS(ESI): *m/z* 432 $[M+Na]^+$, 448 $[M+K]^+$. MS(EI) *m/z* 409 (M^+, 1), 363 (31), 136 (10), 91 (100). HRMS calcd for $C_{22}H_{19}NO_5S$, 409.0984; found 409.0982.

*4.4.6. (E)-1-[2-(Benzylsulfonyl)phenyl]-2-(4-chlorophenyl)-1-nitroethene (**9f**).* Yield (802 mg, 97%). Yellow solid, mp 191–192 °C (ethanol/dioxane); ν_{max} (Nujol) 1651, 1584, 1567, 1524, 1409, 1319, 1302, 1250, 1211, 1197, 1161, 1116, 1091, 1008 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.26 (1H, d, *J* 13.5 Hz), 4.37 (1H, d, *J* 13.8 Hz), 6.94 (2H, d, *J* 8.7 Hz), 7.19 (2H, d, *J* 9.0 Hz), 7.22–7.24 (2H, m), 7.28–7.39 (4H, m), 7.45–7.51 (2H, m), 7.60–7.68 (1H, m), 8.33 (1H, s); ^{13}C NMR ($CDCl_3$) δ 61.7, 127.6, 128.7, 129.0, 129.3, 129.3, 130.4, 130.6, 131.3, 132.3, 132.6, 133.2, 134.6, 134.8, 137.3, 138.0, 147.5. MS(ESI): *m/z* 436 $[M+Na]^+$, 452 $[M+K]^+$. MS(EI) *m/z* 367 (M−46, 30), 349 (23), 212 (20), 176 (22), 165 (16), 91 (100). Anal. Calcd for $C_{21}H_{16}ClNO_4S$ (MW 413.87): C, 60.9; H, 3.9; N, 3.4%. Found: C, 60.7; H, 3.9; N, 3.5%.

*4.4.7. (E)-1-[2-(Benzylsulfonyl)phenyl]-2-(4-bromophenyl)-1-nitroethene (**9g**).* Yield (910 mg, 99%). Yellow solid, mp 185–186 °C (ethanol/dioxane). ν_{max} (Nujol) 1657, 1579, 1522, 1319, 1159, 1116, 1073, 1004 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.27 (1H, d, *J* 13.8 Hz), 4.37 (1H, d, *J* 13.8 Hz), 6.86 (2H, d, *J* 8.7 Hz), 7.21–7.25 (2H, m), 7.28–7.38 (6H, m), 7.47–7.50 (2H, m), 7.60–7.68 (1H, m), 8.31 (1H, s); ^{13}C NMR ($CDCl_3$) δ 61.7, 125.9, 127.6, 128.7, 129.0, 129.7, 130.4, 130.6, 131.3, 132.3, 132.4, 132.6, 133.2, 134.6, 134.9, 138.0, 147.6; MS(ESI): *m/z* 480 $[M+Na]^+$, 496 $[M+K]^+$. MS(EI) *m/z* 413 (M−46, 10), 176 (10), 91 (100). Anal. Calcd for $C_{21}H_{16}BrNO_4S$ (MW 457.90): C, 55.0; H, 3.5; N, 3.1%. Found: C, 55.1; H, 3.4; N, 3.2%.

*4.4.8. (E)-1-[2-(Benzylsulfonyl)phenyl]-2-(1-naphthyl)-1-nitroethene (**9h**).* Yield (849 mg, 99%). Yellow solid, mp 197–198 °C (ethanol/dioxane); ν_{max} (Nujol) 1658, 1525, 1321, 1247, 1196, 1162, 1154, 1118 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.26 (1H, d, *J* 13.8 Hz), 4.39 (1H, d, *J* 13.8 Hz), 7.06 (1H, d, *J* 7.2 Hz), 7.14–7.21 (4H, m), 7.26–7.43 (6H, m), 7.56 (1H, app t, *J* 6.7 Hz), 7.64 (1H, app t, *J* 7.0 Hz), 7.77 (1H, d, *J* 8.1 Hz), 7.84 (1H, d, *J* 8.1 Hz), 8.14 (1H, d, *J* 8.4 Hz), 9.04 (1H, s); ^{13}C NMR ($CDCl_3$) δ 61.6, 123.7, 125.3, 126.7, 127.5, 127.7, 128.2, 128.6, 128.9, 128.9, 129.0, 130.0, 130.6, 130.8, 131.3, 131.9, 132.2, 133.3, 133.6, 133.8, 134.0, 138.2, 149.7. MS(ESI): *m/z* 452 $[M+Na]^+$, 468 $[M+K]^+$. MS(EI) *m/z* 429 (M^+, 2), 383 (13), 228 (11), 91 (100). HRMS calcd for $C_{25}H_{19}NO_4S$, 429.1035; found 429.1035.

*4.4.9. (E)-1-[2-(Benzylsulfonyl)phenyl]-1-nitro-2-(2-thienyl)ethene (**9i**).* Yield (747 mg, 97%). Yellow/orange solid, mp 178–179 °C (ethanol/dioxane); ν_{max} (Nujol) 1631, 1501, 1339, 1312, 1245, 1159, 1150, 1119, 1066 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.21 (1H, d, *J* 13.8 Hz), 4.32 (1H, d, *J* 13.8 Hz), 7.04 (1H, dd, *J* 5.1, 3.6 Hz), 7.20–7.22 (2H, m), 7.27–7.36 (4H, m), 7.41 (1H, d, *J* 4.8 Hz), 7.50 (1H, d, *J* 8.1 Hz), 7.55–7.58 (2H, m), 7.72–7.78 (1H, m), 8.61 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 60.5, 127.3, 128.2, 128.3, 128.6, 128.9, 130.0, 131.0, 131.6, 131.7, 134.1, 134.5, 135.2, 135.3, 138.1, 138.5, 143.2. MS(ESI): *m/z* 408 $[M+Na]^+$, 424 $[M+K]^+$. MS(EI) *m/z* 339 (M−46, 72), 184 (36), 171 (10), 136 (11), 91 (100). Anal. Calcd for $C_{19}H_{15}NO_4S_2$ (MW 385.46): C, 59.2; H, 3.9; N, 3.6%. Found: C, 59.1; H, 3.9; N, 3.7%.

*4.4.10. (E)-1-[2-(Benzylsulfonyl)phenyl]-1-nitro-2-(3-thienyl)ethene (**9j**).* Yield (762 mg, 99%). Pale yellow solid, mp 127–128 °C (ethanol); ν_{max} (Nujol) 1649, 1518, 1332, 1309, 1252, 1199, 1152, 1131, 1118 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.20 (1H, d, *J* 13.8 Hz), 4.33 (1H, d, *J* 13.5 Hz), 6.34 (1H, dd, *J* 5.4, 1.2 Hz), 7.16 (1H, dd, *J* 5.1, 3.0 Hz), 7.19–7.22 (2H, m), 7.27–7.37 (4H, m), 7.43 (1H, d, *J* 7.2 Hz), 7.49–7.56 (2H, m), 7.68–7.74 (1H, m), 8.41 (1H, s); ^{13}C NMR ($CDCl_3$) δ 61.8, 127.2, 127.6, 127.7, 128.6, 128.9, 130.2, 130.5, 130.9, 131.2, 132.5, 132.8, 133.2, 133.5, 134.5, 137.9, 145.4. MS(ESI): *m/z* 408 $[M+Na]^+$, 424 $[M+K]^+$. MS(EI) *m/z* 339 (M−46, 76), 184 (46), 171 (16), 139 (15), 91 (100). Anal. Calcd for $C_{19}H_{15}NO_4S_2$ (MW 385.46): C, 59.2; H, 3.9; N, 3.6%. Found: C, 59.0; H, 3.7; N, 3.5%.

4.5. Reaction of sulfones 9a–j with LHMDS at room temperature or at −78 °C

Reactions at 22 °C were performed on 0.3 mmol of the appropriate **9**, at first according to the conditions described in Ref. 4. Yields are reported in Table 1. The crude solid residues showed at the ^{1}H NMR analysis three series of signals, due to the presence in different relative quantities of three pairs of diastereomers [indicated as **A** (*cis*,*trans*), **B** (*trans*,*cis*), **C** (*trans*,*trans*)]. In all cases, the spectroscopic data reported refer to the crude mixture; in some cases (**10a–d**, **h**) stereoisomer A was obtained in a pure form by crystallization from ethanol, and could be fully characterized; in

addition, for compound **10h**, a change in the crystallization solvent (ethanol/dioxane) allowed to obtain stereoisomer **B** as a pure solid, fully characterized by spectroscopic data.

When the reactions just described above were performed at −78 °C instead of 22 °C, the crude solid residues, obtained in yields (see Table 3) always comparable to those obtained at room temperature (see Table 1), were generally pure by ^{1}H NMR analysis and showed a change in the diastereomeric ratios of compounds **10**, the reactions being much more stereoselective. In all cases, crystallization of the crude residues from ethanol afforded diastereomerically pure **A**.

*4.5.1. 4-Nitro-2,3-diphenylthiochroman S,S-dioxide (**10a**).* Yield (94 mg, 83%, mixture of three racemic pairs). ^{1}H NMR ($CDCl_3$) δ 4.66 (1H **A**, d, *J* 3.9 Hz), 4.70 (1H **C**, d, *J* 11.7 Hz), 4.84 (1H **B**, dd, *J* 12.9, 4.8 Hz), 5.00 (1H **C**, dd, *J* 11.4, 9.3 Hz), 5.20 (1H **A**, dd, *J* 11.4, 3.6 Hz), 5.98 (1H **B**, d, *J* 12.9 Hz), 6.13 (1H **B**, d, *J* 4.8 Hz), 6.19 (1H **C**, d, *J* 9.3 Hz), 6.34 (1H **A**, d, *J* 12.0 Hz), 6.70–8.18 (14H of **A**, 14H of **B**, 14H of **C**). **A** could be isolated as a white solid after crystallizations from ethanol, mp 193–194 °C; ν_{max} (Nujol) 1603, 1550, 1306, 1215, 1151, 1124, 1071 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.65 (1H, d, *J* 3.9 Hz), 5.20 (1H, dd, *J* 11.1, 3.6 Hz), 6.34 (1H, d, *J* 12.0 Hz), 6.72 (2H, d, *J* 7.5 Hz), 6.90 (2H, d, *J* 7.2 Hz), 7.21–7.39 (6H, m), 7.56–7.59 (1H, m), 7.71–7.79 (2H, m), 8.16–8.19 (1H, m); ^{13}C NMR ($CDCl_3$) δ 47.6, 70.4, 86.9, 125.4, 127.2, 128.4, 128.7, 128.9, 128.9, 129.0, 129.5, 129.9, 131.6, 133.8, 134.1, 139.0 (two carbons are accidentally isochronous); MS: *m*/*z* 380.1 (M+H)$^+$. HRMS [M+H]$^+$ calcd for $C_{21}H_{18}NO_4S$, 380.0957; found 380.0911.

*4.5.2. 4-Nitro-2-phenyl-3-(o-tolyl)thiochroman S,S-dioxide (**10b**).* Yield (97 mg, 82%, mixture of three racemic pairs). ^{1}H NMR ($CDCl_3$) δ 2.54 (3H **A**, 3H **B**, 3H **C**, s), 4.49 (1H **A**, d, *J* 3.3 Hz), 4.56 (1H **C**, d, *J* 9.9 Hz), 5.04 (1H **B**, dd, *J* 12.6, 4.8 Hz), 5.32 (1H **C**, dd, *J* 10.8, 8.4 Hz), 5.56 (1H **A**, dd, *J* 12.0, 3.6 Hz), 5.96 (1H **B**, d, *J* 12.6 Hz), 6.04 (1H **B**, d, *J* 4.8 Hz), 6.15 (1H **C**, d, *J* 8.1 Hz), 6.34 (2H **A**, app d, *J* 11.1 Hz), 6.66–8.20 (12H of **A**, 13H of **B**, 13H of **C**). **A** could be isolated as a white solid by crystallization from ethanol, mp 206–207 °C; ν_{max} (Nujol) 1551, 1316, 1226, 1199, 1150, 1128, 1071 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.54 (3H, s), 4.49 (1H, d, *J* 3.3 Hz), 5.56 (1H, dd, *J* 12.0, 3.6 Hz), 6.34 (2H, app d, *J* 11.1 Hz), 6.67 (2H, d, *J* 7.2 Hz), 6.92 (1H, t, *J* 7.2 Hz), 7.15–7.25 (4H, m), 7.33–7.38 (1H, app t, *J* 7.4 Hz), 7.57 (1H, dd, *J* 6.6, 2.1 Hz), 7.71–7.80 (2H, m), 8.18–8.21 (1H, m); ^{13}C NMR (CD_3COCD_3) δ 19.4, 43.6, 69.0, 87.9, 125.7, 126.6, 128.0, 128.6, 129.3, 129.51, 129.9, 130.3, 130.4, 131.2, 132.1, 132.5, 133.6, 134.7, 137.8, 140.0; MS: *m*/*z* 394.1 (M+H)$^+$. HRMS [M+H]$^+$ calcd for $C_{22}H_{20}NO_4S$, 394.1113; found 394.1103.

*4.5.3. 4-Nitro-2-phenyl-3-(m-tolyl)thiochroman S,S-dioxide (**10c**).* Yield (104 mg, 88%, mixture of three racemic pairs). ^{1}H NMR ($CDCl_3$) δ 2.23 (3H **A**, s), 2.29 (3H **B** or **C**, s), 2.33 (3H **C** or **B**, s), 4.63 (1H **A**, d, *J* 3.6 Hz), 4.68 (1H **C**, d, *J* 11.1 Hz), 4.79 (1H **B**, dd, *J* 12.6, 4.5 Hz), 4.95 (1H **C**, dd, *J* 11.7, 9.6 Hz), 5.16 (1H **A**, dd, *J* 12.0, 3.6 Hz), 5.96 (1H **B**, d, *J* 12.6 Hz), 6.12 (1H **B**, d, *J* 4.8 Hz), 6.18 (1H **C**, d, *J* 9.0 Hz), 6.32 (1H **A**, d, *J* 12.0 Hz), 6.61–8.18 (13H of **A**, 13H of **B**, 13H of **C**). **A** could be isolated as a white solid by crystallization from ethanol, mp 174–175 °C; ν_{max} (Nujol) 1608, 1553, 1309, 1240, 1186, 1153, 1131, 1070 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.23 (3H, s), 4.63 (1H, d, *J* 3.9 Hz), 5.16 (1H, dd, *J* 11.7, 3.6 Hz), 6.31 (1H, d, *J* 11.7 Hz), 6.61–6.64 (1H, m), 6.70–6.72 (3H, m), 7.10 (2H, d, *J* 4.8 Hz), 7.21–7.26 (2H, m), 7.34–7.39 (1H, m), 7.55–7.58 (1H, m), 7.71–7.79 (2H, m), 8.16–8.19 (1H, m); ^{13}C NMR (CD_3COCD_3) δ 21.3, 48.7, 70.5, 88.0, 125.6, 126.3, 129.1, 129.4, 129.5, 129.9, 130.2, 130.3, 130.4, 130.5, 131.2, 132.5, 134.7, 135.7, 139.2, 139.8; MS: *m*/*z* 394.1 (M+H)$^+$. HRMS [M+H]$^+$ calcd for $C_{22}H_{20}NO_4S$, 394.1113; found 394.1075.

*4.5.4. 4-Nitro-2-phenyl-3-(p-tolyl)thiochroman S,S-dioxide (**10d**).* Yield (116 mg, 98%, mixture of three racemic pairs). ^{1}H NMR ($CDCl_3$) δ 2.15 (3H **B** or **C**, s), 2.19 (3H **C** or **B**, s), 2.28 (3H **A**, s), 4.64 (1H **A**, d, *J* 3.6 Hz), 4.73 (1H **C**, d, *J* 11.7 Hz), 4.80 (1H **B**, dd, *J* 12.6, 4.2 Hz), 4.94 (1H **C**, dd, *J* 11.4, 10.8 Hz), 5.15 (1H **A**, dd, *J* 11.7, 3.6 Hz), 5.95 (1H **B**, d, *J* 12.9 Hz), 6.10 (1H **B**, d, *J* 4.5 Hz), 6.17 (1H **C**, d, *J* 9.3 Hz), 6.31 (1H **A**, d, *J* 12.0 Hz), 6.71–8.15 (13 of **A**, 13H of **B**, 13H of **C**). **A** could be isolated as a white solid by crystallization from ethanol, mp 207–208 °C; ν_{max} (Nujol) 1551, 1314, 1230, 1191, 1149, 1127, 1069 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.30 (3H, s), 4.64 (1H, d, *J* 3.6 Hz), 5.15 (1H, dd, *J* 11.7, 3.9 Hz), 6.31 (1H, d, *J* 12.0 Hz), 6.73 (2H, d, *J* 7.8 Hz), 6.77 (2H, d, *J* 8.1 Hz), 7.03 (2H, d, *J* 7.8 Hz), 7.24 (2H, app t, *J* 7.2 Hz), 7.36 (1H, app t, *J* 7.5 Hz), 7.54–7.57 (1H, m), 7.70–7.78 (2H, m), 8.15–8.18 (1H, m); ^{13}C NMR (CD_3COCD_3) δ 21.0, 48.4, 70.5, 88.2, 125.6, 129.10, 129.4, 129.6, 129.9, 130.2, 130.3, 130.5, 131.3, 132.5, 132.8, 134.7, 139.3, 139.7; MS: *m*/*z* 394.1 (M+H)$^+$. HRMS [M+H]$^+$ calcd for $C_{22}H_{20}NO_4S$, 394.1113; found 394.1109.

*4.5.5. 3-(p-Methoxyphenyl)-4-nitro-2-phenylthiochroman S,S-dioxide (**10e**).* Yield (101 mg, 82%, mixture of three racemic pairs). ^{1}H NMR ($CDCl_3$) δ 3.70 (3H **B** or **C**, s), 3.71 (3H **C** or **B**, s), 3.77 (3H **A**, s), 4.63 (1H **A**, d, *J* 3.9 Hz), 4.66 (1H **C**, d, *J* 11.7 Hz), 4.78 (1H **B**, dd, *J* 12.6, 4.5 Hz), 4.93 (1H **C**, dd, *J* 11.7, 9.3 Hz), 5.13 (1H **A**, dd, *J* 11.7, 3.9 Hz), 5.93 (1H **B**, d, *J* 12.6 Hz), 6.10 (1H **B**, d, *J* 4.5 Hz), 6.16 (1H **C**, d, *J* 9.3 Hz), 6.27 (1H **A**, d, *J* 11.4 Hz), 6.70–8.19 (13H of **A**, 13H of **B**, 13H of **C**). Crystallization of the crude residue from ethanol brought to only a slight modification of the diastereomeric ratio; the crystallized material was a yellow solid, mp 120–150 °C. **A** as a pure product was obtained by reaction at low temperature. Pale yellow solid, mp 148–150 °C; ν_{max} (Nujol) 1610, 1553, 1512, 1309, 1255, 1180, 1153, 1128, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.76 (3H, s), 4.63 (1H, d, *J* 3.9 Hz), 5.13 (1H, dd, *J* 11.7, 3.9 Hz), 6.28 (1H, d, *J* 12.0 Hz), 6.73–6.81 (5H, m), 7.22–7.39 (4H, m), 7.53–7.56 (1H, m), 7.70–7.78 (2H, m), 8.14–8.18 (1H, m); ^{13}C NMR ($CDCl_3$) δ 46.9, 55.2, 70.4, 87.2, 114.2, 125.3, 125.9, 127.2, 128.7, 128.8, 129.0, 129.5, 129.6, 129.9, 131.5, 133.7, 138.8, 159.8. MS(ESI): *m*/*z* 432 [M+Na]$^+$, 408 [M−H]$^-$. HRMS calcd for $C_{22}H_{19}NO_5S$, 409.0984; found 409.0980.

*4.5.6. 3-(p-Chlorophenyl)-4-nitro-2-phenylthiochroman S,S-dioxide (**10f**).* Yield (111 mg, 90%, mixture of three racemic pairs). ^{1}H NMR ($CDCl_3$) δ 4.62 (1H **A**, d, *J* 3.6 Hz), 4.67 (1H **C**, d, *J* 11.7 Hz), 4.83 (1H **B**, dd, *J* 12.9, 4.5 Hz), 4.98 (1H **C**, dd, *J* 11.1, 9.9 Hz), 5.17 (1H **A**, dd, *J* 11.7, 3.9 Hz), 5.92 (1H **B**, d, *J* 12.9 Hz), 6.10 (1H **B**, d, *J* 4.5 Hz), 6.15 (1H **C**, d, *J* 9.6 Hz), 6.28 (1H **A**, d, *J* 11.4 Hz), 6.73–8.18 (13H of **A**, 13H of **B**, 13H of **C**). Crystallization of the crude residue from ethanol brought to only a slight modification of the diastereomeric ratio; the crystallized material was a white solid, mp 130–150 °C. **A** as a pure product was obtained by reaction at low temperature. White solid, mp 173–174 °C; ν_{max} (Nujol) 1552, 1310, 1153, 1127, 1092, 1014 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.62 (1H, d, *J* 3.6 Hz), 5.17 (1H, dd, *J* 11.7, 3.9 Hz), 6.28 (1H, d, *J* 11.4 Hz), 6.74 (2H, d, *J* 7.5 Hz), 6.83 (2H, d, *J* 8.4 Hz), 7.21–7.29 (4H, m), 7.38 (1H, app t, *J* 7.3 Hz), 7.55–7.57 (1H, m), 7.72–7.80 (2H, m) 8.15–8.18 (1H, m); ^{13}C NMR (CD_3SOCD_3) δ 46.6, 67.4, 86.1, 124.5, 128.5, 128.6, 128.8, 129.0, 129.1, 129.3, 130.3, 130.5, 131.8, 133.1, 133.8, 134.1, 137.1. MS(ESI): *m*/*z* 436 [M+Na]$^+$, 412 [M−H]$^-$. HRMS calcd for $C_{21}H_{16}ClNO_4S$, 413.0489; found 413.0479.

*4.5.7. 3-(p-Bromomophenyl)-4-nitro-2-phenylthiochroman S,S-dioxide (**10g**).* Yield (134 mg, 97%, mixture of three racemic pairs). ^{1}H NMR ($CDCl_3$) δ 4.62 (1H **A**, d, *J* 3.6 Hz), 4.70 (1H **C**, d, *J* 11.6 Hz), 4.82 (1H **B**, dd, *J* 12.8, 4.7 Hz), 4.96 (1H **C**, dd, *J* 11.5, 9.5 Hz), 5.15 (1H **A**, dd, *J* 11.4, 3.6 Hz), 5.91 (1H **B**, d, *J* 12.8 Hz), 6.11 (1H **B**, d, *J* 4.7 Hz), 6.15 (1H **C**, d, *J* 9.5 Hz), 6.27 (1H **A**, d, *J* 11.7 Hz), 6.72–8.16 (13H of **A**, 13H of **B**, 13H of **C**). **A** as a pure product was obtained by reaction at low temperature. White solid, mp 196–197 °C (ethanol); ν_{max} (Nujol) 1552, 1310, 1185, 1153, 1128, 1070, 1010 cm^{-1}; ^{1}H NMR: δ 4.62 (1H, d, *J* 3.6 Hz), 5.15 (1H, dd, *J* 11.4, 3.6 Hz), 6.27 (1H, d, *J* 11.7 Hz), 6.76 (4H, app t, *J* 8.7 Hz), 7.24–7.29 (2H, app t, *J* 7.9 Hz),

7.37–7.41 (3H, m), 7.55–7.58 (1H, m), 7.73–7.80 (2H, m), 8.15–8.18 (1H, m); ^{13}C NMR ($CDCl_3$) δ 47.1, 70.0, 86.8, 123.4, 125.4, 127.2, 128.3, 128.5, 129.2, 129.7, 129.9, 130.1, 131.7, 132.2, 133.0, 133.9, 138.8. MS(ESI): *m/z* 480 $[M+Na]^+$, 458 $[M-H]^-$. HRMS calcd for $C_{21}H_{16}BrNO_4S$, 456.9983; found 456.9980.

*4.5.8. 3-(1-Naphthyl)-4-nitro-2-phenylthiochroman S,S-dioxide (**10h**).* Yield (121 mg, 94%, mixture of three racemic pairs). ^{1}H NMR ($CDCl_3$) δ 4.78 (1H **C**, d, *J* 9.9 Hz), 4.80 (1H **A**, d, *J* 3.3 Hz), 5.74 (1H **B**, dd, *J* 12.6, 4.2 Hz), 6.06 (1H **C**, dd, *J* 10.5, 8.4 Hz), 6.14 (1H **B**, d, *J* 12.6 Hz), 6.23 (1H **A**, dd, *J* 12.0, 3.0 Hz), 6.27 (1H **B**, d, *J* 4.2 Hz), 6.29 (1H **C**, d, *J* 8.4 Hz) 6.47–6.51 (3H, 1**A**+ 2 Ar, m), 6.68–8.43 (14H of **A**, 16H of **B**, 16H of **C**). **A** could be isolated as a white solid after crystallizations from ethanol, mp 211–212 °C; ν_{max} (Nujol) 1552, 1310, 1232, 1153, 1129, 1069 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.80 (1H, d, *J* 3.0 Hz), 6.23 (1H, dd, *J* 12.3, 3.0 Hz), 6.47–6.51 (3H, 1**A**+2 Ar, m), 6.69 (1H, d, *J* 7.2 Hz), 7.12–7.33 (4H, m), 7.58–7.64 (2H, m), 7.72–7.83 (4H, m), 7.93 (1H, d, *J* 7.8 Hz), 8.25 (1H, dd, *J* 7.5, 1.8 Hz), 8.42 (1H, d, *J* 8.4 Hz); ^{13}C NMR ($CDCl_3$) δ 42.0, 68.8, 86.0, 121.9, 124.5, 124.7, 125.4, 126.5, 126.9, 128.0, 128.6, 128.8, 129.2, 129.3, 129.3, 129.5, 129.6, 130.6, 131.6, 133.8, 134.3, 139.2 (two carbons are accidentally isochronous). **B** was isolated by crystallization from ethanol/dioxane as a white solid, mp 242–243 °C; ^{1}H NMR ($CDCl_3$) δ 5.74 (1H, dd, *J* 12.3, 4.2 Hz), 6.14 (1H, d, *J* 12.3 Hz), 6.27 (1H, d, *J* 4.2 Hz), 6.96 (1H, d, *J* 7.2 Hz), 7.15–7.22 (4H, m), 7.34–7.36 (2H, m), 7.52 (1H, d, *J* 7.5 Hz), 7.60 (1H, d, *J* 7.2 Hz), 7.66–7.72 (3H, m), 7.77 (1H, app t, *J* 7.8 Hz), 7.91 (1H, d, *J* 7.8 Hz), 8.18 (1H, d, *J* 8.7 Hz), 8.24 (1H, d, *J* 7.8 Hz); ^{13}C NMR ($CDCl_3$) δ 39.9, 62.7, 89.1, 120.8, 125.3, 125.4, 126.2, 127.0, 127.3, 127.7, 128.6, 129.1, 129.2, 129.4, 129.4, 130.0, 130.7, 131.2, 132.1, 133.4, 134.0, 139.8 (two carbons are accidentally isochronous); MS: *m/z* 430.1 $(M+H)^+$. HRMS $[M+H]^+$ calcd for $C_{25}H_{20}NO_4S$, 430.1113; found 430.1072.

*4.5.9. 4-Nitro-2-phenyl-3-(2-thienyl)thiochroman S,S-dioxide (**10i**).* Yield (107 mg, 93%, mixture of three racemic pairs). ^{1}H NMR ($CDCl_3$) δ 4.64 (1H **C**, d, *J* 11.7 Hz), 4.74 (1H **A**, d, *J* 4.2 Hz), 5.09 (1H **B**, dd, *J* 12.6, 4.8 Hz), 5.38 (1H **C**, dd, *J* 11.7, 9.0 Hz), 5.53 (1H **A**, dd, *J* 11.1, 4.2 Hz), 5.96 (1H **B**, d, *J* 12.6 Hz), 6.18–6.21 (1H **B**+ 1H **C**, m), 6.25 (1H **A**, d, *J* 11.1 Hz), 6.69–8.16 (12H of **A**, 12H of **B**, 12H of **C**). Crystallization of the crude residue from ethanol brought to only a slight modification of the diastereomeric ratio; the crystallized material was a white solid, mp 202–204 °C. **A** as a pure product was obtained by reaction at low temperature. White solid, mp 202–203 °C; ν_{max} (Nujol) 1547, 1298, 1232, 1153, 1133, 1069 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.75 (1H, d, *J* 4.2 Hz), 5.54 (1H, dd, *J* 11.1, 3.9 Hz), 6.26 (1H, d, *J* 10.8 Hz), 6.70 (1H, d, *J* 3.3 Hz), 6.84–6.90 (3H, m), 7.22 (1H, d, *J* 4.5 Hz), 7.25–7.30 (2H, m), 7.39 (1H, t, *J* 7.5 Hz), 7.59–7.62 (1H, m), 7.72–7.79 (2H, m), 8.13–8.16 (1H, m); ^{13}C NMR ($CDCl_3$) δ 43.2, 70.0, 88.6, 125.4, 126.5, 126.9, 127.5, 127.9, 128.4, 128.5, 129.1, 129.8, 130.1, 131.7, 133.9, 136.2, 138.5. MS(ESI): *m/z* 407.6 $[M+Na]^+$, 423.6 $[M+K]^+$. MS(EI) *m/z* 385 (M^+, 2), 338 (96), 321 (32), 274 (100), 241 (38), 197 (40), 186 (80), 173 (58), 91 (33). HRMS calcd for $C_{19}H_{15}NO_4S_2$, 385.0443; found 385.0446.

*4.5.10. 4-Nitro-2-phenyl-3-(3-thienyl)thiochroman S,S-dioxide (**10j**).* Yield (95 mg, 82%, mixture of three racemic pairs). ^{1}H NMR ($CDCl_3$) δ 4.63 (1H **C**, d, *J* 11.1 Hz), 4.71 (1H **A**, d, *J* 3.9 Hz), 4.98 (1H **B**, dd, *J* 13.2, 4.8 Hz), 5.17 (1H **C**, dd, *J* 11.1, 9.3), 5.32 (1H **A**, dd, *J* 11.1, 3.9 Hz), 5.94 (1H **B**, d, *J* 12.6 Hz), 6.13–6.17 (1H **B**+ 1H **C**, m), 6.20 (1H **A**, d, *J* 11.1 Hz), 6.59–8.16 (12H of **A**, 12H of **B**, 12H of **C**). Crystallization of the crude residue from ethanol brought to only a slight modification of the diastereomeric ratio; the crystallized material was a white solid, mp 183–185 °C. **A** as a pure product was obtained by reaction at low temperature. White solid, mp 199–200 °C; ν_{max} (Nujol) 1553, 1310, 1231, 1193, 1151, 1124, 1071 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.71 (1H, d, *J* 3.6 Hz), 5.32 (1H, dd, *J* 11.1, 3.6 Hz), 6.21 (1H, d, *J* 11.1 Hz), 6.60 (1H, d, *J* 5.1 Hz), 6.80 (2H, app d, *J* 7.2 Hz), 6.90 (1H, d, *J* 1.5 Hz), 7.23–7.28 (3H, m), 7.37 (1H, app t, *J* 7.4 Hz), 7.55–7.57 (1H, m), 7.71–7.79 (2H, m), 8.14–8.17 (1H, m); ^{13}C NMR ($CDCl_3$) δ 43.3, 69.4, 87.7, 124.6, 125.3, 126.8, 126.8, 127.4, 128.6, 128.8, 129.0, 129.6, 129.8, 131.6, 133.8, 134.6, 138.9. MS(ESI): *m/z* 408 $[M+Na]^+$, 384 $[M-H]^-$. HRMS calcd for $C_{19}H_{15}NO_4S_2$, 385.0443; found 385.0444.

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