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A new route to thiopyran *S*,*S*-dioxide derivatives via an overall ring-enlargement protocol from 3-nitrothiophene

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ABSTRACT

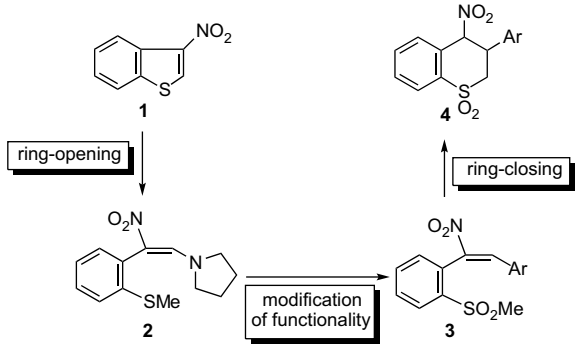
(1*E*,3*Z*)-1-Aryl-4-methanesulfonyl-2-nitro-1,3-butadienes (**8**), derived from the initial ring-opening of 3-nitrothiophene (**5**), have been found to undergo a facile base-induced cyclization leading to thiopyran *S*,*S*-dioxides (**9**), thus furnishing a further example of effective ring-enlargement from 5- to 6-membered sulfur heterocycles. Compounds **9** are obtained as single racemic mixtures in satisfactory yields; they still contain a nitrovinylic moiety, which can be exploited for further modifications targeted to new derivatives endowed with either synthetic or pharmacological potentialities e.g., in the field of L-type Ca^{2+}-channel blockers.

1. Introduction

We have recently shown that the initial ring-opening of 3-nitrobenzothiophene (**1**) with pyrrolidine/$AgNO_3$ in EtOH followed by MeI quenching can lead, after proper modifications of the functionalities of the resulting nitroenamine **2**, to the thiochroman *S*,*S*-dioxides **4** (Scheme 1) in generally more than satisfactory overall yields.[1] The pivotal step of the ring-opening/ring-closing procedure is represented by an intramolecular Michael-type addition of a sulfonyl-stabilized carbanion (**3**$^-$) onto a nitrovinyl moiety.

Significance to the synthesis of **4** is surely provided by the continuous general interest in sulfur heterocycles,[2] justified by their ubiquitous presence both in basic organic chemistry and in biologically or pharmacologically active derivatives.

Aside from their benzocondensed counterparts,[3] the availability of thiopyrans themselves (and/or derivatives therefrom) has recently experienced renewed attention by the scientific community[4] thanks to well-acknowledged applicative potentialities, which encompass their employment as building blocks in organic synthesis[5,6] or as precursors of either natural or suitably designed molecules of biological or medicinal interest;[4c,6] accordingly, the development of original and versatile preparative routes has been fostered, so as to provide chemists and biochemists with more and more variously functionalized structures.



Scheme 1.

On these grounds, within a research project finalized to the synthesis of diverse *O*-, *N*- and/or *S*-heterocycles from nitrothiophenes,[7] we felt it worthwhile evaluating the possibility of targeting the synthetic procedure of Scheme 1 to the thiopyran nucleus, and relevant results are reported herein.

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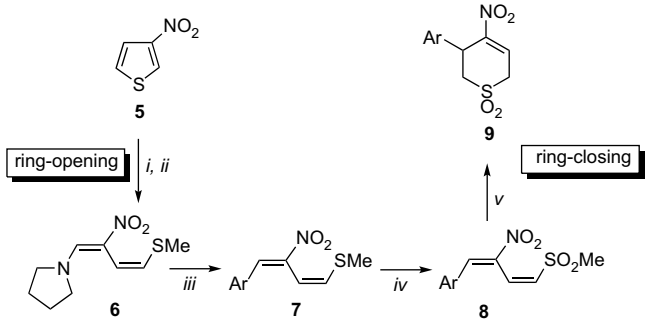
2. Results and discussion

2.1. Ring-opening and ring-closing: from 3-nitrothiophene (5) to thiopyran *S*,*S*-dioxides (9)

The extension of the ring-opening/ring-closing protocol of Scheme 1, aimed at the synthesis of thiopyran derivatives, has been thoroughly investigated on 3-nitrothiophene (**5**) as the model starting heterocycle. As previously reported from our laboratories,[8] the transformation of **5** into sulfonyl derivatives **8** can be effectively performed (Scheme 2) via ring-opening (steps i and ii),[8a] chemo- and stereo-selective replacement of the amino group with aryl Grignard reagents (step iii) and sulfur oxidation (step iv),[8b] under experimental conditions, which closely parallel those relevant to the corresponding steps of Scheme 1.



Scheme 2. (i) Pyrrolidine (2 mol equiv)/$AgNO_3$ (2 mol equiv), abs EtOH, rt, overnight; (ii) excess MeI, 0 °C to rt, 2 h; (iii) ArMgBr (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, 0 °C, 4 h, followed by NH_4Cl quenching.

When treated with the non-nucleophilic base lithium bis(trimethylsilyl)amide (LHMDS) in anhydrous THF at 0 °C, followed by acidic (NH_4Cl) quenching, nitrosulfonylbutadienes **8a–f** did undergo the desired intramolecular Michael-type addition: the final work-up allowing the isolation of the relevant thiopyran *S*,*S*-dioxides (**9a–f**) as crude racemic mixtures. These manifested a rather low stability (see Section 4) both thermal and on chromatographic supports, purification being performed by solubilization in dichloromethane and precipitation with light petroleum at room temperature: brownish solids were generally obtained, characterized by very large melting intervals (with eventual carbonization and gas evolution), which nonetheless allowed full spectroscopic (IR, ^1H and ^{13}C NMR and GC–MS or HRMS) characterization. The brownish solids were used as such for the follow-up chemical transformations described below. The yields reported in Table 1 have been calculated by means of quantitative ^1H NMR spectroscopic analysis on the crude racemic mixtures above (see Section 4).

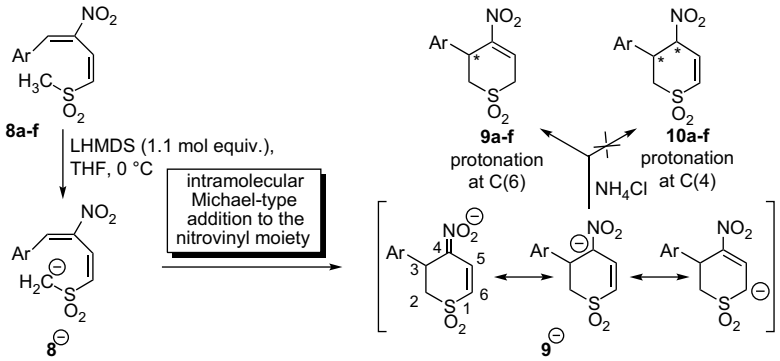
Table 1
Yields (%) of thiopyran *S*,*S*-dioxides **9** from nitrobutadienes **8** (Scheme 2) (calculated on crude racemic mixtures by ^1H NMR spectroscopic analysis)

Substrate	Ar	9
8a	C_6H_5	**9a**: 60
8b	2-MeC_6H_4	**9b**: 73
8c	3-MeC_6H_4	**9c**: 75
8d	4-MeC_6H_4	**9d**: 78
8e	4-$MeOC_6H_4$	**9e**: 66
8f	4-ClC_6H_4	**9f**: 44

The structural assignment to **9** is based on spectroscopic (^1H and ^{13}C NMR) evidence. Particular significance is definitely attached, in this respect, to the presence of only one vinylic proton ($\delta \geq 6.99$ ppm), although in most cases not resolved from the aromatic ones (see Section 4), and of two couples of diastereotopic methylene protons ($^2J \approx 15$ and 18 Hz, respectively).

In principle, after the deprotonation of the methanesulfonyl group of **8** and the intramolecular addition to the nitrovinyl moiety (Scheme 3), the acidic (NH_4Cl) quenching of the resulting resonance-stabilized cyclic anion could lead to either the isolated allylsulfone **9** (as single racemic isomers) or to the isomeric vinylsulfone **10** (as a pair of diastereomers). Actually, the experimental outcome herein lines-up very well with the long-known propensity of conjugated nitronates (i.e., nitronate ions deriving from conjugated nitroalkenes or nitrodienes) to protonate under kinetic control at the terminal C-position of the conjugated system;[9] nonetheless, our case could represent a particular one, as far as the formation of an alternative stabilized system (i.e., the vinylsulfonyl moiety of **10**) could in principle effectively compete. Thus, in order to gain further information on the observed regiochemistry of the protonation step we performed quantum mechanical calculations[10–14] on the species involved, with reference to the model system **a** (Ar=Ph).

In summary, the results show that in **9a**$^-$: (i) the C(6)–SO_2 bond length is significantly shorter (by 0.07 Å) than C(2)–SO_2, supporting a significant sp^2 character of C(6); (ii) C(2)–C(3) and C(3)–C(4) bonds exhibit length values typical of sp^3–sp^3 single bonds (1.52 and 1.55 Å, respectively), while C(4)–NO_2, C(4)–C(5) and C(5)–C(6) are much shorter (1.37, 1.42 and 1.37 Å, respectively); (iii) a C(2′)–C(1′)–C(3)–C(2) dihedral angle of 47.3° indicates that the phenyl group is significantly rotated with respect to the average plane of the thiopyran ring; on the other hand, an O–N–C(4)–C(3) dihedral angle of only 10.9° shows that the nitrogroup is nearly coplanar to it; (iv) the nitrogroup oxygens, C(4) and C(6) host significant negative Mulliken charges (−0.310, −0.367, −0.850 and −0.437, respectively). On the whole, the calculations herein provide the picture of an anion whose negative charge is strongly localized on the C(4)NO_2 moiety and thus, in principle, prone to undergo a kinetically controlled protonation at C(4), in contrast with the herein



Scheme 3.

Table 2
Calculated relative energies (kcal/mol), selected dihedral angles (°) and bond lengths (Å) for the conformations of **9a** and **10a**

Conformation	RHF/6-31G[10]				B3LYP/6-31+G*[a] SCRF-CPCM[11–14]			
	Energy	Ph rotn[b] (°)	NO_2 rotn[c] (°)	C(4)–N (Å)	Energy	Ph rotn[b] (°)	NO_2 rotn[c] (°)	C(4)–N (Å)
9a (eq Ph)	*0.00*[d]	73.4	27.2	1.46	*0.00*[d]	51.3	33.1	1.48
9a (ax Ph)	*1.45*	75.0	22.9	1.47	*1.90*	36.7	−17.3	1.48
trans-**10a** (eq Ph, eq NO_2)	*4.80*	58.1	44.9	1.505	*3.01*	60.4	74.1	1.53
cis-**10a** (eq Ph, ax NO_2)	*4.48*	43.7	63.7	1.51	*3.75*	90.0	59.4	1.55
cis-**10a** (ax Ph, eq NO_2)	*7.46*	30.7	60.1	1.50	*7.20*	37.0	−4.7	1.53
trans-**10a** (ax Ph, ax NO_2)	*8.29*	31.0	14.6	1.52	*8.05*	35.7	78.2	1.54

[a] For the benzene ring a 3-21G basis set was used.
[b] Reported as the C(2′)–C(1′)–C(3)–C(2) torsion angle.
[c] Reported as the O–N–C(4)–C(3) torsion angle.
[d] Reference value.

experimentally observed protonation at C(6); thus, a thermodynamically driven process towards a more stable product must be operative in our case. In order to verify this conclusion, compounds **9**, *trans*-**10** and *cis*-**10** have been studied at both the RHF and the DFT levels[11] for the model system **a** (Ar=Ph), and the results are reported in Table 2.

In any case the energy-minimization protocol has singled out half-chair structures, characterized by a small C–S–C and a large O–S–O angle, as a consequence of substantial negative charges on the oxygen atoms (which exhibit Mulliken charges of −0.6, according to DFT calculations).

The data in Table 2 show that RHF and DFT calculations concordantly place both half-chair conformations of **9a** at an energy level significantly lower than those relevant to either *trans*-**10a** or *cis*-**10a**, thus definitely justifying on thermodynamic grounds the experimentally observed protonation at C(6) with exclusive formation of the nitrovinyl moiety. The stabilization above very likely arises from the conjugative interaction between the nitrogroup and the C(4)–C(5) double bond, whose significance is also mirrored by the low values, exhibited by **9a**, of both the C(4)–NO_2 bond length and the nitrogroup rotation out of the double-bond plane (see Table 2). Evidently, as expected from the known electronic effects of the sulfonyl group,[15] structure **10a** cannot take advantage of a quantitatively comparable resonance stabilization: significant information on the different ability of nitro and sulfonyl groups to give conjugative effects can be gained when considering, in particular, $(\sigma_p^- - \sigma_p)$ values (0.44 and 0.32, respectively) or σ_R^- values (0.41 and 0.31, respectively).[15]

Interestingly enough, the energy values reported in Table 2 show that, whatever the structure under examination (**9a**, *trans*-**10a** or *cis*-**10a**), an axial orientation of the phenyl moiety plays a significant destabilizing role: a reasonable outcome when considering that the 1,3 pseudo-diaxial interaction between a phenyl group and a sulfonyl oxygen is expected to be highly repulsive in both **9a** and **10a** (see Chart 1). Conversely an axial orientation of the nitrogroup in **10a** seems to produce only a minor effect, because the 1,3 di-pseudoaxial interaction with the positively charged hydrogens α to the sulfonyl group could even be not repulsive (see Chart 1). Thus, the half chair of **9** with an equatorial phenyl group represents the overall energy minimum.

The effectiveness of the Michael-type cyclization process has been also investigated by means of DFT calculations on the model **8a**$^-$→**9a**$^-$ system (Ar=Ph; Chart 2), carried out both in the gas phase and in solution (THF: data in brackets).

Actually, the cyclization is characterized by a relatively low activation energy (3.65 and 8.20 kcal/mol in gas phase and in THF, respectively) and by a very favourable energetic balance (−54.0 and −54.3 kcal/mol in gas phase and in THF, respectively), thus suggesting an early transition state (**TS**$^{\#}$) along the reaction coordinate. This hypothesis is strongly supported by the comparison among the calculated distance between the anionic carbon of the SO_2–CH_2^- system and the sp^2 C(1) in the starting *s-cis*-**8a**$^-$ (4.44 Å), the length

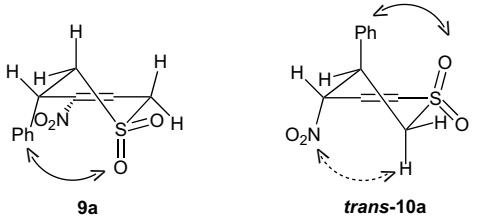


Chart 1. The 1,3 diaxial interactions in the higher-energy half-chair conformation of **9a** and of the hypothetical *trans*-**10a**.

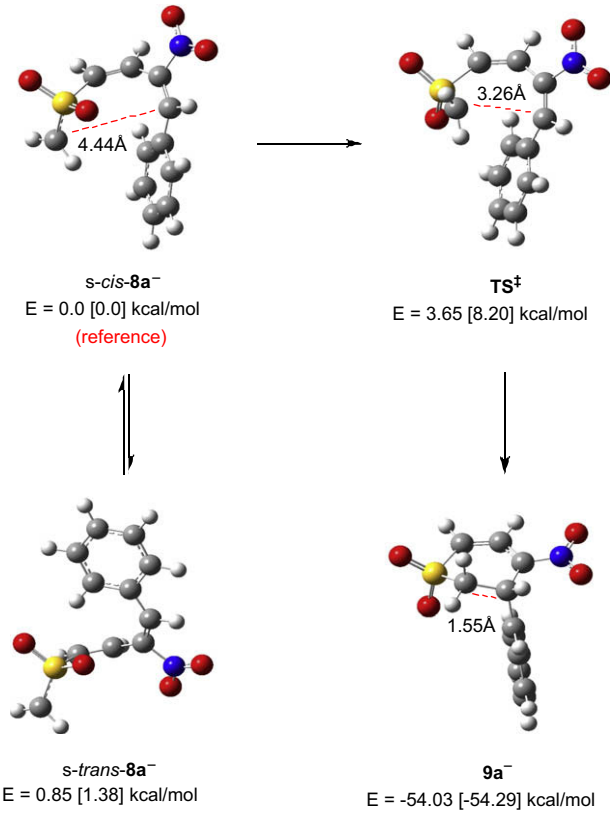


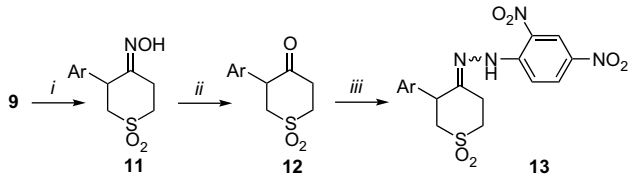
Chart 2.

of the forming C(2)–C(3) bond in the relevant **TS**$^{\#}$ (3.26 Å) and the length of the formed C(2)–C(3) bond in **9a**$^{-}$ (1.55 Å).

Interestingly enough, the *s-cis* conformation necessary for the cyclization to occur results to be slightly favoured over the *s-trans* conformer both in the gas phase and in THF (0.85 and 1.38 kcal/mol, respectively).

2.2. Synthesis of oximes and ketones from thiopyran *S,S*-dioxides 9

The foreseeable versatility of compounds **9**, e.g., due to the nitrovinylic moiety, has been confirmed herein by further transformation of such a functionality via reduction to the oximes **11** (Scheme 4) followed by hydrolysis to the ketones **12**, according to reported methodologies.[16,17] Yields are reported in Table 3. Unfortunately, much as the precursors **9** (see above in the discussion and Section 4), compounds **11** and **12** showed difficulties in their purification due to a relatively low stability, possibly linked to the presence of the sulfonyl group. A satisfactory characterization of **12** (and hence of the precursors **9** and **11**) was eventually obtained by their conversion into the corresponding, thermally stable, 2,4-dinitrophenylhydrazones (**13**), which could be suitably crystallized and fully characterized (see Section 4).



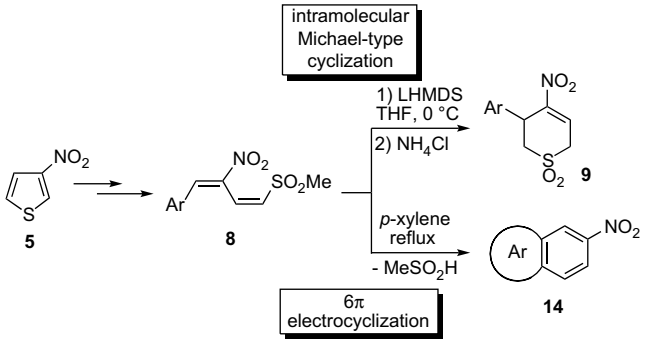
Scheme 4. Functional transformations of thiopyran *S,S*-dioxides **9**. Reagents and conditions: (i) [**9**]: ca. 0.20 M in AcOEt, $SnCl_2 \cdot H_2O$ (2 mol equiv), rt, 1 h; (ii) [**11**]: 0.15 M in CH_3COCH_3/H_2O 10:1, Amberlyst 15, 4 h, reflux; (iii) [**12**]: ca. 0.10 M in EtOH, 2,4-dinitrophenylhydrazine (1.1 mol equiv), 100 °C, 10 min.

3. Conclusions

The results herein significantly enlarge our knowledge on the synthetic applications of nitrothiophenes and of the highly functionalized nitrobutadienic building blocks, which derive from their amine-induced ring-opening.[7] The overall ring-enlargement of Scheme 3 allows access to thiopyran *S,S*-dioxides endowed with residual reactive functionalities, and thus represents a versatile route to molecular arrays whose interest both in synthetic and biological applications has been recently renewed.[4–6]

In this line, particular interest is attached to some recent results on compounds showing a significant activity as L-type Ca^{2+}-channels blockers (LTCCBs):[18] considering that several of them contained a sulfonyl group,[18] and that the nitrogroup is a well known pharmacophore often present in some LTCCBs drugs,[19] as well as in new classes of molecules endowed with promising potential anticancer properties,[20] both nitrothiopyrans **9** and nitrothiochromans **4** (and derivatives thereof) seem promising candidates deserving of closer inspection targeted to the individuation of yet new classes of heterocycles with potential pharmacological activities.

Finally, it should be remarked that the results described above represent just one aspect of the reactivity of the versatile nitrosulfonylbutadienes **8**. Intriguingly enough, the same substrates have been recently found to be appealing precursors of nitrobenzene ring-fused derivatives (**14**, Y: 72–92%; Scheme 5) under different experimental conditions (reflux in *p*-xylene) via an unprecedently mild 6π-electrocyclization driven by a concerted β-elimination of methanesulfinic acid.[8b]



Scheme 5. Dichotomic behaviour of nitrosulfonylbutadienes **8** under different experimental conditions.

Thus, it is surely rewarding that, thanks to a multifaceted, versatile functionalization, a molecular array such as the nitrobutadiene **8** can dichotomically participate in diverse reaction pathways depending on the reaction conditions. As a matter of fact, the involvement of analogous derivatives in yet more types of reactions (e.g., such as Diels–Alder cycloadditions) is presently under investigation and results will be reported in due time.

4. Experimental

4.1. General

^{1}H NMR and ^{13}C NMR spectra were recorded at 200 or 300 MHz and 50 or 60 MHz, respectively; chemical shifts (TMS as internal reference) are reported as δ values (ppm); 1,4-bis(chloromethyl)-benzene was used as internal standard in the quantitative determinations. ESI-MS analyses were recorded on either an Agilent 1100 LC/MSD-SL ion trap mass spectrometer or a Micromass ZOMD Waters instrument. GC–MS were carried out on a HP-5971A instrument, using a HP-1 column (12 m long, 0.2 mm id, 0.33 μm), electron impact at 70 eV, and a temperature of about 170 °C. Only $m/z>33$ were detected, all analyses were performed with a constant He flow of 0.9 ml/min, and with an initial temperature of 70 °C, initial time 2 min, rate 15 °C/min, final T 280 °C, final t 5 min, injection T 200 °C, detector T 280 °C; t_R are in min. HRMS were recorded on a FINNIGAN MAT95XP apparatus. Melting points were determined with a Büchi 535 apparatus and are uncorrected.

4.2. Materials

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 (petroleum ether, ethyl acetate, methylene chloride) being distilled before use. Tetrahydrofuran (THF) was purified by standard methods and distilled over potassium benzophenone ketyl before use. 4-Methoxy- and 4-chlorophenylmagnesium bromides were commercial solutions (0.5 M in THF and 1 M in Et_2O, respectively), titrated[21] just before use. All commercially available reagents were used as received. Compounds **6**,[8a] **7a–d** and **8a–d**[8b] were prepared

Table 3
Yields (%) of compounds **11** and **12** according to Scheme 4, calculated by ^{1}H NMR analysis with respect to an internal standard

Entry	Ar	11	12
1	C_6H_5	**11a**: 72	**12a**: 57
2	2-MeC_6H_4	**11b**: 73	**12b**: 61
3	3-MeC_6H_4	**11c**: 74	**12c**: 62
4	4-MeC_6H_4	**11d**: 73	**12d**: 59
5	4-$MeOC_6H_4$	**11e**: 56	**12e**: 82
6	4-ClC_6H_4	**11f**: 54	**12f**: 81

as previously reported, while **7e**,**f** and **8e**,**f** are new compounds, synthesized according with the same methodology[8b] starting from **6** (0.5 g, 2.33 mmol) and **7e** or **7f** (2 mmol), respectively.

*4.2.1. 1-Methoxy-4-[(1E,3Z)-4-methylsulfanyl-2-nitro-1,3-butadienyl]benzene (**7e**)*

Yield 0.55 g, 93%; yellow oil; ν_{max} (neat) 3007, 2922, 2836, 2616, 2565, 2513, 2319, 2047, 1910, 1639, 1598, 1504, 1456, 1438, 1427, 1384, 1301, 1263, 1220, 1176, 1117, 1018 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.73 (3H, s), 3.86 (3H, s), 6.46 (1H, d, *J* 10.2 Hz), 6.60 (1H, d, *J* 10.5 Hz), 6.92 (2H, half AA′BB′, *J* 8.7 Hz), 7.55 (2H, half AA′BB′, *J* 8.7 Hz), 8.05 (1H, s); ^{13}C NMR ($CDCl_3$) δ 17.56, 55.38, 114.27, 114.69, 123.63, 133.06, 134.56, 138.43, 142.72, 161.68; HRMS calcd for $C_{12}H_{13}NO_3S$: 251.0616; found 251.0614.

*4.2.2. 1-Chloro-4-[(1E,3Z)-4-methylsulfanyl-2-nitro-1,3-butadienyl]benzene (**7f**)*

Yield 0.37 g, 62%; yellow oil; ν_{max} ($CHCl_3$ solution) 3062, 3026, 2996, 2927, 2525, 2317, 1706, 1589, 1514, 1488, 1404, 1359, 1321, 1195, 1092, 1013 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.72 (3H, s), 6.45 (1H, d, *J* 10.5 Hz), 6.62 (1H, d, *J* 10.5 Hz), 7.37 (2H, half AA′BB′, *J* 8.7 Hz), 7.48 (2H, half AA′BB′, *J* 8.4 Hz), 7.99 (1H, s); ^{13}C NMR ($CDCl_3$) δ 13.70, 113.77, 129.08, 129.78, 131.89, 132.88, 136.66, 139.42, 145.23; HRMS calcd for $C_{11}H_{10}ClNO_2S$: 255.0121; found 255.0124.

*4.2.3. 1-[(1E,3Z)-4-Methanesulfonyl-2-nitro-1,3-butadienyl]-4-methoxybenzene (**8e**)*

Yield 0.55 g, 96%; yellow solid, mp 135–136 °C (ethanol); ν_{max} (Nujol) 1649, 1600, 1561, 1503, 1426, 1296, 1269, 1191, 1179, 1141, 1054, 1033 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.02 (3H, s), 3.88 (3H, s), 6.76 (1H, d, *J* 11.7 Hz), 6.92–7.00 (3H, m), 4.48 (2H, half AA′BB′, *J* 8.7 Hz), 8.16 (1H, d, *J* 1.2 Hz); ^{13}C NMR ($CDCl_3$) δ 41.38, 55.58, 114.84, 123.15, 130.89, 133.70, 135.32, 137.97, 139.51, 162.70; HRMS calcd for $C_{12}H_{13}NO_5S$: 283.0514; found 283.0514.

*4.2.4. 1-Chloro-4-[(1E,3Z)-4-methanesulfonyl-2-nitro-1,3-butadienyl]benzene (**8f**)*

Yield 0.57 g, 98%; yellow solid, mp 163–164 °C (ethanol); ν_{max} (Nujol) 1655, 1587, 1522, 1404, 1296, 1141, 1093, 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.02 (3H, s), 6.80 (1H, d, *J* 11.4 Hz), 6.90 (1H, dd, *J* 11.1 and 1.5 Hz), 7.45 (4H, app s), 8.14 (1H, d, *J* 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 41.50, 129.02, 129.61, 130.06, 132.41, 136.34, 136.37, 138.22, 141.96; HRMS calcd for $C_{11}H_{10}ClNO_4S$: 287.0019; found 287.0022.

4.3. Base-induced cyclization of 8 to nitrothiopyrans 1,1-dioxides 9

The appropriate **8** (1 mmol) was dissolved under argon in THF (63 mL) at 0 °C and LHMDS 1 M (1.1 mol equiv, 1.1 mL) was added by syringe under magnetic stirring. After a standard reaction time (4 h), the mixture was poured into saturated aqueous NH_4Cl (150 mL), and extracted with dichloromethane (3×50 mL), the organic extracts being then dried over Na_2SO_4. After filtration, the solvent was evaporated under reduced pressure. Because of high thermolability and instability of **9** on different chromatographic supports (SiO_2 or neutral Al_2O_3), the reported yields have been determined by quantitative ^1H NMR analysis on crude final residues; these were then purified by solubilization in dichloromethane and precipitation with light petroleum. Over the very large melting-range, compounds **9a–f** always showed modification, finally carbonizing with gas evolution.

*4.3.1. 4-Nitro-3-phenyl-3,6-dihydro-2H-thiopyran 1,1-dioxide (**9a**)*

Yield 0.152 g, 60%; pale brown solid (methylene chloride/petroleum ether); ν_{max} (Nujol) 1555, 1529, 1494, 1321, 1253, 1130, 1057 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.29 (1H, dd, *J* 15.0 and 10.4 Hz), 3.52 (1H, ddd, *J* 15.0, 6.3 and 3.5 Hz), 3.88 (1H, dm, *J* 18.6 Hz), 4.13 (1H, br dt, *J* 18.6 Hz), 4.84 (1H, br m), 7.10–7.50 (6H, m); ^{13}C NMR (CDCl3) δ 42.92, 48.63, 53.89, 125.32, 126.94, 128.56, 129.57, 136.66, 151.65; HRMS calcd for $C_{11}H_{11}NO_4S$: 253.0409; found 253.0405.

*4.3.2. 4-Nitro-3-(2-methylphenyl)-3,6-dihydro-2H-thiopyran 1,1-dioxide (**9b**)*

Yield 0.195 g, 73%; pale brown solid (methylene chloride/petroleum ether); ν_{max} (Nujol) 1532, 1329, 1132, 1054 cm^{-1}; ^1H NMR (300, $CDCl_3$) δ 2.48 (3H, s), 3.21 (1H, dd, *J* 15.0 and 10.6 Hz), 3.44 (1H, ddd, *J* 15.0, 6.0 and 3.9 Hz), 3.88 (1H, dm, *J* 18.3 Hz), 4.15 (1H, dt, *J* 18.3 and 2.9 Hz), 5.05 (1H, m), 7.01 (1H, app d), 7.10–7.30 (4H, m); ^{13}C NMR ($CDCl_3$) δ 19.16, 38.93, 48.53, 52.75, 124.91, 125.47, 127.26, 128.46, 131.55, 135.06, 135.55, 152.25; HRMS calcd for $C_{12}H_{13}NO_4S$: 267.0565; found 267.0565.

*4.3.3. 4-Nitro-3-(3-methylphenyl)-3,6-dihydro-2H-thiopyran 1,1-dioxide (**9c**)*

Yield 0.200 g, 75%; pale brown solid (methylene chloride/petroleum ether); ν_{max} (Nujol) 1531, 1317, 1130, 1056 cm^{-1}; ^1H NMR (300, $CDCl_3$) δ 2.33 (3H, s), 3.27 (1H, dd, *J* 15.0 and 10.6 Hz), 3.50 (1H, ddd, *J* 15.0, 6.0 and 3.9 Hz), 3.87 (1H, dm, *J* 18.3 Hz), 4.12 (1H, dt, *J* 18.3 and 3.0 Hz), 4.80 (1H, m), 6.99 (1H, app d), 7.05–7.30 (4H, m); ^{13}C NMR ($CDCl_3$) δ 21.39, 42.93, 48.66, 54.04, 123.90, 124.98, 127.56, 129.39, 129.47, 136.58, 139.50, 151.89; HRMS calcd for $C_{12}H_{13}NO_4S$: 267.0565; found 267.0562.

*4.3.4. 4-Nitro-3-(4-methylphenyl)-3,6-dihydro-2H-thiopyran 1,1-dioxide (**9d**)*

Yield 0.208 g, 78%; pale brown solid (methylene chloride/petroleum ether); ν_{max} (Nujol) 1530, 1322, 1281, 1175, 1131, 1114 cm^{-1}; ^1H NMR (300, $CDCl_3$) δ 2.32 (3H, s), 3.27 (1H, dd, *J* 14.8 and 10.4 Hz), 3.50 (1H, ddd, *J* 14.8, 6.0 and 3.5 Hz), 3.87 (1H, dm, *J* 18.6 Hz), 4.11 (1H, dt, *J* 18.6 and 3.0 Hz), 4.80 (1H, m), 7.05–7.20 (5H, m); ^{13}C NMR ($CDCl_3$) δ 21.07, 42.56, 48.64, 53.96, 124.88, 126.81, 130.22, 133.54, 138.49, 151.90; HRMS calcd for $C_{12}H_{13}NO_4S$: 267.0565; found 267.0564.

*4.3.5. 3-(4-Methoxyphenyl)-4-nitro-3,6-dihydro-2H-thiopyran 1,1-dioxide (**9e**)*

Yield 0.187 g, 66%; pale brown solid (methylene chloride/petroleum ether); ν_{max} (Nujol) 1599, 1509, 1305, 1250, 1176, 1127, 1029 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.26 (1H, dd, *J* 14.7 and 10.2 Hz), 3.50 (1H, ddd, *J* 14.7, 6.0 and 3.6 Hz), 3.78 (3H, s), 3.82–3.92 (1H, m), 4.11 (1H, td, *J* 18.3 and 3.0 Hz), 4.80 (1H, m), 6.87 (2H, half AA′BB′, *J* 8.7 Hz), 7.13 (3H, m); ^{13}C NMR ($CDCl_3$) δ 42.14, 48.60, 53.88, 55.30, 114.87, 124.74, 128.21, 128.33, 151.92, 159.56; GC–MS: t_R 13.86; *m*/*z* (%) 283 (M^+, 47), 266 (14), 236 (19), 218 (24), 202 (72), 172 (78), 157 (57), 149 (81), 134 (100), 128 (62), 121 (93), 115 (62), 102 (15), 91 (49), 77 (39), 64 (34), 51 (21), 39 (22), 30 (7); HRMS calcd for $C_{12}H_{13}NO_5S$: 283.0514; found 283.0511.

*4.3.6. 3-(4-Chlorophenyl)-4-nitro-3,6-dihydro-2H-thiopyran 1,1-dioxide (**9f**)*

Yield 0.127 g, 44%; pale brown solid (methylene chloride/petroleum ether); ν_{max} (Nujol) 1529, 1304, 1130, 1091, 1012 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.26 (1H, dd, *J* 14.4 and 9.9 Hz), 3.52 (1H, ddd, *J* 15.0, 6.0 and 3.3 Hz), 3.91 (1H, dm, *J* 18.0 Hz), 4.12 (1H, dt, *J* 18.6 and 3.3 Hz), 4.85 (1H, m), 7.16 (2H, half AA′BB′, *J* 8.4 Hz), 7.24 (1H, m), 7.35 (2H, half AA′BB′, *J* 8.8 Hz); ^{13}C NMR ($CDCl_3$) δ 42.29, 48.65, 53.61, 125.92, 128.39, 129.78, 134.59, 135.08, 151.08; GC–MS: t_R 13.62; *m*/*z* (%) 287 (M^+, 5) [and 289 $(M+2)^+$, 2] (the isotopic pattern shows the presence of a chlorine atom), 224 (9), 222 (29), 208 (14), 206 (34), 192 (7), 176 (22), 162 (10), 153 (36), 141 (100), 138 (63), 125 (70), 115 (48), 103 (29), 89 (17), 75 (33), 63 (23), 51 (21), 39 (16), 30 (10); HRMS calcd for $C_{11}H_{10}ClNO_4S$: 287.0019; found 287.0014.

4.4. Reduction of 9 to oximes 11

The procedure is a slight modification of a previously reported one.[16] In an Erlenmeyer flask, the appropriate **9** (0.4 mmol) was dissolved in ethyl acetate (2 mL), and $SnCl_2 \cdot 2H_2O$ (0.8 mmol) was added under magnetic stirring. After 1 h at room temperature, the reaction mixture was poured into ice, and the solid product, which separated was filtered under reduced pressure. The obtained crude oximes **11a–f** proved very sensitive to heat and were therefore characterized after washing with petroleum ether in the cold. The reported yields have been determined by quantitative ^{1}H NMR analysis on crude final residues.

*4.4.1. 1,1-Dioxo-3-phenyltetrahydro-1λ^6-thiopyran-4-one oxime (**11a**)*

Yield 0.069 g, 72%; whitish solid; ν_{max} (Nujol) 3275 (br), 1619, 1556, 1306, 1128 cm^{-1}; ^{1}H NMR (300, CD_3COCD_3) δ 2.53–2.66 (1H, m), 3.20–3.37 (3H, m), 3.72 (1H, dt, *J* 15.3 and 4.4 Hz), 3.86 (1H, t, *J* 12.6 Hz), 4.24 (1H, dd, *J* 12.6 and 4.2 Hz), 7.31 (5H, br m), 11.00 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 20.90, 45.39, 48.42, 54.41, 126.67, 127.86, 128.75, 137.90, 153.10; HRMS calcd for $C_{11}H_{13}NO_3S$: 239.0616; found 239.0614.

*4.4.2. 1,1-Dioxo-3-(2-methylphenyl)tetrahydro-1λ^6-thiopyran-4-one oxime (**11b**)*

Yield 0.074 g, 73%; whitish solid; ν_{max} (Nujol) 3280 (br), 1556, 1305, 1176, 1132, 1006 cm^{-1}; ^{1}H NMR (300, CD_3COCD_3) δ 2.26 (3H, s), 2.47–2.59 (1H, m), 3.20–3.39 (3H, m), 3.78–3.96 (2H, dt (*J* 14.8 and 4.2 Hz) and t (*J* 13.2 Hz) partially overlapping), 4.39 (1H, dd, *J* 13.2 and 3.3 Hz), 7.16 (4H, m), 10.13 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 19.02, 21.01, 41.59, 48.50, 54.06, 125.62, 126.54, 127.64, 129.75, 135.76, 136.30, 152.31; HRMS calcd for $C_{12}H_{15}NO_3S$: 253.0773; found 253.0774.

*4.4.3. 1,1-Dioxo-3-(3-methylphenyl)tetrahydro-1λ^6-thiopyran-4-one oxime (**11c**)*

Yield 0.075 g, 74%; whitish solid; ν_{max} (Nujol) 3247 (br), 1608, 1555, 1290, 1122 cm^{-1}; ^{1}H NMR (300, CD_3COCD_3) δ 2.31 (3H, s), 2.54–2.69 (1H, m), 3.17–3.35 (3H, m), 3.71 (1H, dt, *J* 15.9 Hz), 3.84 (1H, t, *J* 12.9 Hz), 4.12–4.24 (1H, m), 7.00–7.30 (4H, br m), 10.15 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 20.93 (two isochronous carbons), 45.39, 48.42, 54.41, 125.83, 127.36, 127.82, 129.43, 136.90, 137.83, 153.17; HRMS calcd for $C_{12}H_{15}NO_3S$: 253.0773; found 253.0771.

*4.4.4. 1,1-Dioxo-3-(4-methylphenyl)tetrahydro-1λ^6-thiopyran-4-one oxime (**11d**)*

Yield 0.074 g, 73%; whitish solid; ν_{max} (Nujol) 3353 (br), 1651, 1557, 1514, 1289, 1241, 1123, 1009 cm^{-1}; ^{1}H NMR (CD_3COCD_3) δ 2.30 (3H, s), 2.50–2.70 (1H, m), 3.16–3.42 (3H, m), 3.69 (1H, dt, *J* 15.4 and 3.6 Hz), 3.82 (1H, t, *J* 13.6 Hz), 4.19 (1H, dd, *J* 12.1 and 3.3 Hz), 7.15 (4H, AA′BB′ system), 10.12 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 20.54, 20.90, 45.07, 48.44, 54.48, 128.46, 128.61, 134.87, 135.84, 153.20; HRMS calcd for $C_{12}H_{15}NO_3S$: 253.0773; found 253.0770.

*4.4.5. 1,1-Dioxo-3-(4-methoxyphenyl)tetrahydro-1λ^6-thiopyran-4-one oxime (**11e**)*

Yield 0.060 g, 56%; whitish solid; ^{1}H NMR (CD_3SOCD_3) δ 2.36–2.47 (1H, m), 3.24–3.40 (3H, m), 3.53 (1H, dt, *J* 14.7 and 3.6 Hz), 3.73 (3H, s), 3.95 (1H, t, *J* 12.9 Hz), 4.12 (1H, dd, *J* 12.6 and 3.3 Hz), 6.86 (2H, half AA′BB′, *J* 9.0 Hz), 7.21 (2H, half AA′BB′, *J* 8.7 Hz), 11.15 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 21.63, 45.45, 49.19, 55.43, 55.74, 114.07, 129.60, 130.53, 154.08, 158.86; HRMS calcd for $C_{12}H_{15}NO_4S$: 269.0722; found 269.0720.

*4.4.6. 3-(4-Chlorophenyl)-1,1-dioxotetrahydro-1λ^6-thiopyran-4-one oxime (**11f**)*

Yield 0.059 g, 54%; whitish solid; ^{1}H NMR (CD_3SOCD_3) δ 2.37–2.47 (1H, m), 3.24–3.40 (3H, m), 3.55 (1H, dt, *J* 15.6 and 4.2 Hz), 4.00 (1H, t, *J* 13.2 Hz), 4.22 (1H, dd, *J* 12.3 and 3.3 Hz), 7.35 (4H, AA′BB′ system), 11.21 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 20.93, 44.74, 48.42, 54.06, 127.82, 130.74, 131.43, 136.98, 135.05; HRMS calcd for $C_{11}H_{12}ClNO_3S$: 273.0226; found 273.0227.

4.5. Hydrolysis of 11 to ketones 12

The procedure is a slight modification of a previously reported one.[17] To a flask equipped with reflux condenser and magnetic stirring bar, a suspension of the appropriate **11** (0.4 mmol) in a mixture acetone/water 10:1 (2.6 mL) was added by Amberlyst 15 (79 mg) and kept at reflux (80 °C) under magnetic stirring. After 4 h, acetone was added and the obtained solution filtered, the removed Amberlyst washed with acetone, the combined organic layers dried over Na_2SO_4 and the solvent removed under reduced pressure. The reported yields have been determined by quantitative ^{1}H NMR analysis on crude final residues; these were then purified by solubilization in dichloromethane and precipitation with light petroleum, their thermal instability preventing the determination of reliable melting points.

*4.5.1. 1,1-Dioxo-3-phenyltetrahydro-1λ^6-thiopyran-4-one (**12a**)*

Yield 0.051 g, 57%; pale brown solid (methylene chloride/light petroleum); ν_{max} (Nujol) 1728, 1601, 1555, 1303, 1128 cm^{-1}; ^{1}H NMR (300, CD_3COCD_3) δ 2.81 (1H, dt, *J* 15.3 and 4.5 Hz), 3.26 (1H, ddd, *J* 15.3, 12.9 and 4.8 Hz), 3.38–3.52 (2H, m), 3.85 (1H, td, *J* 13.5 and 4.4 Hz), 4.15 (1H, t, *J* 13.5 Hz), 4.47 (1H, dd, *J* 13.5 and 4.5 Hz), 7.20–7.50 (5H, br m); ^{13}C NMR (CD_3COCD_3) δ 38.78, 50.64, 53.79, 55.64, 128.28, 129.13, 129.63, 129.93, 202.71; MS (ESI): *m*/*z* 246.9 $(M+Na)^+$, 222.8 (M−1); HRMS calcd for $C_{11}H_{12}O_3S$: 224.0507; found 224.0507.

*4.5.2. 1,1-Dioxo-3-(2-methylphenyl)tetrahydro-1λ^6-thiopyran-4-one (**12b**)*

Yield 0.058 g, 61%; pale brown solid (methylene chloride/light petroleum); ν_{max} (Nujol) 1712, 1557, 1319, 1283, 1121 cm^{-1}; ^{1}H NMR (300, CD_3COCD_3) δ 2.26 (3H, s), 2.85 (1H, app dt, *J* 16.2 Hz), 3.29 (1H, ddd, *J* 16.2, 12.9 and 4.8 Hz), 3.38–3.55 (2H, m), 3.88 (1H, td, *J* 13.2 and 4.2 Hz), 4.17 (1H, t, *J* 13.5 Hz), 4.64 (1H, dd, *J* 13.2 and 4.2 Hz), 7.20 (4H, s); ^{13}C NMR (CD_3COCD_3) δ 19.59, 38.90, 50.14, 50.50, 55.01, 126.77, 128.22, 129.24, 131.08, 135.54, 137.28, 202.49; MS (ESI): *m*/*z* 260.9 $(M+Na)^+$, 236.9 (M−1); HRMS calcd for $C_{12}H_{14}O_3S$: 238.0664; found 238.0661.

*4.5.3. 1,1-Dioxo-3-(3-methylphenyl)tetrahydro-1λ^6-thiopyran-4-one (**12c**)*

Yield 0.059 g, 62%; pale brown solid (methylene chloride/light petroleum); ν_{max} (Nujol) 1717, 1607, 1556, 1316, 1127 cm^{-1}; ^{1}H NMR (300, CD_3COCD_3) δ 2.31 (3H, s), 2.81 (1H, dt, *J* 15.6 and 4.2 Hz), 3.31 (1H, ddd, *J* 15.6, 13.2 and 4.8 Hz), 3.35–3.52 (2H, m), 3.85 (1H, td, *J* 13.4 and 4.3 Hz), 4.14 (1H, t, *J* 13.8 Hz), 4.42 (1H, dd, *J* 13.8 and 4.3 Hz), 7.00–7.30 (4H, br m); ^{13}C NMR (CD_3COCD_3) δ 21.35, 38.78, 50.62, 53.75, 55.67, 126.95, 128.95, 129.04, 130.56, 137.03, 138.55, 202.75; MS (ESI): *m*/*z* 260.9 $(M+Na)^+$, 236.9 (M−1); HRMS calcd for $C_{12}H_{14}O_3S$: 238.0664; found 238.0663.

*4.5.4. 1,1-Dioxo-3-(4-methylphenyl)tetrahydro-1λ^6-thiopyran-4-one (**12d**)*

Yield 0.056 g, 59%; pale brown solid (methylene chloride/light petroleum); ν_{max} (Nujol) 1722, 1555, 1324, 1280, 1128 cm^{-1}; ^{1}H NMR (300, CD_3COCD_3) δ 2.31 (3H, s), 2.80 (1H, dt, *J* 15.3 and 4.5 Hz), 3.24 (1H, ddd, *J* 15.3, 12.9 and 5.3 Hz), 3.35–3.51 (2H, m), 3.83 (1H,

td, *J* 13.4 and 4.3 Hz), 4.12 (1H, t, *J* 13.8 Hz), 4.42 (1H, dd, *J* 13.8 and 4.7 Hz), 7.15 (4H, AA′BB′ system); ^{13}C NMR (CD_3COCD_3) δ 21.03, 38.74, 50.62, 53.43, 55.73, 129.75, 129.77, 134.11, 137.78, 202.84; MS (ESI): *m*/*z* 260.9 $(M+Na)^+$, 236.9 (M−1); HRMS calcd for $C_{12}H_{14}O_3S$: 238.0664; found 238.0664.

*4.5.5. 1,1-Dioxo-3-(4-methoxyphenyl)tetrahydro-1λ^6-thiopyran-4-one (**12e**)*

Yield 0.083 g, 82%; pale brown solid (methylene chloride/light petroleum); ^{1}H NMR (CD_3COCD_3) δ 2.79 (1H, dt, *J* 15.3 and 4.4 Hz), 3.23 (1H, ddd, *J* 15.3, 12.9 and 5.1 Hz), 3.35–3.50 (2H, m), 3.77–3.87 (4H, m), 4.10 (1H, t, *J* 13.5 Hz), 4.41 (1H, dd, *J* 13.8 and 4.8 Hz), 6.90 (2H, half AA′BB′, *J* 8.7 Hz), 7.17 (2H, half AA′BB′, *J* 9.0 Hz); ^{13}C NMR (CD_3COCD_3) δ 38.69, 50.62, 53.03, 55.47, 55.89, 114.51, 129.05, 130.95, 160.03, 203.01; HRMS calcd for $C_{12}H_{14}O_4S$: 254.0613; found 254.0612.

*4.5.6. 3-(4-Chlorophenyl)-1,1-dioxotetrahydro-1λ^6-thiopyran-4-one (**12f**)*

Yield 0.084 g, 81%; pale brown solid (methylene chloride/light petroleum); ^{1}H NMR (CD_3COCD_3) δ 2.81 (1H, dt, *J* 15.6 and 4.2 Hz), 3.26 (1H, ddd, *J* 15.6, 13.5 and 5.1 Hz), 3.42–3.52 (2H, m), 3.85 (1H, td, *J* 13.5 and 4.5 Hz), 4.16 (1H, t, *J* 13.5 Hz), 4.53 (1H, dd, *J* 13.8 and 4.8 Hz), 7.30 (2H, half AA′BB′, *J* 8.7 Hz), 7.39 (2H, half AA′BB′, *J* 8.7 Hz); ^{13}C NMR (CD_3COCD_3) δ 38.69, 50.55, 53.07, 55.30, 129.11, 131.71, 133.64, 135.95, 202.46; HRMS calcd for $C_{11}H_{11}ClO_3S$: 258.0117; found 258.0115.

4.6. Derivatization of ketones 12 as 2,4-dinitrophenylhydrazones 13

To a solution of the appropriate crude **12** (0.8 mmol) in ethanol (2.5 mL), 2,4-dinitrophenylhydrazine (0.88 mmol) in ethanol (5 mL) and HCl 37% (0.75 mL) were added and the reaction mixture kept at 100 °C under magnetic stirring for 10 min. The hydrazones **13a**–**f**, which separated as orange powders, were filtered and crystallized.

*4.6.1. N-(2,4-Dinitrophenyl)-N′-(1,1-dioxo-3-phenyltetrahydro-1λ^6-thiopyran-4-ylidene)hydrazine (**13a**)*

Yield 0.048 g, 15%; orange solid, mp 263–265 °C (ethanol/dioxane); ν_{max} (Nujol) 3326, 1615, 1595, 1500, 1335, 1120 cm^{-1}; ^{1}H NMR (CD_3SOCD_3) δ 2.87–2.98 (1H, m), 3.30 (1H, app dt), 3.49–3.57 (3H, m), 4.05 (1H, t, *J* 12.9 Hz), 4.46 (1H, dd, *J* 12.6 and 3.9 Hz), 7.12 (1H, d, *J* 9.4 Hz), 7.32–7.44 (5H, m), 8.22 (1H, dd, *J* 9.4 and 2.5 Hz), 8.82 (1H, dd, *J* 2.5 Hz), 10.94 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 24.22, 47.39, 48.24, 54.66, 115.47, 122.82, 127.11, 127.98, 128.81, 129.65, 129.87, 137.23, 137.56, 144.72, 155.91; MS (ESI): *m*/*z* 427 $(M+Na)^+$, 403 (M−1); HRMS calcd for $C_{17}H_{16}N_4O_6S$: 404.0791; found 404.0792.

*4.6.2. N-(2,4-Dinitrophenyl)-N′-[1,1-dioxo-3-(2-methylphenyl)-tetrahydro-1λ^6-thiopyran-4-ylidene]hydrazine (**13b**)*

Yield 0.073 g, 22%; orange solid, mp 196–197 °C (ethanol/dioxane); ν_{max} (Nujol) 3331, 1617, 1595, 1559, 1499, 1335, 1310, 1294, 1282, 1192, 1123, 1083 cm^{-1}; ^{1}H NMR (CD_3SOCD_3) δ 2.27 (3H, s), 2.87–3.00 (1H, m), 3.3 ca. (1H, app dt), 3.45–3.65 (3H, m), 4.08 (1H, t, *J* 13.3 Hz), 4.51 (1H, dd, *J* 12.6 and 2.7 Hz), 6.98 (1H, d, *J* 9.6 Hz), 7.20–7.35 (4H, m), 8.18 (1H, dd, *J* 9.6 and 2.1 Hz), 8.80 (1H, d, *J* 2.1 Hz), 10.93 (1H, s); ^{1}H NMR (CD_3COCD_3) δ 2.35 (3H, s), 3.06–3.20 (1H, m), 3.40–3.74 (4H, m), 4.05 (1H, t, *J* 13.4 Hz), 4.72 (1H, dd, *J* 13.4 and 3.8 Hz), 7.15–7.41 (5H, m), 8.16 (1H, dd, *J* 9.6 and 2.4 Hz), 8.93 (1H, d, *J* 2.4 Hz), 11.13 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 19.20, 24.43, 43.65, 48.25, 54.19, 115.24, 122.84, 125.65, 126.97, 127.94, 129.59, 129.78, 129.88, 135.89, 135.96, 137.17, 144.77, 155.55; MS (ESI): *m*/*z* 441 $(M+Na)^+$, 417 (M−1). Anal. Calcd for $C_{18}H_{18}N_4O_6S$ (418.42): C, 51.67; H, 4.34; N, 13.39%. Found: C, 51.54; H, 4.30; N, 13.34%.

*4.6.3. N-(2,4-Dinitrophenyl)-N′-[1,1-dioxo-3-(3-methylphenyl)-tetrahydro-1λ^6-thiopyran-4-ylidene]hydrazine (**13c**)*

Yield 0.092 g, 28%; orange solid, mp 246–247 °C (ethanol/dioxane); ν_{max} (Nujol) 3327, 1616, 1594, 1533, 1500, 1334, 1294, 1192, 1120, 1088 cm^{-1}; ^{1}H NMR (CD_3SOCD_3) δ 2.35 (3H, s), 2.86–2.97 (1H, m), 3.25 (1H, dt, *J* 11.1 and 4.8 Hz), 3.45–3.56 (3H, m), 4.02 (1H, t, *J* 13.2 Hz), 4.40 (1H, dd, *J* 12.3 and 4.2 Hz), 7.14–7.20 (4H, m), 7.29 (1H, t, *J* 7.5 Hz), 8.24 (1H, dd, *J* 9.3 and 2.4 Hz), 8.81 (1H, d, *J* 3.0 Hz), 10.93 (1H, s); ^{1}H NMR (CD_3COCD_3) δ 2.39 (3H, s), 3.07–3.15 (1H, m), 3.43–3.67 (4H, m), 4.00 (1H, t, *J* 12.6 Hz), 4.52 (1H, dd, *J* 12.3 and 3.9 Hz), 7.19–7.39 (5H, m), 8.24 (1H, br d, *J* 9.9 Hz), 8.96 (1H, br s), 11.14 (1H, br s); ^{13}C NMR (CD_3SOCD_3) δ 20.95, 24.19, 47.38, 48.22, 54.76, 115.49, 122.81, 125.90, 127.71, 127.87, 129.44, 129.63, 129.81, 137.01, 137.21, 137.43, 144.75, 155.85; MS (ESI): *m*/*z* 441 $(M+Na)^+$, 417 (M−1); HRMS calcd for $C_{18}H_{18}N_4O_6S$: 418.0947; found 418.0941. Anal. Calcd for $C_{18}H_{18}N_4O_6S$ (418.42): C, 51.67; H, 4.34; N, 13.39%. Found: C, 51.58; H, 4.34; N, 13.33%.

*4.6.4. N-(2,4-Dinitrophenyl)-N′-[1,1-dioxo-3-(4-methylphenyl)-tetrahydro-1λ^6-thiopyran-4-ylidene]hydrazine (**13d**)*

Yield 0.099 g, 30%; orange solid, mp 248–252 °C (ethanol/dioxane); ν_{max} (Nujol) 3328, 1739, 1614, 1596, 1535, 1500, 1360, 1335, 1314, 1294, 1244, 1174, 1138, 1122, 1090, 1063, 1029 cm^{-1}; ^{1}H NMR (300, CD_3SOCD_3) δ 2.34 (3H, s), 2.91 (1H, app q), 3.24 (1H, app dt), 3.40–3.56 (3H, m), 4.01 (1H, t, *J* 12.9 Hz), 4.40 (1H, dd, *J* 12.2 and 3.8 Hz), 7.15–7.28 [5H in all, AA′BB′(*J* 7.8 Hz) and d (*J* 9.6 Hz)], 8.27 (1H, dd, *J* 9.6 and 2.3 Hz), 8.82 (1H, d, *J* 2.3 Hz), 10.94 (1H, s); ^{1}H NMR (CD_3COCD_3) δ 2.39 (3H, s), 3.04–3.17 (1H, m), 3.40–3.69 (4H, m), 3.98 (1H, t, *J* 13.1 Hz), 4.53 (1H, dd, *J* 12.6 and 4.2 Hz), 7.26 (2H, half AA′BB′, *J* 8.0 Hz), 7.34 (2H, half AA′BB′, *J* 8.0 Hz), 7.40 (1H, d, *J* 9.6 Hz), 8.23 (1H, dd, *J* 9.6 and 2.7 Hz), 8.95 (1H, d, *J* 2.7 Hz), 11.20 (1H, br s); ^{13}C NMR (CD_3SOCD_3) δ 20.65, 24.15, 47.03, 48.19, 54.87, 115.56, 122.78, 128.54, 128.59, 129.61, 129.86, 134.49, 136.13, 137.18, 144.73, 156.04; MS (ESI): *m*/*z* 441 $(M+Na)^+$, 417 (M−1); HRMS calcd for $C_{18}H_{18}N_4O_6S$: 418.0947; found 418.0948. Anal. Calcd for $C_{18}H_{18}N_4O_6S$ (418.42): C, 51.67; H, 4.34; N, 13.39%. Found: C, 51.54; H, 4.35; N, 13.34%.

*4.6.5. N-(2,4-Dinitrophenyl)-N′-[1,1-dioxo-3-(4-methoxyphenyl)-tetrahydro-1λ^6-thiopyran-4-ylidene]hydrazine (**13e**)*

Yield 0.081 g, 23%; yellow solid, mp 241–242 °C (ethanol/dioxane); ν_{max} (Nujol) 3330, 1614, 1336, 1116, 1023 cm^{-1}; ^{1}H NMR (CD_3SOCD_3) δ 2.90 (1H, app q), 3.20–3.30 (1H, m), 3.45 (1H, d, *J* 13.5 Hz), 3.50–3.58 (2H, m), 3.79 (3H, s), 3.99 (1H, t, *J* 12.9 Hz), 4.40 (1H, dd, *J* 12.9 and 4.2 Hz), 6.96 (2H, half AA′BB′, *J* 8.7 Hz), 7.21 (1H, d, *J* 9.6 Hz), 7.30 (2H, half AA′BB′, *J* 8.4 Hz), 8.29 (1H, dd, *J* 9.3 and 2.4 Hz), 8.82 (1H, d, *J* 2.7 Hz), 10.95 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 24.16, 46.68, 48.23, 55.00, 55.10, 113.40, 115.58, 122.85, 129.42, 129.62, 129.87, 129.97, 137.19, 144.76, 156.22, 158.24; MS (ESI): *m*/*z* 435 $(M+H)^+$, 457 $(M+Na)^+$. Anal. Calcd for $C_{18}H_{18}N_4O_7S$ (434.47): C, 49.76; H, 4.18; N, 12.90%. Found: C, 49.68; H, 4.16; N, 12.91%.

*4.6.6. N-[3-(4-Chlorophenyl)-1,1-dioxotetrahydro-1λ^6-thiopyran-4-ylidene]-N′-(2,4-dinitrophenyl)hydrazine (**13f**)*

Yield 0.123 g, 35%; yellow solid, mp 249–250 °C (ethanol/dioxane); ν_{max} (Nujol) 3327, 1616, 1594, 1499, 1337, 1312, 1289, 1121, 1090 cm^{-1}; ^{1}H NMR (CD_3SOCD_3) δ 2.91 (1H, app q), 3.24–3.29 (1H, m), 3.50–3.55 (3H, m), 4.03 (1H, t, *J* 12.9 Hz), 4.49 (1H, dd, *J* 12.3 and 3.9 Hz), 7.15 (1H, d, *J* 9.6 Hz), 7.42 (2H, half AA′BB′, *J* 8.7 Hz), 7.47 (2H, half AA′BB′, *J* 8.7 Hz), 8.29 (1H, dd, *J* 9.6 and 2.4 Hz), 8.82 (1H, d, *J* 2.7 Hz), 10.94 (1H, s); ^{13}C NMR (CD_3SOCD_3) δ 24.26, 46.74, 48.26, 54.52, 115.49, 122.86, 127.99, 129.75, 130.01, 130.78, 131.73, 136.62, 137.26, 144.70, 155.86; MS (ESI): *m*/*z* 439 $(M+H)^+$, 461 $(M+Na)^+$. Anal. Calcd for $C_{17}H_{15}ClN_4O_6S$ (438.88): C, 46.52; H, 3.45; N, 12.77%. Found: C, 46.50; H, 3.40; N, 12.70%.

4.7. Computational details

Calculation at the RHF/6-31G has been performed with GAUSSIAN 98;[10] for all other computations the Gaussian 03 package was used. The molecular structures were fully optimized both in the gas phase and in the presence of the solvent at the DFT level. The B3LYP hybrid functional was used in all calculations. To save computational time the phenyl groups have been described using a less accurate (3-21G) basis set with respect the one (6-31+G*) used to describe the other atoms, including the reacting ones. The solvent (THF, ε=7.58) was simulated using the SCRF-CPCM[13] method. The nature of all critical points was ascertained by means of frequency calculation; while for all minima no imaginary frequencies were found, for the **TS**$^{\#}$'s the single imaginary frequency corresponds to a normal mode mainly composed by the length of the forming bond.

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Supplementary data

Full citation of Refs. 10 and 12; energies and geometries for the chemical species reported in Table 2 and in Chart 2. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.10.046.

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