Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron
Tetrahedron 60 (2004) 4967–4973

Easy access to 4-nitrothiochroman *S*,*S*-dioxides via ring-enlargement from 3-nitrobenzo[*b*]thiophene☆

Lara Bianchi,[a] Carlo Dell'Erba,[a] Massimo Maccagno,[a] Stefano Morganti,[b] Marino Novi,[a] Giovanni Petrillo,[a,*] Egon Rizzato,[b] Fernando Sancassan,[a] Elda Severi,[a] Domenico Spinelli[b] and Cinzia Tavani[a]

[a]*Dipartimento di Chimica e Chimica Industriale, Università di Genova, Via Dodecaneso 31, I-16146 Genova, Italy*
[b]*Dipartimento di Chimica Organica 'A. Mangini', Università di Bologna, Via S. Donato 15, I-40127 Bologna, Italy*

Received 13 February 2004; revised 25 March 2004; accepted 14 April 2004

Abstract—The (*E*)-2-aryl-1-[2-(methylthio)phenyl]-1-nitroethylenes **5** can easily be oxidized to the relevant sulfones **6** and effectively subjected to cyclization via an intramolecular Michael addition after metallation with lithium bis(trimethylsilyl)amide in THF. After quenching with ammonium chloride the 3-aryl-4-nitrothiochroman *S*,*S*-dioxides **2** are obtained as diastereomeric mixtures in good to excellent yields. Both yields and stereochemistry of the ring-closure step appear to be influenced by steric effects of the 3-aryl moiety. As sulfides **5** derive from an initial ring opening of 3-nitrobenzo[*b*]thiophene (**1**), the overall **1** to **2** process can be considered as an effective 5 to 6 ring enlargement of the sulfur heterocycle. A conformational ^{1}H NMR and molecular-mechanics investigation on the isolated diastereomeric **2** has also been accomplished.

1. Introduction

A number of reports from the recent literature clearly testify for a renewed interest in the synthetic approach to thiopyrans and benzothiopyrans (thiochromans).[2,3] The quest for new synthetic routes has been boosted by the importance which has been attached in the last decade to such heterocycles, both in pharmacology and in medicine:[4] an occurrence which has also contributed to partially fill, from both a synthetic and applicative point of view, the gap with the oxygen counterparts (pyrans and benzopyrans, respectively), whose long-recognised abundance in nature has always fostered a good deal of research relevant to preparations and properties.[5]

Many thiochromans have been synthesized through reduction of the corresponding thiochromens[6] and thiochromanones,[7] via Claisen rearrangement of allyl phenyl sulfides,[8] or via thermal decomposition of 2-azidobenzo[*b*]thiophenes in the presence of alkenes.[9] More recent synthetic approaches to thiochromans utilize the cycloaddition of sulfur-stabilized carbocations to alkenes.[2b] Some substituted thiochromans have also been prepared through condensation of dilithiated methylthio- and isopropylthio-benzene with α-diketones.[10]

Within the framework of our long-standing project on the synthetic exploitation of the ring-opening of nitrothiophenes[11] we now report on a novel approach to thiochroman *S*,*S*-dioxides **2** (Scheme 1) which takes advantage of an intramolecular Michael addition of the lithium salts of compounds **6** to the nitrovinyl moiety (Scheme 2) and which can be envisaged, starting from 3-nitrobenzo[*b*]thiophene (**1**), as an overall 5 to 6 enlargement of the sulfur heterocycle. It should be pointed out that, at least to our knowledge, compounds **2** represent the first example of thiochroman derivatives with a nitrogroup at C(4).

2. Results and discussion

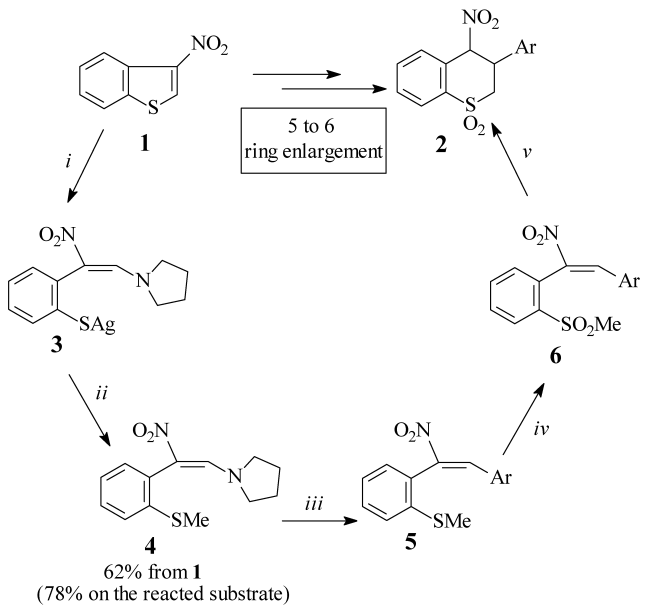
Substrates **6** have been prepared (Scheme 1 and Table 1) by oxidation of **5**, in turn easily obtainable via a preliminary ring opening of 3-nitrobenzo[*b*]thiophene (**1**), according to a methodology previously described for the preparation of **5d** (Ar=*p*-tolyl).[12]

Treatment of **6** with lithium bis(trimethylsilyl)amide (LHMDS) in anhydrous THF at room temperature, followed by acidic (NH_4Cl) quenching allowed us to isolate, in good

☆ See Ref. 1.

Keywords: Thiochromans; Nitrothiophenes; 3-Nitrobenzo[*b*]thiophene; Ring-opening/ring-closure reactions; Ring enlargement; Conformations.
* Corresponding author. Tel.: +39-10-3536121; fax: +39-10-3536118; e-mail address: petrillo@chimica.unige.it

0040–4020/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2004.04.039



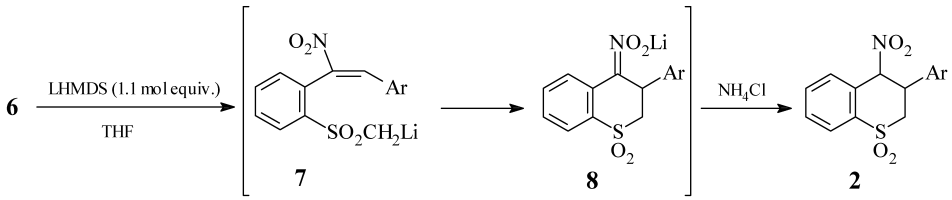
Scheme 1. (i) Pyrrolidine (2 mol equiv.)/$AgNO_3$ (2 mol equiv.), abs. EtOH, rt, overnight; (ii) excess MeI, 0 °C to rt, 2 h; (iii) ArMgX or ArLi (1.1 mol equiv.), THF, −78 °C, 15–45 min, followed by acidic quenching; (iv) MCPBA (2 mol equiv.), CH_2Cl_2, rt; (v) LHMDS (1.1 mol equiv.), THF, rt, 4 h,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

the mesityl-substituted **6e**, evidencing that the overall process is highly sensitive to the bulk of the aryl moiety in the substrate.

The assignment of the structure to the reaction products is based both on microanalytical results and on spectral data [IR, ^1H and ^{13}C NMR, MS(ESI): see Experimental Section]. In particular, the same molecular weight as for **6**, the absence of the nitrovinyl and of the CH_3SO_2 protons, and the presence of a CH–CH–CH_2 moiety in the ^1H NMR spectra represent definitive confirmation of the proposed structure for **2**.

Nitrothiochromans **2** can be reasonably envisaged to originate from the non isolated nitronates **8**, which are in turn the result of an intramolecular Michael addition undergone by the initially formed lithium salts **7** (Scheme 2). Consistant with this proposed mechanism, if the reaction of **6d** is quenched with ND_4Cl in D_2O, 4-deutero-4-nitro-3-(*p*-tolyl)thiochroman *S*,*S*-dioxide (**2′d**) is formed.

The ^1H NMR spectra of crude nitroderivatives **2** are consistent with the concomitant presence of two racemic diastereoisomers, non separable by chromatography, corresponding to the *trans* and *cis* configurations at the C(3)–C(4) bond; thus, in order to better rationalize the results, it seemed worth carrying out an accurate conformational analysis on such thiochromans. While the sulphur atom and C(4) have to be 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 side (generating two non equivalent boats): in the latter case, though, severe eclipsing at the C(2)–C(3) bond can be expected. Another possibility is represented by sofa conformations, exhibiting just one carbon out of the plane and possibly less effective eclipsing than the boats. For this reason sofa conformations received much attention as possible competitors of half-chairs in related systems.[2b,13]



Scheme 2.

Table 1. Yields of compounds **5**, **6** and **2** (Scheme 1, steps iii, iv and v, respectively)[a]

	Ar	5 (Yield %)	6 (Yield %)	2 (Yield %)[b]	2 *trans*/*cis* Ratio[c]
a	Ph	99	99	78	1:1.4
b	2-MeC_6H_4	95	97	80	1:2.2
c	3-MeC_6H_4	87	99	80	1:1.3
d	4-MeC_6H_4	94[d]	94	88	1:1.2
e	2,4,6-$Me_3C_6H_2$	41 (99)[e]	99	[f]	
f	4-ClC_6H_4	99	99	78	1:1.0
g	1-Naphthyl	99	99	99[g]	1:3.0
h	2-Thienyl	99[h]	99	70	1:0.9

[a] Yields of chromatographically-isolated compounds, if not otherwise stated.
[b] Yields of crude diastereoisomeric mixtures.
[c] Isomeric ratios have been determined by ^1H NMR, on the basis of the ratios of the H(4) signals in the mixture.
[d] See Ref. 12.
[e] Yield based on the reacted substrate.
[f] Unaltered substrate recovered after 48 h, with no trace of products.
[g] Reaction time: 30 h.
[h] Reaction time: 4 h.

to excellent yields, the 3-aryl-4-nitrothiochroman *S*,*S*-dioxides **2** (Scheme 1 and Table 1). It should be pointed out that the formation of the product is much slower for the naphthyl-substituted **6g** and even completely suppressed for

We have approached the problem by running molecular-mechanics calculations (PCMODEL program[14]) for the *trans* and *cis* forms of **2a** (Ar=Ph). Results are collected in Table 2. In both cases the most stable conformation is calculated to be one of the two possible half-chairs, the *trans* form adopting a pseudo-equatorial (*peq*) arrangement of the nitro and the phenyl substituents while the *cis* form prefers a pseudo-axial (*pax*) nitrogroup and a *peq* phenyl moiety (Fig. 1). It stands out that the two forms differ mainly for the orientation of the 4-NO_2 substituent and consequently for the H(3)–C(3)–C(4)–H(4) dihedral angle, which is

Table 2. Calculated dihedral angles (°) and dipole moments (D) for the half-chair conformations of *trans*- and *cis*-**2a**

	C(4a)–C(8a)–S(1)–C(2)	C(8a)–C(4a)–C(4)–C(3)	$H(2)_{pax}$–C(2)–C(3)–H(3)	$H(2)_{peq}$–C(2)–C(3)–H(3)	H(3)–C(3)–C(4)–H(4)	Dipole moment
trans	−17.6	−9.0	172.3	−65.8	164.3	5.054
cis	−16.8	−15.1	173.4	−65.3	55.0	4.341

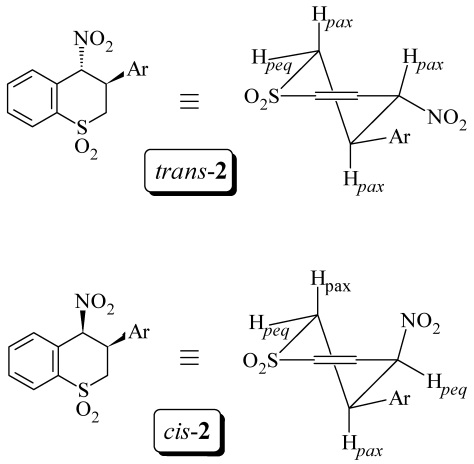


Figure 1. Configuration and preferred half-chair conformation of the two diastereoisomers of **2** (only one enantiomer shown).

calculated to be rather close to 180° for the *trans* form and rather close to 60° for the *cis* one.

Although other conformations cannot be completely ruled out and could be present as minor components, nevertheless these results provide a valuable key to the interpretation of ^{1}H NMR spectra. In fact, the Karplus-Conroy rule[15] predicts high $J_{3,4}$ values (10–15 Hz) for the *quasi-trans* 1,2-pseudodiaxial interaction of H(3) and H(4) in the *trans* form and low values (2–5 Hz) for the staggered 1,2-pseudoaxial-pseudoequatorial interaction of the same protons in the *cis* form. Thus the non aromatic ^{1}H NMR signals of the two racemic pairs of **2** can be fully interpreted and assignments are given in Table 3. It stands out that diastereomeric pairs exhibit striking differences not only, as expected, in $J_{3,4}$ but also in $\delta_{H(2)_{pax}}$ values because of 1,3-pseudodiaxial deshielding interactions between $H(2)_{pax}$ and 4-NO_2 in the *cis* form. Similarly significant variations are observed also in the chemical shifts of H(3) and H(4) on going from *cis*-**2** to *trans*-**2**.

From the *trans*-**2**/*cis*-**2** ratios observed in the crude final mixtures (Table 1) it appears that the cyclization occurs with no significant stereoselectivity but for the 1-naphthyl derivative: in this case, the ca. threefold predominance of the *cis* racemic couple is remarkable and presumably the result of steric effects. It should be also pointed out that a crystallization of the crude from ethanol allows, in the case of the just cited 1-naphthyl derivative, the recovering of an almost pure *cis* isomer, while no appreciable alteration of the *trans*/*cis* ratio has been observed in the other cases; on the other hand, the use of a less polar mixed solvent (viz. ethanol/dioxane) in the case of the model compound **2d** leads to a significant increase in the percentage of the more polar *trans* isomer (see Table 2) in the recovered crystals (the *trans*/*cis* ratio changing from 1:1.2 to 1:0.7 and 1:0.5 after one and two crystallizations, respectively).

3. Conclusions

The results herein enlighten an original and attractive access to the thiochroman *S*,*S*-dioxide ring system, which originates from the ring-opening of 3-nitrobenzo[*b*]thiophene (**1**) and whose key step is represented by an intramolecular Michael-type addition of a sulfonyl-stabilized carbanion onto a nitrovinylic moiety (**6**→**2**: see Schemes 1 and 2).

Table 3. ^{1}H NMR Data (see Section 4) for the non-aromatic protons of the diastereomeric *cis*/*trans* racemic pairs of thiochromans **2**[a]

Isomer	$\delta_{H(2)_{pax}}$	$\delta_{H(2)_{peq}}$	$\delta_{H(3)}$	$\delta_{H(4)}$	$J_{2_{pax},2_{peq}}$	$J_{2_{pax},3}$	$J_{2_{peq},3}$	$J_{3,4}$
trans-**2a**	3.73(dd)	3.60 (dd)	4.62 (app td)	6.13 (d)	14.2	12.0	4.0	11.4
cis-**2a**	4.74 (app t)	3.56 (dd)	4.45 (ddd)	6.00 (d)	13.6	13.8	2.2	4.4
trans-**2b**	3.60 (dd)	3.48[b]	4.99 (app td)	6.30 (d)	14.3	12.1	4.2	11.0
cis-**2b**	4.76 (app t)	3.48[b]	4.62 (dd)	5.94 (d)	12.4	14.0	[c]	4.0
trans-**2c**	3.71 (dd)	3.55[b]	4.56 (app td)	6.14 (d)	13.8	12.5	3.5	11.0
cis-**2c**	4.72 (app t)	3.55[b]	4.39 (ddd)	5.99 (d)	13.6	13.8	2.4	4.1
trans-**2d**	3.71 (dd)	3.58 (dd)	4.57 (app td)	6.10 (d)	14.3	12.0	4.1	11.0
cis-**2d**	4.72 (app t)	3.54 (dd)	4.40 (ddd)	5.97 (d)	13.4	13.6	2.2	4.4
trans-**2f**	3.70 (dd)	3.58 (dd)	4.60 (app td)	6.09 (d)	14.2	11.8	4.4	11.0
cis-**2f**	4.70 (app t)	3.52 (dd)	4.42 (ddd)	5.97 (d)	13.6	13.8	2.2	4.4
trans-**2g**[d]	4.23 (br app t)	3.86 (dd)	5.61 (br app t)	7.03 (d)	14.1	13[e]	2.6	10.6
cis-**2g**[d]	4.78 (app t)	3.88 (dd)	5.36 (ddd)	6.59 (d)	14.0	13.2	2.2	4.1
trans-**2h**[d]	4.21 (dd)	3.87 (dd)	4.9[b]	6.57 (d)	14.2	12.6	3.0	10.2
cis-**2h**[d]	4.57 (app t)	3.91 (dd)	4.9[b]	6.47 (d)	13.6	13.5	2.6	4.4

[a] Chemical shifts as δ ppm from internal TMS, coupling constants in Hz. Solvent: $CDCl_3$, unless otherwise specified; *pax*=pseudoaxial, *peq*=pseudoequatorial. No long-range coupling between non-aromatic and aromatic protons could be detected at 200 MHz (see Ref. 16).
[b] Overlapping signals.
[c] In this product $J_{2_{peq},3}$ is very low and not detectable, possibly because of some little difference in ring conformation as a consequence of the steric requirement of the 2-MeC_6H_4 group.
[d] In acetone-d_6.
[e] Broadening of the relevant triplets does not allow a more accurate measurement.

A ^{1}H NMR study, together with molecular-mechanics calculations, has allowed to gain insights into the configuration of compounds **2** and their conformation.

It should be finally emphasized that the overall **1→2** protocol described herein represents a further example of heterocyclic synthesis by means of a ring-opening/ring-closing procedure which takes advantage of the non-benzenoid behaviour of nitrothiophene derivatives towards secondary nucleophilic amines.[11]

4. Experimental

4.1. General

^{1}H NMR and ^{13}C NMR spectra were recorded at 200 and 50 MHz, respectively; chemical shifts (TMS as internal reference) are reported as δ values (ppm). MS(ESI) analyses were recorded on a Micromass Z0MD Waters instrument (30 V, 13.2 kV). Melting points were determined with a Büchi 535 apparatus and are uncorrected. Petroleum ether and light petroleum refer to the fractions with bp 40–60 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. Compound **4** was synthesized as previously reported.[12] Commercial lithium bis(trimethylsilyl)amide (LHMDS, 1 M in THF) was used as received. All other commercially available reagents were used as received.

Organometallic reagents. All the reagents were THF or Et_2O solutions titrated[17] just before use. Phenyl-, 4-methylphenyl-, 2,4,6-trimethylphenyl-, 1-naphthyl-magnesium bromides, 2-methylphenyl-, 3-methylphenyl-magnesium chlorides were commercial solutions in THF; 4-chlorophenylmagnesium bromide and 2-thienyllithium were commercial solutions in Et_2O.

4.2. Reactions of 4 with aromatic organometallic reagents

The reactions were performed on 1 g of compound **4**[12] (3.78 mmol) following the procedure previously reported for the synthesis of **5d**.[12] Yields of compounds **5** are collected in Table 1.

4.2.1. (*E*)-1-[2-(Methylthio)phenyl]-1-nitro-2-phenylethylene (5a). (1.02 g, 99%). Yellow solid, mp 95–96 °C (light petroleum); ν_{max} (Nujol) 1649, 1584, 1513, 1324, 1212, 1166, 1069 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.41 (3H, s), 7.09 (2H, app d), 7.17–7.56 (7H, m), 8.30 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 14.52, 125.58, 125.99, 128.78, 128.95, 130.70, 130.78, 130.97, 131.02, 131.21, 136.20, 139.50, 147.44. Anal. Calcd for $C_{15}H_{13}NO_2S$: C, 66.4; H, 4.8; N, 5.2%. Found: C, 66.3; H, 4.7; N, 5.2%.

4.2.2. (*E*)-1-[2-(Methylthio)phenyl]-1-nitro-2-(*o*-tolyl)-ethylene (5b). (1.02 g, 95%). Yellow solid, mp 94–96 °C (light petroleum); ν_{max} (Nujol) 1647, 1581, 1513, 1323, 1288, 1228, 1161, 1070 cm^{-1}; ^{1}H NMR (CD_3COCD_3) δ 2.47 (3H, s), 2.51 (3H, s), 6.80–6.99 (2H, m), 7.15–7.32 (4H, m), 7.42–7.53 (2H, m), 8.51 (1H, s); ^{13}C NMR ($CDCl_3$) δ 16.04, 20.15, 125.64, 125.94, 126.84, 129.00, 130.00, 130.23, 130.39, 130.51, 130.58, 131.46, 134.21, 139.10, 140.14, 148.93. Anal. Calcd for $C_{16}H_{15}NO_2S$: C, 67.3; H, 5.3; N, 4.9%. Found: C, 67.5; H, 5.2; N, 4.8%.

4.2.3. (*E*)-1-[2-(Methylthio)phenyl]-1-nitro-2-(*m*-tolyl)-ethylene (5c). (0.94 g, 87%). Yellow solid, mp 65–66 °C (petroleum ether); ν_{max} (Nujol) 1646, 1581, 1504, 1314, 1173, 1070 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.22 (3H, s), 2.42 (3H, s), 6.84 (1H, app d), 6.95 (1H, s), 7.05–7.32 (4H, m), 7.38–7.58 (2H, m), 8.27 (1H, s); ^{13}C NMR ($CDCl_3$) δ 15.99, 21.25, 125.93, 126.92, 127.80, 128.70, 130.23, 130.81, 130.95, 131.16, 131.88, 132.16, 136.48, 138.48, 140.07, 147.80. Anal. Calcd for $C_{16}H_{15}NO_2S$: C, 67.3; H, 5.3; N, 4.9%. Found: C, 67.2; H, 5.2; N, 4.8%.

4.2.4. (*E*)-1-[2-(Methylthio)phenyl]-1-nitro-2-(*p*-tolyl)-ethylene (5d). (1.02 g, 94%). Yellow solid, mp 56–57 °C (light petroleum).[12]

4.2.5. (*E*)-1-[2-(Methylthio)phenyl]-1-nitro-2-(2,4,6-trimethylphenyl)ethylene (5e). [0.49 g, 41% (99% based on the unreacted substrate)]. Yellow solid, mp 128–129 °C (light petroleum); ν_{max} (Nujol) 1645, 1609, 1585, 1518, 1328, 1172, 1067, 1040 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.08 (6H, s), 2.22 (3H, s), 2.44 (3H, s), 6.75–6.83 (3H, m), 7.00 (1H, td, *J*=7.3, 1.4 Hz), 7.31 (1H, td, *J*=7.5, 1.4 Hz), 7.40 (1H, dd, *J*=7.8, 1.4 Hz), 8.18 (1H, s); ^{13}C NMR ($CDCl_3$) δ 17.40, 20.36, 21.01, 125.78, 127.82, 128.59, 129.12, 130.36, 130.93, 131.39, 135.51, 136.16, 138.61, 139.31, 151.87. Anal. Calcd for $C_{18}H_{19}NO_2S$: C, 69.0; H, 6.1; N, 4.5%. Found: C, 69.2; H, 6.0; N, 4.4%.

4.2.6. (*E*)-2-(4-Chlorophenyl)-1-[2-(methylthio)phenyl]-1-nitroethylene (5f). (1.14 g, 99%). Yellow solid, mp 96–98 °C (light petroleum); ν_{max} (Nujol) 1655, 1583, 1519, 1491, 1407, 1325, 1207, 1166, 1092, 1069, 1011 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.42 (3H, s), 7.02 (2H, d, *J*=8.4 Hz), 7.14–7.31 (4H, m), 7.40 (1H, d, *J*=7.8 Hz), 7.52 (1H, td, *J*=7.5, 1.4 Hz), 8.24 (1H, s); ^{13}C NMR ($CDCl_3$) δ 15.79, 125.94, 126.73, 129.18, 129.43, 129.50, 131.01, 131.06, 132.03, 134.87, 137.17, 140.09, 148.29. Anal. Calcd for $C_{15}H_{12}ClNO_2S$: C, 58.9; H, 4.0; N, 4.6%. Found: C, 59.1; H, 3.9; N, 4.7%.

4.2.7. (*E*)-1-[2-(Methylthio)phenyl]-2-(1-naphthyl)-1-nitroethylene (5g). (1.20 g, 99%). Yellow solid, mp 158–159 °C (toluene/light petroleum); ν_{max} (Nujol) 1641, 1584, 1518, 1355, 1322, 1243, 1169, 1071, 1017 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.44 (3H, s), 7.05–7.27 (4H, m), 7.33–7.48 (2H, m), 7.50–7.69 (2H, m), 7.74–7.90 (2H, m), 8.16 (1H, d, *J*=8.4 Hz), 9.01 (1H, s); ^{13}C NMR ($CDCl_3$) δ 16.07, 123.52, 125.13, 125.60, 126.45, 126.77, 127.27, 128.05, 128.21, 128.87, 129.98, 130.55, 130.86, 131.41, 131.95, 133.33, 133.78, 140.31, 150.14. Anal. Calcd for $C_{19}H_{15}NO_2S$: C, 71.0; H, 4.7; N, 4.4%. Found: C, 71.2; H, 4.6; N, 4.4%.

4.2.8. (*E*)-1-[2-(Methylthio)phenyl]-1-nitro-2-(2-thienyl)ethylene (5h). [1.04 g, 99% (reaction time: 4 h)]. Yellow solid, mp 106–108 °C (light petroleum); ν_{max} (Nujol) 1632, 1583, 1500, 1415, 1311, 1286, 1250, 1237, 1214, 1052, 1040 cm^{-1}; ^{1}H NMR (CD_3SOCD_3) δ 2.40 (3H,

s), 7.16 (1H, dd, *J*=4.8, 3.8 Hz), 7.33–7.40 (2H, m), 7.51 (1H, app d, *J*=8.2 Hz), 7.56–7.68 (1H, m), 7.74–7.83 (2H, m), 8.75 (1H, s); ^{13}C NMR (CD_3COCD_3) δ 15.45, 126.90, 127.69, 128.55, 129.80, 131.13, 132.30, 132.75, 135.24, 135.83, 138.07, 141.58, 145.90. Anal. Calcd for $C_{13}H_{11}NO_2S_2$: C, 56.3; H, 4.1; N, 5.1%. Found: C, 56.3; H, 4.0; N, 5.0%.

4.3. Oxidation of compounds 5 to 6

The reaction was performed on 2 mmol of the appropriate **5**, according to the conditions described in Ref. 11. Yields are reported in Table 1.

4.3.1. (*E*)-1-[2-(Methylsulfonyl)phenyl]-1-nitro-2-phenylethylene (6a). (600 mg, 99%). Yellow solid, mp 116–117 °C (ethanol); ν_{max} (Nujol) 1643, 1598, 1512, 1322, 1306, 1213, 1152, 1122 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.97 (3H, s), 7.02 (2H, d, *J*=7.2 Hz), 7.18–7.40 (4H, m), 7.67–7.83 (2H, m), 8.22 (1H, dd, *J*=7.3, 1.9 Hz), 8.37 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 43.23, 128.99, 129.24, 130.26, 130.39, 131.01, 131.27, 131.75, 133.39, 134.78, 135.09, 139.63, 146.35. Anal. Calcd for $C_{15}H_{13}NO_4S$: C, 59.4; H, 4.3; N, 4.6%. Found: C, 59.3; H, 4.3; N, 4.5%.

4.3.2. (*E*)-1-[2-(Methylsulfonyl)phenyl]-1-nitro-2-(*o*-tolyl)ethylene (6b). (616 mg, 97%). Yellow solid, mp 174–175 °C (ethanol); ν_{max} (Nujol) 1650, 1530, 1336, 1305, 1266, 1232, 1151, 1121, 1073 cm^{-1}; ^{1}H NMR (CD_3SOCD_3) δ 2.47 (3H, s), 3.09 (3H, s), 6.61 (1H, d, *J*=7.6 Hz), 6.95 (1H, t, *J*=7.3 Hz), 7.18–7.33 (2H, m), 7.45 (1H, app dd, *J*=7.0, 1.8 Hz), 7.69–7.86 (2H, m), 8.17 (1H, app dd, *J*=7.4, 1.8 Hz), 8.49 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 19.54, 43.09, 125.82, 128.60, 128.82, 129.88, 130.06, 130.37, 130.61, 131.46, 133.38, 133.74, 134.19, 139.23, 139.99, 147.78. Anal. Calcd for $C_{16}H_{15}NO_4S$: C, 60.6; H, 4.8; N, 4.4%. Found: C, 60.4; H, 4.7; N, 4.3%.

4.3.3. (*E*)-1-[2-(Methylsulfonyl)phenyl]-1-nitro-2-(*m*-tolyl)ethylene (6c). (630 mg, 99%). Yellow solid, mp 155–156 °C (ethanol); ν_{max} (Nujol) 1646, 1523, 1337, 1307, 1246, 1181, 1150, 1124 cm^{-1}; ^{1}H NMR (CD_3SOCD_3) δ 2.16 (3H, s), 3.00 (3H, s), 6.81 (1H, d, *J*=7.4 Hz), 6.98 (1H, s), 7.13–7.27 (2H, m), 7.56–7.63 (1H, m), 7.84–7.97 (2H, m), 8.19–8.26 (1H, m), 8.36 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 20.69, 43.25, 127.80, 128.85, 129.39, 130.26, 130.33, 131.71, 131.96, 132.07, 133.41, 134.76, 135.19, 138.27, 139.60, 146.23. Anal. Calcd for $C_{16}H_{15}NO_4S$: C, 60.6; H, 4.8; N, 4.4%. Found: C, 60.7; H, 4.7; N, 4.4%.

4.3.4. (*E*)-1-[2-(Methylsulfonyl)phenyl]-1-nitro-2-(*p*-tolyl)ethylene (6d). (600 mg, 94%). Yellow solid, mp 160–161 °C (ethanol); ν_{max} (Nujol) 1655, 1605, 1513, 1330, 1314, 1192, 1168, 1156, 1125 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.30 (3H, s), 2.95 (3H, s), 6.89 (2H, d, *J*=8.3 Hz), 7.05 (2H, d, *J*=8.3 Hz), 7.35–7.41 (1H, m), 7.67–7.83 (2H, m), 8.18–8.27 (1H, m), 8.35 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 20.79, 43.23, 127.48, 129.43, 129.56, 130.15, 130.98, 131.54, 133.30, 134.65, 135.09, 139.59, 141.70, 145.47. Anal. Calcd for $C_{16}H_{15}NO_4S$: C, 60.6; H, 4.8; N, 4.4%. Found: C, 60.5; H, 4.8; N, 4.3%.

4.3.5. (*E*)-1-[2-(Methylsulfonyl)phenyl]-1-nitro-2-(2,4,6-trimethylphenyl)ethylene (6e). (684 mg, 99%). Pale yellow solid, mp 202–203 °C (ethanol); ν_{max} (Nujol) 1649, 1611, 1530, 1339, 1305, 1265, 1156, 1119, 1071 cm^{-1}; ^{1}H NMR (CD_3SOCD_3) δ 2.07 (6H, s), 2.17 (3H, s), 3.20 (3H, s), 6.80 (2H, s), 6.94 (1H, dd, *J*=7.7, 1.5 Hz), 7.53 (1H, td, *J*=7.5, 1.3 Hz), 7.69 (1H, td, *J*=7.7, 1.4 Hz), 8.12 (1H, dd, *J*=7.9, 1.3 Hz), 8.36 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 19.87, 20.47, 43.23, 127.51, 128.26, 128.32, 130.40, 131.32, 132.90, 133.45, 135.59, 135.83, 138.30, 139.21, 149.99. Anal. Calcd for $C_{18}H_{19}NO_4S$: C, 62.6; H, 5.6; N, 4.1%. Found: C, 62.4; H, 5.5; N, 4.0%.

4.3.6. (*E*)-2-(4-Chlorophenyl)-1-[2-(methylsulfonyl)-phenyl]-1-nitroethylene (6f). (670 mg, 99%). Yellow solid, mp 149–150 °C (ethanol); ν_{max} (Nujol) 1649, 1584, 1527, 1407, 1313, 1208, 1151, 1120, 1089, 1011 cm^{-1}; ^{1}H NMR (CD_3SOCD_3) δ 3.04 (3H, s), 7.12 (2H, d, *J*=8.6 Hz), 7.41 (2H, d, *J*=8.6 Hz), 7.54–7.63 (1H, m), 7.83–7.97 (2H, m), 8.19–8.27 (1H, m), 8.43 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 43.26, 128.84, 129.16, 129.42, 130.32, 131.92, 132.58, 133.32, 133.95, 134.87, 135.99, 139.67, 146.83. Anal. Calcd for $C_{15}H_{12}ClNO_4S$: C, 53.3; H, 3.6; N, 4.1%. Found: C, 53.2; H, 3.6; N, 4.2%.

4.3.7. (*E*)-1-[2-(Methylsulfonyl)phenyl]-2-(1-naphthyl)-1-nitroethylene (6g). (707 mg, 99%). Yellow solid, mp 213–214 °C (ethanol/dioxane); ν_{max} (Nujol) 1646, 1510, 1310, 1243, 1153, 1119, 1069 cm^{-1}; ^{1}H NMR (CD_3SOCD_3) δ 3.12 (3H, s), 7.03 (1H, d, *J*=7.4 Hz), 7.27–7.39 (2H, m), 7.57–7.80 (4H, m), 7.96 (2H, app t, *J*=8.8 Hz), 8.15 (1H, dd, *J*=7.9, 1.3 Hz), 8.22 (1H, d, *J*=7.6 Hz), 8.97 (1H, s); ^{13}C NMR ($CDCl_3$) δ 43.16, 124.06, 125.12, 126.72, 127.39, 127.88, 128.19, 128.63, 128.73, 130.05, 130.62, 131.16, 131.43, 132.89, 133.02, 133.57, 134.08, 140.06, 149.23. Anal. Calcd for $C_{19}H_{15}NO_4S$: C, 64.6; H, 4.3; N, 4.0%. Found: C, 64.4; H, 4.2; N, 4.0%.

4.3.8. (*E*)-1-[2-(Methylsulfonyl)phenyl]-1-nitro-2-(2-thienyl)ethylene (6h). (612 mg, 99%). Yellow solid, mp 151–152 °C (ethanol); ν_{max} (Nujol) 1627, 1337, 1305, 1246, 1152, 1120, 1052 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.93 (3H, s), 7.06 (1H, dd, *J*=5.1, 3.7 Hz), 7.38 (1H, d, *J*=3.7 Hz), 7.42 (1H, dd, *J*=5.1, 0.7 Hz), 7.46–7.55 (1H, m), 7.77–7.89 (2H, m), 8.20–8.29 (1H, m), 8.58 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 43.48, 128.13, 128.31, 129.88, 130.54, 132.24, 134.04, 134.18, 135.06, 135.27, 138.58, 139.72, 143.04. Anal. Calcd for $C_{13}H_{11}NO_4S_2$: C, 50.5; H, 3.6; N, 4.5%. Found: C, 50.5; H, 3.5; N, 4.4%.

4.4. Reaction of compounds 6 with LHMDS

In a flask, the appropriate **6** (0.3 mmol) was dissolved under Argon in THF (19 mL) and LHMDS 1 M (1.1 mol equiv., 0.33 mL) was added by a syringe under magnetic stirring. The proceeding of the reaction was followed by TLC and, after completion, the mixture was poured into saturated aqueous NH_4Cl (50 mL), and extracted with dichloromethane (2×20 mL), the organic extracts being dried over Na_2SO_4. The crude solid residue, obtained by filtration and removal of the solvent under reduced pressure, was generally pure by ^{1}H NMR analysis, being a diastereomeric *cis*/*trans* mixture of compounds **2**. Yields of compounds **2**

are reported in Table 1 together with the relevant *cis*/*trans* ratios. As mentioned in the text, the crystallization of the crude residues from ethanol brings about only minor variations in the diastereomeric ratio in all cases but for the 1-naphthyl derivative **2g**, for which the pure *cis* stereoisomer can be recovered: therefore, the spectroscopic data reported below refer to the crystallized mixture in every case but for **2g**. For the latter, ^{1}H NMR data for the crude residue, where both diastereoisomers are present, are reported, together with a full spectroscopic characterization of the crystallized *cis* stereoisomer. In the ^{1}H NMR spectra of compounds **2** some signals appeared as triplets, as a consequence of the similar values of the two coupling constants involved; in these cases, as the frequency difference between the outer lines corresponds to the sum of the two *J* values, if one of them was known the other was calculated accordingly.

4.4.1. 4-Nitro-3-phenylthiochroman *S*,*S*-dioxide (2a). (71 mg, 78%, mixture of *trans*:*cis* isomers 1:1.4). White solid, mp 162–170 °C (ethanol); ν_{max} (Nujol) 1556, 1296, 1247, 1225, 1158, 1126, 1070 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.56 (1H *cis*, dd, *J*=13.6, 2.2 Hz), 3.60 (1H *trans*, dd, *J*=14.2, 4.0 Hz), 3.73 (1H *trans*, dd, *J*=14.2, 12.0 Hz), 4.45 (1H *cis*, ddd, *J*=13.8, 4.4, 2.2 Hz), 4.62 (1H *trans*, app td, *J*=12.0, 11.4, 4.0 Hz), 4.74 (1H *cis*, app t, *J*=13.8, 13.6 Hz), 6.00 (1H *cis*, d, *J*=4.4 Hz), 6.13 (1H *trans*, d, *J*=11.4 Hz), 7.18–7.80 (8H *cis* and 8H *trans*), 8.04–8.18 (1H *cis* and 1H *trans*, m); ^{13}C NMR ($CDCl_3$) δ 41.40, 43.13, 48.57, 53.48, 88.55, 90.72, 124.51, 124.59, 127.02, 127.08, 127.25, 127.65, 128.54, 129.21, 129.28, 129.54, 129.61, 129.73, 131.09, 132.16, 133.43, 133.75, 135.45, 136.25, 138.16, 139.05; MS(ESI): *m*/*z* 326.3 (M+Na)$^+$, 302.0 (M−1). Anal. Calcd for $C_{15}H_{13}NO_4S$: C, 59.4; H, 4.3; N, 4.6%. Found: C, 59.2; H, 4.3; N, 4.5%.

4.4.2. 4-Nitro-3-(*o*-tolyl)thiochroman *S*,*S*-dioxide (2b). (76 mg, 80%, mixture of *trans*:*cis* isomers 1:2.2). White solid, mp 187–189 °C (ethanol); ν_{max} (Nujol) 1552, 1413, 1327, 1306, 1267, 1253, 1234, 1197, 1166, 1156, 1132, 1072 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.44 (3H *trans*, s), 2.48 (3H *cis*, s), 3.48 (1H *cis* and 1H *trans*, overlapping multiplets), 3.60 (1H *trans*, dd, *J*=14.3, 12.1 Hz), 4.62 (1H *cis*, dd, *J*=14.0, 4.0 Hz), 4.76 (1H *cis*, app t, *J*=14.0, 12.4 Hz), 4.99 (1H *trans*, app td, *J*=12.1, 11.0, 4.2 Hz), 5.94 (1H *cis*, d, *J*=4.0 Hz), 6.30 (1H *trans*, d, *J*=11.0 Hz), 6.98 (1H *cis*, d, *J*=7.0 Hz), 7.20–7.34 (3H *cis* and 4H *trans*, m), 7.43 (1H *trans*, m), 7.52 (1H *cis*, m), 7.61–7.79 (2H *cis* and 2H *trans*, m), 8.05–8.19 (1H *cis* and 1H *trans*, m); ^{13}C NMR ($CDCl_3$) δ 19.41, 37.64, 38.40, 49.02, 53.97, 86.64, 89.57, 124.52, 124.68, 125.40, 125.81, 127.01, 127.25, 127.44, 127.73, 128.78, 128.83, 129.05, 129.59, 131.08, 131.36, 131.81, 132.14, 133.42, 133.59, 133.69, 134.49, 135.35, 136.44, 139.10 (two pairs of carbons are accidentally isochronous); MS(ESI): *m*/*z* 340.2 (M+Na)$^+$, 316.2 (M−1). Anal. Calcd for $C_{16}H_{15}NO_4S$: C, 60.6; H, 4.8; N, 4.4%. Found: C, 60.6; H, 4.7; N, 4.5%.

4.4.3. 4-Nitro-3-(*m*-tolyl)thiochroman *S*,*S*-dioxide (2c). (76 mg, 80%, mixture of *trans*:*cis* isomers 1:1.3). White solid, mp 179–180 °C (ethanol); ν_{max} (Nujol) 1552, 1300, 1265, 1244, 1219, 1195, 1155, 1129, 1073 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.37 (3H *cis* and 3H *trans*, 2 s overlapped), 3.55 (1H *cis* and 1H *trans*, overlapping multiplets), 3.71 (1H *trans*, dd, *J*=13.8, 12.5 Hz), 4.39 (1H *cis*, ddd, *J*=13.8, 4.1, 2.4 Hz), 4.56 (1H *trans*, app td, *J*=12.5, 11.0, 3.5 Hz), 4.72 (1H *cis*, app t, *J*=13.8, 13.6 Hz), 5.99 (1H *cis*, d, *J*=4.1 Hz), 6.14 (1H *trans*, d, *J*=11.0 Hz), 6.98–7.78 (7H *cis* and 7H *trans*, m), 8.09 (1H *cis* and 1H *trans*, m); ^{13}C NMR (CD_3COCD_3) δ 21.38, 41.54, 44.64, 49.24, 53.41, 89.70, 91.88, 124.69, 124.76, 125.19, 125.47, 128.09, 128.86, 129.18, 129.39, 129.81, 130.04, 130.08, 130.32, 130.89, 131.81, 132.84, 134.16, 134.45, 137.54, 138.15, 139.53, 139.84, 139.88, 140.53 (two pairs of carbons are accidentally isochronous); MS(ESI): *m*/*z* 340.2 (M+Na)$^+$, 316.1 (M−1). Anal. Calcd for $C_{16}H_{15}NO_4S$: C, 60.6; H, 4.8; N, 4.4%. Found: C, 60.4; H, 4.7; N, 4.4%.

4.4.4. 4-Nitro-3-(*p*-tolyl)thiochroman *S*,*S*-dioxide (2d). (84 mg, 88%, mixture of *trans*:*cis* isomers 1:1.2). White solid, mp 194–196 °C (ethanol); ν_{max} (Nujol) 1553, 1513, 1402, 1366, 1343, 1302, 1264, 1247, 1225, 1158, 1131, 1073 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.37 (3H *cis* and 3H *trans*, 2 s overlapped), 3.54 (1H *cis*, dd, *J*=13.4, 2.2 Hz), 3.58 (1H *trans*, dd, *J*=14.3, 4.1 Hz), 3.71 (1H *trans*, dd, *J*=14.3, 12.0 Hz), 4.40 (1H *cis*, ddd, *J*=13.6, 4.4, 2.2 Hz), 4.57 (1H *trans*, app td, *J*=12.0, 11.0, 4.1 Hz), 4.72 (1H *cis*, app t, *J*=13.6, 13.4 Hz), 5.97 (1H *cis*, d, *J*=4.4 Hz), 6.10 (1H *trans*, d, *J*=11.0 Hz), 7.06–7.78 (7H *cis* and 7H *trans*, m), 8.04–8.18 (1H *cis* and 1H *trans*, m); ^{13}C NMR ($CDCl_3$) δ 21.14, 41.05, 42.80, 48.67, 53.57, 88.64, 90.87, 124.47, 124.54, 126.83, 127.03, 127.07, 127.71, 128.58, 129.52, 130.23, 130.34, 131.03, 132.10, 132.45, 133.21, 133.37, 133.68, 138.17, 139.05, 139.12, 139.21 (the methyl carbons of the two isomers are accidentally isochronous); MS(ESI): *m*/*z* 340.3 (M+Na)$^+$, 316.1 (M−1). Anal. Calcd for $C_{16}H_{15}NO_4S$: C, 60.6; H, 4.8; N, 4.4%. Found: C, 60.5; H, 4.8; N, 4.4%. The ^{1}H NMR for the 4-deutero-4-nitro-3-(*p*-tolyl)thiochroman *S*,*S*-dioxide (**2′d**) is analogous to that of **2d** but for the signals at δ 4.40 and 4.57 which are (1H *cis*, dd, *J*=13.6, 2.2 Hz) and (1H *trans*, dd, *J*=12.2, 4.3 Hz), respectively.

4.4.5. 3-(*p*-Chlorophenyl)-4-nitrothiochroman *S*,*S*-dioxide (2f). (79 mg, 78%, mixture of *trans*:*cis* isomers ca. 1:1). White solid, mp 189–195 °C (ethanol); ν_{max} (Nujol) 1552, 1308, 1157, 1131, 1096, 1015 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.52 (1H *cis*, dd, *J*=13.6, 2.2 Hz), 3.58 (1H *trans*, dd, *J*=14.2, 4.4 Hz), 3.70 (1H *trans*, dd, *J*=14.2, 11.8 Hz), 4.42 (1H *cis*, ddd, *J*=13.8, 4.4, 2.2 Hz), 4.60 (1H *trans*, app td, *J*=11.8, 11.0, 4.4 Hz), 4.70 (1H *cis*, app t, *J*=13.8, 13.6 Hz), 5.97 (1H *cis*, d, *J*=4.4 Hz), 6.09 (1H *trans*, d, *J*=11.0 Hz), 7.13–7.80 (7H *cis* and 7H *trans*, m), 8.04–8.17 (1H *cis* and 1H *trans*, m); ^{13}C NMR ($CDCl_3$) δ 40.85, 42.56, 48.44, 53.28, 88.28, 90.53, 124.53, 124.64, 127.02, 127.34, 128.26, 128.41, 128.66, 129.55, 129.86, 129.99, 131.20, 132.28, 133.54, 133.86, 134.70, 135.38, 138.01, 138.90 (two pairs of carbons are accidentally isochronous); MS(ESI): *m*/*z* 360.2 (M+Na)$^+$, 336.2 (M−1). Anal. Calcd for $C_{15}H_{12}ClNO_4S$: C, 53.3; H, 3.6; N, 4.2%. Found: C, 53.2; H, 3.5; N, 4.1%.

4.4.6. 3-(1-Naphthyl)-4-nitrothiochroman *S*,*S*-dioxide (2g). (105 mg, 99%, mixture of *trans*:*cis* isomers 1:3.0). ^{1}H NMR (CD_3COCD_3) δ 3.86 (1H *trans*, dd, *J*=14.1, 2.6 Hz), 3.88 (1H *cis*, dd, *J*=14.0, 2.2 Hz), 4.23 (1H *trans*,

br t, J=13 Hz), 4.78 (1H *cis*, app t, J=14.0, 13.2 Hz), 5.36 (1H *cis*, ddd, J=13.2, 4.1, 2.2 Hz), 5.61 (1H *trans*, br t, J=13 Hz), 6.59 (1H *cis*, d, J=4.1 Hz), 7.03 (1H *trans*, d, J=10.6 Hz), 7.1–8.8 (11H *cis* and 11H *trans*, m) (assignments supported by decoupling experiments). A crystallization from ethanol afforded a white solid, mp 224–226 °C, which was identified as the pure *cis*-diastereoisomer by spectroscopic data; ν_{max} (Nujol) 1551, 1509, 1415, 1305, 1252, 1160, 1133, 1073 cm^{-1}; ^1H NMR (CD_3COCD_3) δ 3.88 (1H, dd, J=14.0, 2.2 Hz), 4.78 (1H, app t, J=14.0, 13.2 Hz), 5.36 (1H, ddd, J=13.2, 4.1, 2.2 Hz), 6.59 (1H, d, J=4.1 Hz), 7.43 (1H, d, J=7.0 Hz), 7.50–7.94 (6H, m), 7.98–8.10 (2H, m), 8.15 (1H, m), 8.56 (1H, m); ^{13}C NMR (CD_3COCD_3) δ 37.69, 49.84, 88.78, 123.36, 124.66, 125.54, 126.44, 127.13, 128.17, 129.54, 130.19, 130.28, 131.24, 131.46, 132.80, 133.40, 134.17, 134.92, 140.57; MS(ESI): *m/z* 376.3 $(M+Na)^+$, 352.2 (M−1). Anal. Calcd for $C_{19}H_{15}NO_4S$: C, 64.6; H, 4.3; N, 4.0%. Found: C, 64.4; H, 4.2; N, 3.9%.

4.4.7. 4-Nitro-3-(2-thienyl)thiochroman *S*,*S*-dioxide (2h). (65 mg, 70%, mixture of *trans*:*cis* isomers 1:0.9). Pale green solid, mp 113–117 °C (ethanol); ν_{max} (Nujol) 1552, 1300, 1246, 1155, 1127, 1069 cm^{-1}; ^1H NMR (CD_3COCD_3) δ 3.87 (1H *trans*, dd, J=14.2, 3.0 Hz), 3.91 (1H *cis*, dd, J=13.6, 2.6 Hz), 4.21 (1H *trans*, dd, J=14.2, 12.6 Hz), 4.57 (1H *cis*, app t, J=13.6, 13.5 Hz), 4.83–4.97 (1H *cis* and 1H *trans*, m), 6.47 (1H *cis*, d, J=4.4 Hz), 6.57 (1H *trans*, d, J=10.2 Hz), 7.10 (1H *cis* and 1H *trans*, m), 7.21 (1H *cis*, m), 7.27 (1H *trans*, m), 7.48–7.57 (2H *cis* and 1H *trans*, m), 7.68–8.12 (3H *cis* and 4H *trans*, m); ^{13}C NMR ($CDCl_3$) δ 37.24, 38.73, 49.56, 53.90, 88.35, 91.32, 124.43, 124.50, 126.09, 126.20, 126.35, 127.00, 127.14, 127.26, 127.58, 127.66, 127.90, 129.63, 131.22, 132.27, 133.47, 133.78, 137.36, 138.07, 138.43, 138.83; MS(ESI): *m/z* 332.2 $(M+Na)^+$, 308.2 (M−1). Anal. Calcd for $C_{13}H_{11}NO_4S_2$: C, 50.5; H, 3.6; N, 4.5%. Found: C, 50.5; H, 3.5; N, 4.6%.

Acknowledgements

Financial support was provided by grants from the Universities of Genova and of Bologna, and from Ministero dell'Istruzione, dell'Università e della Ricerca (MIUR, PRIN-2002).

References and notes

1. Synthetic Exploitation of the Ring-Opening of Nitrothiophenes, Part XVI. For part XV, see Ref. 11.
2. (a) Saito, T.; Horikoshi, T.; Otani, T.; Matsuda, Y.; Karakasa, T. *Tetrahedron Lett.* **2003**, *44*, 6513–6517. (b) Katritzky, A. R.; Button, M. A. C. *J. Org. Chem.* **2001**, *66*, 5595–5600. (c) Ram, V. J.; Srivastava, P.; Saxena, A. S. *J. Org. Chem.* **2001**, *66*, 5333–5337. (d) Hori, M.; Kataoka, T.; Shimizu, H.; Imai, E.; Iwata, N.; Kawamura, N.; Kurono, M.; Nakano, K.; Kido, M. *Chem. Pharm. Bull.* **1989**, *37*, 1282–1286.
3. (a) Ingall, A. H. *Comprehensive Heterocyclic Chemistry*; Boulton, A. J., McKillop, A., Eds.; Pergamon: Oxford, 1984; Vol. 3, pp 885–942. (b) Ingall, A. H. *Comprehensive Heterocyclic Chemistry II*; McKillop, A., Ed.; Pergamon: Oxford, 1996; Vol. 5, p 501.
4. (a) Al-Nakib, T.; Bezjak, V.; Rashid, S.; Fullam, B.; Meegan, M. J. *Eur. J. Med. Chem.* **1991**, *26*, 221–230. (b) Al-Nakib, T.; Bezjak, V.; Meegan, M. J.; Chandy, R. *Eur. J. Med. Chem.* **1990**, *25*, 455–457. (c) Van Vliet, L. A.; Rodenhuis, N.; Dijkstra, D.; Wikstroem, H.; Pugsley, T. A.; Serpa, K. A.; Meltzer, L. T.; Heffner, T. G.; Wise, L. D.; Lajiness, M. E.; Huff, R. M.; Svensson, K.; Sundell, S.; Lundmark, M. *J. Med. Chem.* **2000**, *43*, 2871–2882. (d) Pigini, M.; Brasili, L.; Giannella, M.; Giardinà, D.; Gulini, U.; Quaglia, W.; Melchiorre, C. *J. Med. Chem.* **1988**, *31*, 2300–2304. (e) Baurmgarth, M.; Beier, N.; Gericke, R. *J. Med. Chem.* **1998**, *41*, 3736–3747. (f) Philip, A.; Jirkovsky, I.; Martel, R. R. *J. Med. Chem.* **1980**, *23*, 1372–1376. (g) Ramalingam, K.; Thyvelikakath, G. X.; Berlin, K. D.; Chesnut, R. W.; Brown, R. A.; Durham, N. N.; Ealick, S. E.; van der Helm, D. *J. Med. Chem.* **1977**, *20*, 647–650. (h) Holshouser, M. H.; Loeffler, L. J.; Hill, I. H. *J. Med. Chem.* **1981**, *24*, 853–858. (i) Holshouser, M. H.; Loeffler, L. J. *J. Pharm. Sci.* **1982**, *71*, 715–717. (j) For less recent reports on the pharmacological (antipyretic, antidepressant and analgesic) properties of thiochromans see: *Adv. Heterocycl. Chem.* **1975**, **18**, 59–97.
5. (a) Brogden, P. J.; Gabbutt, C. D.; Hepworth, J. D. *Comprehensive Heterocyclic Chemistry*; Boulton, A. J., McKillop, A., Eds.; Pergamon: Oxford, 1984; Vol. 3, pp 573–883. (b) Miyazaki, H.; Honda, K.; Asami, M.; Inoue, S. *J. Org. Chem.* **1999**, *64*, 9507–9511. (c) Yadav, J. S.; Reddy, B. V. S.; Rao, C. V.; Rao, K. V. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1401–1404.
6. Tilak, B. D.; Vaidya, V. M. *Tetrahedron Lett.* **1963**, *8*, 487–495.
7. Takido, T.; Tagagi, Y.; Itabashi, K. *J. Heterocycl. Chem.* **1995**, *32*, 687–690.
8. Meyers, C. Y.; Rinaldi, C.; Bonoli, L. *J. Org. Chem.* **1963**, *28*, 2440–2442.
9. Funicello, M.; Spagnolo, P.; Zanirato, P. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2971–2978.
10. Cabiddu, M. G.; Cabiddu, S.; Cadoni, E.; Demurtas, P.; Fattuoni, C.; Floris, C.; Melis, S. *Synthesis* **1998**, 1098–1100.
11. Bianchi, L.; Dell'Erba, C.; Maccagno, M.; Mugnoli, A.; Novi, M.; Petrillo, G.; Sancassan, F.; Tavani, C. *J. Org. Chem.* **2003**, *68*, 5254–5260, and previous papers in the series.
12. Dell'Erba, C.; Gabellini, A.; Novi, M.; Petrillo, G.; Tavani, C.; Cosimelli, B.; Spinelli, D. *Tetrahedron* **2001**, *57*, 8159–8165.
13. (a) Bolger, B. J.; Hirwe, A.; Marathe, K. G.; Philbin, E. M.; Vickars, M. A.; Lillya, C. P. *Tetrahedron* **1966**, *22*, 621–628. (b) Clark-Lewis, J. W. *Aust. J. Chem.* **1968**, *21*, 2059–2075. (c) Katekar, G. F. *Aust. J. Chem.* **1966**, *19*, 1251–1257.
14. PC Model Version 7.0 Serena Software, Box 3076, Bloomington, In, USA, 1998.
15. (a) Karplus, M. *J. Chem. Phys.* **1959**, *30*, 11–18. (b) Conroy, H. H. *Adv. Org. Chem.* **1960**, *2*, 265–268.
16. Katekar, G. F.; Moritz, A. G. *Aust. J. Chem.* **1967**, *20*, 2235–2241.
17. Bergbreit, D. E.; Pendergrass, E. *J. Org. Chem.* **1981**, *46*, 219–220.