Cycloadditions with 2,2-Dialkyl-3-thioxochroman-4-one *S*-Sulfides Including an Unprecedented [3 + 5] Cycloaddition

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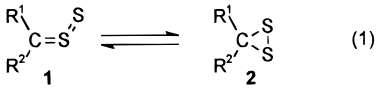
Received July 31, 1998

We report the facile generation of the chroman-4-one-derived thiosulfines **10** under mild conditions by our well-established nucleophilic "unzipping" of the corresponding acetyl α-chloroalkyl disulfides **9** which in turn can be prepared from the corresponding α-chloro sulfenyl chlorides **8**. Spontaneous partial loss of sulfur from **10**, most probably by the disproportionation of **10** to **11** and **12**, generates the expectedly reactive *β*-oxo thioketones **11** which partly dimerize in a precedented Diels−Alder fashion, to give the 1,3,4-oxadithiins **13**, and partly cycloadd to **10** to form the 1,2,4-trithiolanes **14** in a well-precedented fashion. Dimerization of **10** can occur in two competing ways: the precedented nonconcerted [3 + 3] cycloaddition (to give 1,2,4,5-tetrathianes **15**) and the unprecedented concerted [3 + 5] addition to give 1,3,4,5,6-oxatetrathiocins **16**. In the latter interaction one molecule of **10** behaves as a 1,5-dipole and a second molecule as a 1,3-dipole. In one case (**10d**) extensive sulfur scrambling takes place with formation of the 1,2,3,4,5,6-hexathiepane **17d**. It is remarkable how sensitive the reactions of **10** are to minor variations of the simple alkyl substituents in the 2-position. In addition to the usual spectroscopic characterization all isolated key compounds were subjected to X-ray single-crystal structure determinations.

Introduction and Background

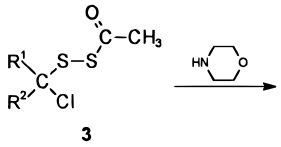
Thiosulfines **1** and dithiiranes **2**, cf. eq 1, are compounds of high topical interest.[1−3] The generation of

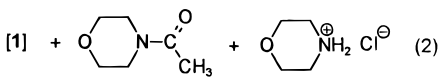


(1)

thiosulfines/dithiiranes **1**/**2** from α-chloroalkanesulfenyl chlorides via acetyl α-chloroalkyl disulfides **3**, in a convenient "unzipping" reaction under mild conditions, cf. eq 2, is a tested and reliable preparative method.[4,5]

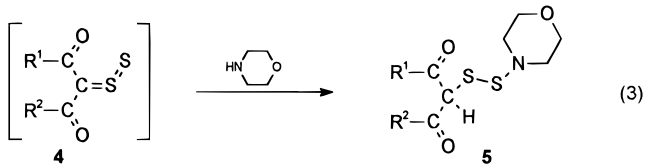
β,*β*′-Dioxo-substituted compounds in the shape of diaroylmethane derivatives exhibited a particular behavior in that the loss of sulfur from the corresponding thiosulfine **4** seen with many other thiosulfines was by and large suppressed. Furthermore, contrary to all other known **1**/**2** systems the observed nucleophilic addition of





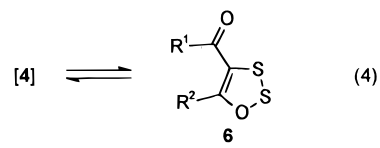
(2)

morpholine giving **5**, cf. eq 3, could be explained either



(3)

in terms of inductive and mesomeric substituent effects on the electron distribution within the thiosulfine moiety, i.e., leading to a preponderance of the resonance contributor **1f**, cf. Scheme 1, or by invoking the intermediacy of a tautomer **6** formed by intramolecular ring closure of **4**, cf. eq 4.



(4)

In our present study we wished to examine the generation and reactive behavior of *β*-monooxo **1**/**2** derived from

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[‡] Chemistry Department, Menoufia University.
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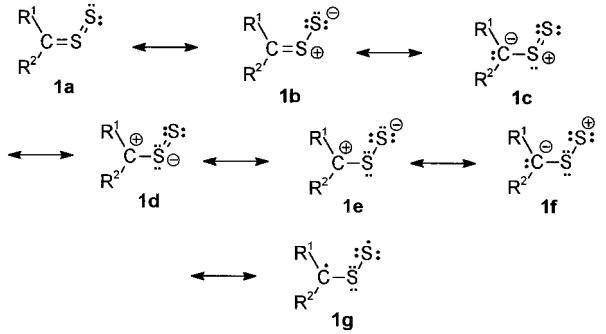
(1) Huisgen, R.; Rapp, J. *Tetrahedron* **1997**, *53*, 939−960 and references cited therein.
(2) Ishii, A.; Akazawa, T.; Ding, M.-X.; Honjo, T.; Maruta, T.; Nakamura, S.-Y.; Nagaya, H.; Ogura, M.; Teramoto, K.; Shiro, M.; Hoshino, M.; Nakayama, J. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 509−523 and literature cited therein.
(3) Fabian, J.; Senning, A. *Sulfur Rep.* **1998**, *21*, 1−42 and literature cited therein.
(4) Senning, A.; Hansen, H. C.; Abdel-Megeed, M. F.; Mazurkiewicz, W.; Jensen, B. *Tetrahedron* **1986**, *42*, 739−746.
(5) Franek, W. *Monatsh. Chem.* **1996**, *127*, 895−907, 909−915.

10.1021/jo981534+ CCC: $15.00
Published on Web 12/04/1998

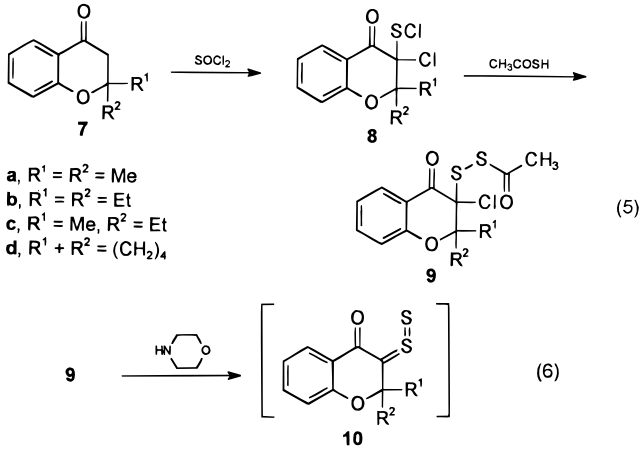
Scheme 1



4-chromanones **7**, i.e., 2,2-dialkyl-3-thioxochroman-4-one *S*-sulfides **10**.

Results and Discussion

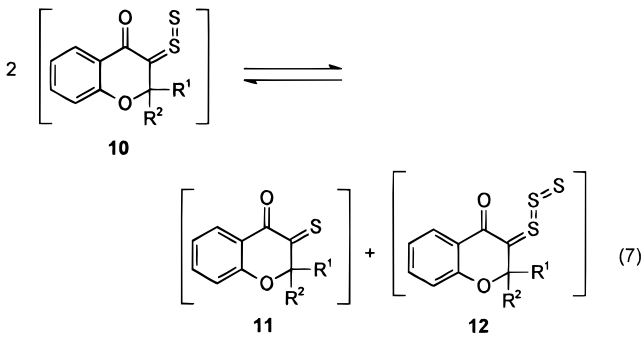
The cycloaddition chemistry ensuing after the smooth formation of **10** according to eqs 5 and 6 is rich and, for



(5)

(6)

so far obscure reasons, noticeably dependent upon the nature of the simple alkyl substituents R^1 and R^2. As shown in eq 7 **10** can disproportionate to the correspond-



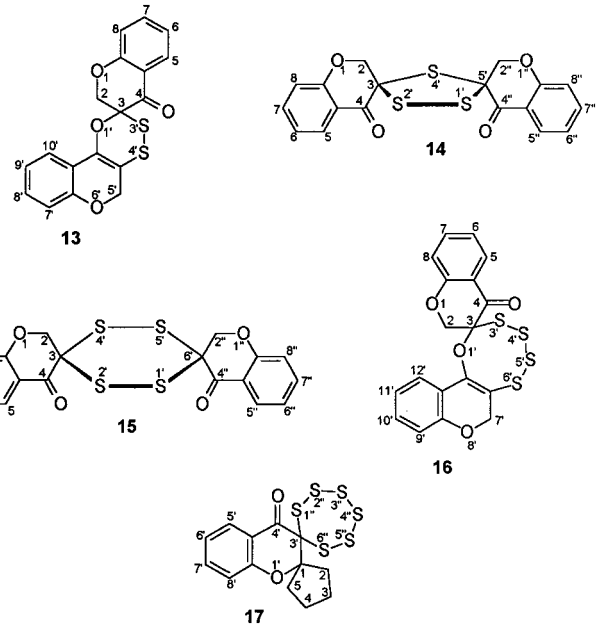
(7)

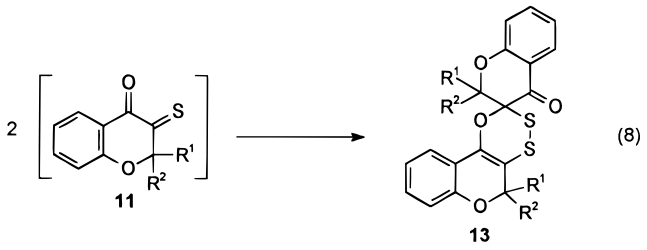
ing, highly reactive, 3-thioxochroman-4-one **11** and its *S*-disulfide **12**. The former can dimerize in a Diels–Alder fashion according to eq 8 and also take part in other cycloaddition reactions such as in eq 9 and, possibly, in eq 12. Disproportionations analogous to (7) have been previously encountered by Huisgen et al.[1] The formation of Diels–Alder dimers such as **13** from α-oxo thioketones has precedent in the work of Crossland.[6] No straightforward evidence for the formation and subsequent fate of **12** can be derived from our present work.

Table 1. Yields of Cycloaddition Products of 10 (%)

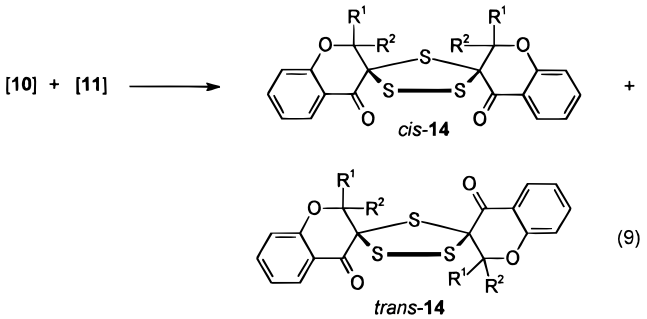
starting material	**13**	*trans*-**14**	*cis*-**15**	**16**	**17**
9a	10	19	9	0	0
9b	0	16	0	16	0
9c	0	38	0	15	0
9d	0	17	6	20	12

Chart 1





(8)



(9)

Table 1 shows the observed formation of heterocyclic products from **10**, generated according to eq 6. The Diels–Alder dimers **13** (see Chart 1) of the corresponding thiones **11** and the 1,2,4-trithiolanes **14** are good indicators of the importance of the disproportionation in eq 7 and, as mentioned before, are well precedented.[6] The 1,2,4-trithiolanes **14** must be formed according to eq 9 in a manner reminiscent of the chemistry which Huisgen *et al.*[1] encountered in the thiation of thioketones. No 1,2,3-trithiolanes were found in our reactions, cf. ref 3. The 1,2,4,5-tetrathianes **15** isolated in our present study

(6) Crossland, I. *Acta Chem. Scand.* **1977**, *B31*, 890–894.

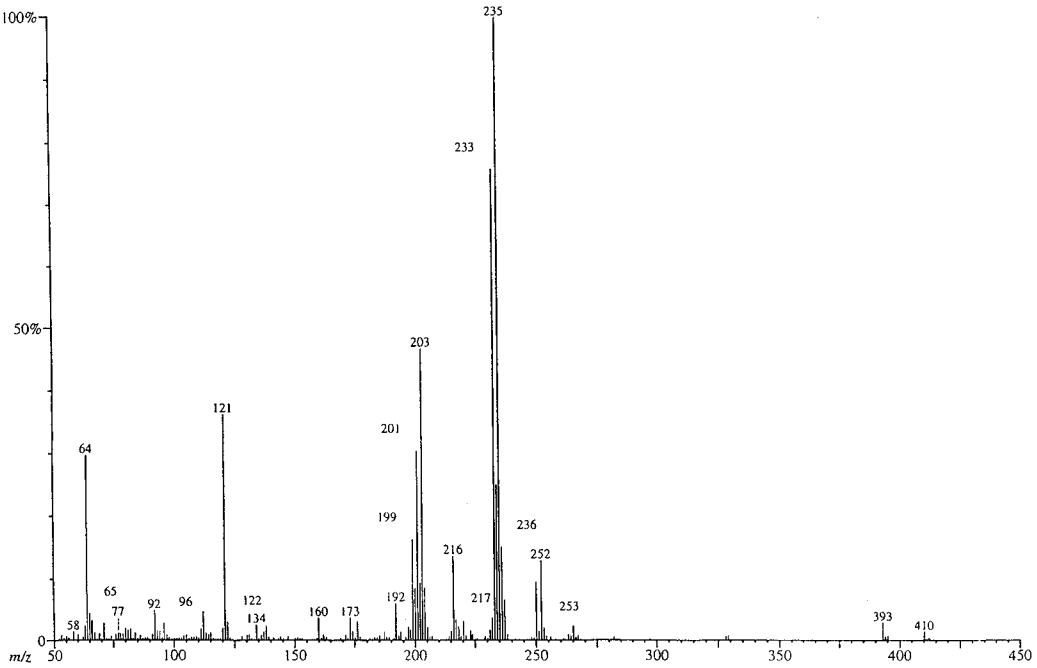
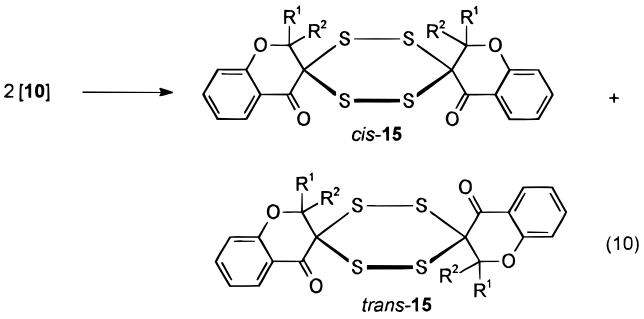


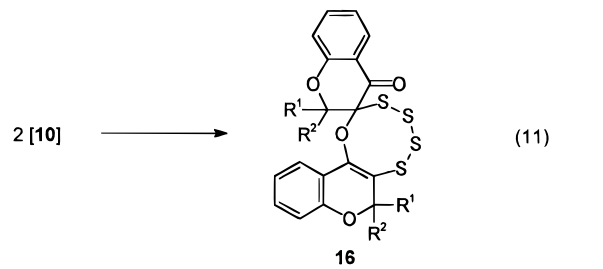
Figure 1. The CI mass spectrum of **17d**.

are most likely formed by a two-step dimerization of **10** according to eq 10 since the concerted [3 + 3] dimerization of **10** is Woodward−Hoffmann forbidden. It should be noted, however, that several authors distrust the possibility of the dimerization of thiosulfines to 1,2,4,5-tetrathianes, cf. ref 3. Again, thiosulfine dimers could in principle also possess the 1,2,3,4-tetrathiane structure, but no such products have been observed by us or others.



(10)

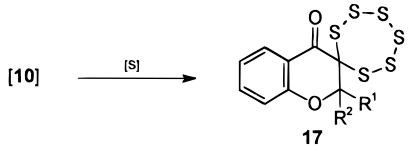
However, in the three cases **10b**−**d** we find the novel reaction mode of a [3 + 5] cycloadditive dimerization according to eq 11, in competition with the previously mentioned reactions. It should be noted that the 1,3,4,5,6-oxatetrathiocins **16** are isomers of the corresponding 1,2,4,5-tetrathianes **15** and thus formed in competition with them. Both the observed [3 + 5] cycloaddition of the Woodward−Hoffmann allowed type [$_{\pi}4_{s}$ + $_{\pi}6_{s}$] and the 1,3,4,5,6-oxatetrathiocin system formed by it are without precedent in the literature. None of the few known [3 + 5] cycloadditions[7] involve conjugated or cumulated π-electron systems such as ours. While we consider the [3 + 5] cycloaddition depicted in eq 11 as the most attractive mechanistic proposal, our data do not rule out the less likely [2 + 6] cycloaddition between **11** and **12**.



(11)

In the case of **10d** also a monomeric product is formed, i.e., the spiro[chroman-2,7′-1,2,3,4,5,6-hexathiepane] **17d**. The formation of sulfur-rich systems such as **17** from relatively simple precursors and unspecified sources of active sulfur has been observed on several occasions.[8]

The formation of **13**−**17** from **10** (eq 12) is the consequence of a remarkably facile sulfur scrambling when one considers the fact that **10** is generated under mild conditions (dilute solution, ambient temperature) and that the reactions are completed within a few minutes.



(12)

The NMR spectra of our compounds by and large follow the pattern predicted by symmetry arguments, i.e., two identical 2,2-substituents in the chroman part are NMR equivalent in the absence of a stereogenic center (as in **7**) but diastereotopic in the presence of one or more stereogenic centers (as in **8**, **9**, and **14**). An interesting case becomes apparent when **15** are examined. Although Fischer projections would predict these compounds to be devoid of chirality, the diastereotopy (apparent from the

(7) Molander, G. A.; Eastwood, P. R. *J. Org. Chem.* **1995**, *60*, 4559−4565.

(8) (a) Jin, Y.-N.; Ishii, A.; Sugihara, Y.; Nakayama, J. *Heterocycles* **1997**, *44*, 255−262. cf.: (b) Steudel, R.; Kustos, M.; Münchow, V.; Westphal, U. *Chem. Ber./Recl.* **1997**, *130*, 757−764. (c) Hartke, K.; Wagner, U. *Chem. Ber.* **1996**, *129*, 663−669. (d) Takeda, N.; Tokitoh, N.; Imakubo, T.; Goto, M.; Okazaki, R. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 2757−2764.

Table 2. Crystal Data for Compounds Whose Structure Has Been Determined by X-ray Crystallography[a]

	compound						
crystal data	**13a**	*trans*-**14a**	*trans*-**14d**	*cis*-**15a**	*cis*-**15d**	**16b**	**16d**
formula	$C_{22}H_{20}O_4S_2$	$C_{22}H_{20}O_4S_3$	$C_{26}H_{24}O_4S_3$	$C_{22}H_{20}O_4S_4$	$C_{26}H_{24}O_4S_4$	$C_{26}H_{28}O_4S_4$	$C_{26}H_{24}O_4S_4$
MW	412.53	444.59	496.67	476.66	528.74	532.77	528.74
mp/°C	145−147	225−230	219−222	236−240	255−260	127−130	155−157
cryst system	monoclinic	monoclinic	monoclinic	monoclinic	tetragonal	triclinic	triclinic
space group	$P2_1/n$	$P2_1/c$	$P2_1/c$	$C2/c$	$I4_1/a$	$P\bar{1}$	$P\bar{1}$
a/Å	10.2025(7)	12.7807(2)	11.5675(3)	16.2480(4)	16.150(2)	7.6946(3)	10.3038(2)
b/Å	9.4499(6)	14.1055(3)	12.5321(2)	11.4790(5)	16.150(2)	12.721(1)	10.6198(2)
c/Å	20.9216(14)	11.4778(3)	16.5050(5)	12.9057(5)	19.148(4)	14.1879(5)	12.3758(3)
α/deg						75.124(2)	79.082(1)
β/deg	95.331(2)	91.665(1)	107.471(1)	116.864(2)		80.053(1)	72.676(1)
γ/deg						77.978(2)	66.029(1)
V/Å^3	2008.5(2)	2068.32(8)	2282.27(10)	2147.29(14)	4994.5(14)	1302.28(8)	1177.64(4)
Z	4	4	4	4	8	2	2
tot. no. of unique reflcns	4364	5269	5616	2350	2202	3977	5702
no. with $I > 2\sigma(I)$	2529	3600	3731	1512	1104	2537	4608
θ-range/deg	1.96−27.00	1.59−29.70	1.85−28.50	2.26−26.99	2.78−24.96	1.50−24.00	1.73−29.58
R (obs data)	757	737	579	608	768	974	460
w*R*2 (all data)	1776	1418	1248	1367	2215	3288	1113

[a] Data, except for that of cis-**15d**, were collected at 296 K on a SMART diffractometer using Mo *K*α radiation. The crystal-to-detector distance was 4.5 cm. For the data collection of cis-**15d** an Enraf-Nonius CAD-4F diffractometer was used. The structures were solved by direct methods (SHELXTL) and refined with the full-matrix least-squares technique.

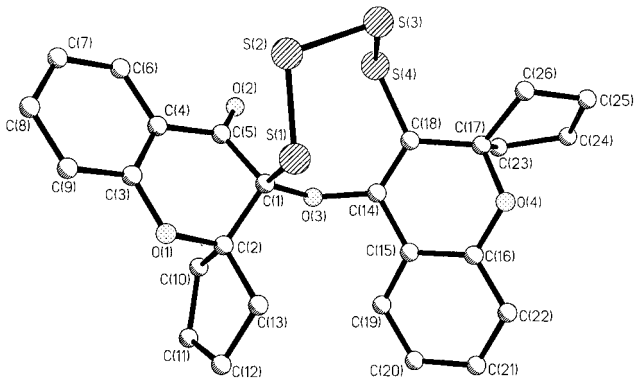


Figure 2. The molecular structure of **16d** as determined by X-ray crystallography.

^{13}C NMR spectrum) of, for instance, C-2 and C-5 of *cis*-**15d** shows that the central 1,2,4,5-tetrathiane ring must be twisted into an unsymmetrical conformation, which is stable in solution, with the consequence that C-3″ and C-6″ have become stereogenic centers. The same is true for *cis*-**15a**. On the other hand, the two benzene rings of *cis*-**15a** are NMR nonequivalent, giving rise to 12 aromatic carbon signals while the two benzene rings of *cis*-**15d** with their total of six aromatic carbon signals appear NMR equivalent, at least within the resolution achievable at 500 MHz. In the case of *trans*-**14a-d** the two benzene rings are NMR equivalent in *trans*-**14a**, *trans*-**14b**, and *trans*-**14d** (with two stereogenic centers each, i.e., C-3′ and C-5 in the two former and C-3″ and C-5″ in the latter) and nonequivalent in **14c** (with four stereogenic centers, i.e., C-2, C-2″, C-3′, and C-5′). Moreover, even in cases where carbon atoms of the two corresponding, more peripheral benzene rings of **14** and **15** are NMR nonequivalent some or all of the carbon atoms of the two corresponding more proximal pyrone systems can be NMR equivalent, for instance in *trans*-**14c**. We find it difficult to rationalize these latter NMR phenomena.

The mass spectra of our compounds are in line with the expected molecular ions and fragmentation patterns. The CI mass spectrum of **17d** is shown in Figure 1. While the weak, but distinct, molecular ions and the clear-cut pattern of sulfur loss confirm the hexathiepane structure of **17d**, the remaining fragmentations are difficult to interpret in terms of a consistent pattern.

The molecular structure of **16d** as determined by X-ray crystallography is shown in Figure 2. Its most prominent feature, the rare tetrasulfide moiety, exhibits the expected bond lengths, bond angles, and dihedral angles. All seven molecular structures which were determined by X-ray crystallography (cf. Table 2) are devoid of undue strain or other anomalies.

Conclusion

We have expanded the scope of our mild "unzipping" of acetyl α-chloroalkyl disulfides **3** to generate thiosulfines **1** as reactive intermediates to the 4-chromanone system **9** and found, contrary to earlier experience with both related and unrelated systems **3**, that the thiosulfines **10** thus generated participate in a plethora of disproportionation and cycloaddition reactions leading to novel sulfur-containing heterocycles **13**−**17**. Among these latter the oxatetrathiocines **16** are unprecedented as is the [3 + 5] cycloaddition of two molecules of **10** leading to them. The precise outcome of the individual reactions depends in a so far obscure manner upon the substituents R^1 and R^2 of **10**. The disproportionation of **10** to the thioketones **11** and thioketone *S*-disulfides **12** plays a key role in our sequence of reactions. Further work will be required to elucidate the dramatic substituent effects in **10**. Also the somewhat puzzling intramolecular symmetries of **14** and **15** in solution as expressed in their NMR spectra deserve future attention.

Experimental Section

General Methods. The IR spectra of solids were recorded with KBr wafers; those of liquids, neat. The ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ with TMS as internal standard. The low-resolution mass spectra were obtained by direct inlet as EI (70 eV) or CI (NH_3) spectra. The elemental analyses were performed by the Microanalytical Laboratory of the Department of Physical Chemistry, University of Vienna, A-1090 Vienna, Austria. The single crystals for the X-ray work (cf. Table 2) were obtained by slow evaporation of the respective hexane/ether (8:1) eluates from the column chromatographic separations (*vide infra*).

2,2-Dialkylchroman-4-ones (7a−d). These syntheses were patterned after a literature procedure.[9] To a solution of 2-hydroxyacetophenone (170.00 g, 1.25 mol) and the appropriate ketone (1.63 mol) in 375 mL of toluene is added pyrrolidine (25.00 g, 0.35 mol) dropwise. The reaction mixture is kept for 1 h and then refluxed for 10 h with a water separator. After the reaction mixture has attained room temperature it is poured onto ice water. The organic layer is subsequently washed with 200 mL of 4 M HCl, 62 mL of 2 M NaOH, and 125 mL water, dried over Na_2SO_4, and evaporated in vacuo. The solid **7a** was recrystallized; the liquids **7b−d** were distilled *in vacuo*.

2,2-Dimethylchroman-4-one (7a): prepared from acetone; mp 88−89 °C (from 2:1 hexane/ether) (lit.[10] mp 88−89 °C); yield 38%; IR $\nu_{C=O}$ 1690 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.49 (6H, s, 2 × CH_3), 2.72 (2H, s, CH_2), 6.90−6.99 (2H, m, 2ArH), 7.40−7.49 (1H, m, ArH), 7.82 (1H, dd, ArH); ^{13}C NMR (125 MHz) δ 26.5 (2C), 48.8, 79.0, 118.2, 120.1, 120.6 (2C), 126.4, 136.0, 159.9, 192.4; MS (EI) *m*/*z* (%) 176 (46, M), 161 (100, M − CH_3), 121 (74, $C_7H_5O_2$), 92 (50, C_6H_4O).

2,2-Diethylchroman-4-one (7b): prepared from pentan-3-one; colorless oil; bp 100 °C/0.5 mmHg; yield 96.46 g (38%); IR $\nu_{C=O}$ 1684 cm^{-1}; ^{1}H NMR (250 MHz) δ 0.95 (6H, t, 2 CH_3-CH_2), 1.68−1.90 (4H, m, 2 CH_3CH_2), 2.75 (2H, s, CH_2), 6.93−6.99 (2H, m, 7-H, 8-H), 7.40−7.49 (1H, m, 6-H), 7.85 (1H, dd, 5-H); ^{13}C NMR (125 MHz) δ 7.5 (2C), 28.2 (2C), 44.7, 83.5, 118.2, 120.3, 120.5, 126.2, 135.9, 159.8, 192.7; MS (EI) *m*/*z* (%) 204 (20, M), 175 (80, M − C_2H_5), 121 (100, $C_7H_5O_2$), 92 (15, C_6H_4O). Anal. Calcd for $C_{13}H_{16}O_2$ (204.27): C, 76.44; H, 7.89. Found: C, 76.39; H 7.91.

2-Ethyl-2-methylchroman-4-one (7c): prepared from butan-2-one; bp 85−90 °C/1.0 mmHg (mentioned in ref 9 without data); yield 71%; IR $\nu_{C=O}$ 1692 cm^{-1}; ^{1}H NMR (500 MHz) δ 0.99 (3H, t, CH_3CH_2), 1.40 (3H, s, CH_3), 1.66−1.85 (2H, m, CH_3CH_2), 2.61−2.80 (2H, m, CH_2), 6.90−7.00 (2H, m, ArH), 7.41−7.50 (1H, m, ArH), 7.82 (1H, dd, ArH); ^{13}C NMR (125 MHz) δ 7.7, 23.1, 31.9, 46.8, 81.2, 118.1, 120.2, 120.4, 126.2, 135.9, 159.7, 192.4; MS (EI) *m*/*z* (%) 190 (35, M), 175 (13, M − CH_3), 161 (75, M − C_2H_5), 121 (100, $C_7H_5O_2$), 92 (30, C_6H_4O).

Spiro[chroman-2,1′-cyclopentan]-4-one (7d): prepared from cyclopentanone; bp 128−130 °C/1.0 mmHg (lit.[9] bp 100−105 °C/0.05 mmHg); yield 80%; IR $\nu_{C=O}$ 1688 cm^{-1}; ^{13}C NMR (50 MHz) δ 23.7 (2C), 37.2 (2C), 46.8, 89.7, 118.3, 120.5, 120.8, 126.5, 135.7, 160.1, 192.9; MS (EI) *m*/*z* (%) 202 (20, M), 173 (45, M − C_2H_5), 121 (100, $C_7H_5O_2$), 92 (20, C_6H_4O).

(*RS*)-3-Chloro-2,2-dialkyl-4-oxochroman-3-sulfenyl Chlorides (8a−d). A general procedure for the conversion of active methylene compounds to α-chloroalkanesulfenyl chlorides[6,11] was followed. Ketone **7** (0.130 mol) is dissolved in thionyl chloride (108 g, 0.910 mol) and the mixture stirred overnight. Removal of excess thionyl chloride *in vacuo* affords a dark brown viscous oil which is crystallized or distilled *in vacuo*.

(*RS*)-3-Chloro-2,2-dimethyl-4-oxochroman-3-sulfenyl chloride (8a): yellow crystals; mp 84−85 °C (lit.[11] mp 84.5−85.5 °C); yield 88%.

(*RS*)-3-Chloro-2,2-diethyl-4-oxochroman-3-sulfenyl chloride (8b): yellow crystals; mp 47−50 °C; obtained by evaporation of a filtered petroleum ether (bp 40−60 °C) solution of the crude product, yield 79%; IR $\nu_{C=O}$ 1709 cm^{-1}; ^{1}H NMR (250 MHz) δ 0.90 (3H, t, CH_3CH_2), 1.25 (3H, t, CH_3CH_2), 1.70−2.38 (4H, m, 2 CH_3CH_2), 6.99−7.02 (1H, m, ArH), 7.09−7.15 (1H, m, ArH), 7.51−7.60 (1H, m, ArH), 7.99 (1H, dd, ArH); ^{13}C NMR (125 MHz) δ 8.0, 9.3, 25.2, 28.6, 88.3, 88.8, 117.8, 118.1, 122.2, 128.5, 136.6, 157.0, 180.1; MS (EI) *m*/*z* (%) 304 (15, M), 269 (30, M − Cl), 233 (15, M − H − Cl_2), 121 (100, $C_7H_5O_2$). Anal. Calcd for $C_{13}H_{14}Cl_2O_2S$ (305.22): C, 51.18; H, 4.59; S, 10.51. Found: C, 51.19; H, 4.62; S, 10.66.

(2*RS*,3*RS*)-3-Chloro-2-ethyl-2-methyl-4-oxochroman-3-sulfenyl chloride (8c): yellow crystals; mp 103−105 °C (lit.[11] mp 103.5−105.5 °C); yield 77%.

(*RS*)-3-Chloro-4-oxospiro[chroman-2,1′-cyclopentane]-3-sulfenyl chloride (8d): yellow crystals; mp 74−76 °C; yield 67%; IR $\nu_{C=O}$ 1703 cm^{-1}; ^{1}H NMR (250 MHz) δ 1.77−2.55 (8H, m, 4 CH_2), 6.92 (1H, dd, ArH), 7.09−7.18 (1H, m, ArH), 7.50−7.60 (1H, m, ArH), 8.00 (1H, dd, ArH); ^{13}C NMR (125 MHz) δ 24.7, 24.9, 34.4, 35.3, 86.6, 96.0, 118.3, 118.6, 122.5, 128.9, 136.4, 157.5, 179.9; MS (EI) *m*/*z* (%) 302 (9, M), 267 (7, M − Cl), 121 (100, $C_7H_5O_2$). Anal. Calcd for $C_{13}H_{12}Cl_2O_2S$ (303.21): C, 51.49, H, 3.98, S, 10.57. Found: C, 51.77, H, 4.03, S, 10.71.

Acetyl (*RS*)-3-Chloro-2,2-dialkyl-4-oxochroman-3-yl Disulfides (9a−d). A general procedure was followed.[4] Equimolar amounts of **8** and thioacetic acid are dissolved in CCl_4 and kept at 50−60 °C until the reaction is complete as judged by TLC. After evaporation of the solvent **9** is obtained by recrystallization from petroleum ether (bp 40−60 °C).

Acetyl (*RS*)-3-chloro-2,2-dimethyl-4-oxochroman-3-yl disulfide (9a): colorless crystals; mp 87−88 °C; yield 83%; IR $\nu_{C=O}$ 1698, 1750 cm^{-1}; ^{1}H NMR (250 MHz) δ 1.55 (3H, s, Me), 1.85 (3H, s, Me), 2.40 (3H, s, Me), 6.90 (1H, dd, ArH), 7.09−7.17 (1H, m, ArH), 7.52−7.60 (1H, m, ArH), 7.85 (1H, dd, ArH); ^{13}C NMR (125 MHz) δ 22.2, 24.1, 28.8, 85.4, 85.4, 118.0, 118.7, 122.1, 128.6, 136.4, 157.0, 180.6, 190.9; MS (CI) *m*/*z* (%) 334 (100, M + NH_4^+), 317 (38, M + H^+), 252 (20, M − S_2). Anal. Calcd for $C_{13}H_{13}ClO_3S_2$ (316.83): C, 49.28, H 4.14; S, 20.24. Found: C, 49.46, H, 4.17; S, 20.16.

Acetyl (*RS*)-3-chloro-2,2-diethyl-4-oxochroman-3-yl disulfide (9b): colorless crystals; mp 85−6 °C; yield 66%; IR $\nu_{C=O}$ 1699, 1750 cm^{-1}; ^{1}H NMR (250 MHz) δ 0.85 (3H, t, CH_3-CH_2), 1.25 (3H, t, CH_3CH_2), 1.76−2.16 (2H, m, CH_3CH_2), 2.38−2.45 (2H, m, CH_3CH_2), 2.42 (3H, s, Me) 6.99 (1H, d, ArH), 7.08−7.18 (1H, m, ArH), 7.58−7.61 (1H, m, ArH), 7.89 (1H, d, ArH); ^{13}C NMR (125 MHz) δ 8.2, 9.3, 25.1, 28.1, 28.8, 87.0, 88.3, 117.9, 118.9, 122.0, 128.4, 136.3, 157.0, 180.6, 191.1; MS (CI) *m*/*z* (%) 362 (100, M + NH_4^+), 345 (30, M + H^+), 280 (10, M − S_2). Anal. Calcd for $C_{15}H_{17}ClO_3S_2$ (344.88): C, 52.24; H, 4.97; Cl,10.28; S, 18.59. Found: C, 52.29; H, 5.07; Cl,10.39; S, 18.53.

Acetyl (2*RS*,3*RS*)-3-chloro-2-ethyl-2-methyl-4-oxochroman-3-yl disulfide (9c): colorless crystals; mp 110−111 °C; yield 96%; IR $\nu_{C=O}$ 1705, 1743 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.18 (3H, t, CH_3CH_2), 1.45 (3H, s, Me), 2.13−2.22 (1H, m, CH_aH_b), 2.39 (3H, s, CH_3CO), 2.47−2.58 (1H, m, CH_aH_b), 6.98 (1H, dd, ArH), 7.09−7.12 (1H, m, ArH), 7.51−7.59 (1H, m, ArH), 7.92 (1H, dd, ArH); ^{13}C NMR (125 MHz) δ 7.1, 18.0, 28.6, 28.8, 86.9, 117.9, 118.0 (2C), 118.7, 128.4, 136.3, 156.9, 180.6, 190.8; MS (CI) *m*/*z* (%) 348 (100, M + NH_4^+), 331 (86, M + H^+). Anal. Calcd for $C_{14}H_{15}ClO_3S_2$ (330.85): C, 50.82, H, 4.57, S, 19.38. Found: C, 50.87, H, 4.43, S, 19.03.

Acetyl (*R,S*)-3-chloro-4-oxospiro[chroman-2,1′-cyclopentan]-3-yl disulfide (9d): colorless crystals; mp 122−123 °C; yield 88%; IR $\nu_{C=O}$ 1695, 1748 cm^{-1}; ^{1}H NMR (250 MHz) δ 1.75−2.61 (8H, m, 4 CH_2), 2.41 (3H, s, Me), 6.92 (1H, dd, ArH), 7.08−7.18 (1H, m, ArH), 7.52−7.60 (1H, m, ArH), 7.91 (1H, dd, ArH); ^{13}C NMR (125 MHz) δ 24.7, 25.2, 34.3, 35.5, 28.7, 85.2, 96.1, 118.3, 119.0, 122.2, 128.2, 136.2, 157.5, 180.5, 190.9; MS (CI) *m*/*z* (%) 360 (90, M + NH_4^+), 343 (100, M + H^+), 278 (25, M − S_2). Anal. Calcd for $C_{15}H_{15}ClO_3S_2$ (342.87): C, 52.55, H, 4.40, S, 18.70. Found: C, 52.44, H, 4.42, S, 18.56.

Reaction of 9a−d with Morpholine. Compound **9** (0.02 mol) was dissolved in 50 mL of ether (or chloroform in the case of **9d**), cooled in an ice bath, and treated, under stirring, with 10.44 g (0.12 mol) of morpholine, dissolved in 25 mL of ether. The rate of the addition was adjusted so as to prevent any appreciable rise in the temperature of the reaction mixture. Then the reaction mixture was extracted three times with water, and the organic phase was dried over $CaCl_2$, filtered, and evaporated *in vacuo*. The remaining crude product was column chromatographed on silica gel (Merck silica gel 60, particle size 0.040−0.063 mm) with hexane/ether (8:1) as eluent.

The following products (in the order of elution) were obtained, cf. Table 1 which also lists the yields: from **9a**, **13a**, *trans*-**14a**, and *cis*-**15a**; from **9b**, **16b** and *trans*-**14b**; from **9c**, **16c** and *trans*-**14c**; from **9d**, **17d**, **16d**, *trans*-**14d**, and *cis*-**15d**.

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2,2,5′,5′-Tetramethylspiro[chroman-3,2′-2*H*-chromeno-[3,4-*e*][1,3,4]oxadithiin]-4-one (13a): yellow crystals; mp 145−147 °C; IR $\nu_{C=O}$ 1700 cm^{-1}; ^{1}H NMR (250 MHz) δ 1.55 (3H, s, Me), 1.60 (3H, s, Me), 1.70 (3H, s, Me), 1.77 (3H, s, Me), 6.85−7.95 (8H, m, 8 ArH); ^{13}C NMR (125 MHz) δ 21.5, 23.3, 26.0, 26.2, 79.5, 83.8, 90.5, 107.5, 116.9, 117.9, 119.1, 119.5, 120.3, 121.0, 121.9, 127.9, 129.8, 135.9, 144.2, 152.2, 157.4, 181.9; MS (EI) *m*/*z* (%) 412 (0.7, M), 397 (0.7, M − CH_3), 206 (40, $C_{11}H_{10}O_2S$), 86 (100, C_4H_6S). Anal. Calcd for $C_{22}H_{20}O_4S_2$ (412.53): C, 64.05, H, 4.89, S, 15.55. Found: C, 63.96, H, 4.80, S, 15.59.

***trans*-2,2,2″,2″-Tetramethyldispiro[chroman-3,3′-[1,2,4]-trithiolane-5′,3″-chroman]-4,4″-dione (*trans*-14a):** colorless crystals; mp 225−230 °C; IR $\nu_{C=O}$ 1688 cm^{-1}; ^{1}H NMR (250 MHz) δ 1.58 (6H, s, 2 Me), 2.18 (6H, s, 2 Me), 6.95 (2H, dd, 2 ArH), 7.04−7.12 (2H, m, 2 ArH), 7.46−7.57 (2H, m, 2 ArH), 7.99 (2H, dd, 2 ArH); ^{13}C NMR (125 MHz) δ 25.0 (2C), 25.7 (2C), 84.3 (2C), 91.2 (2C), 118.1 (2C), 118.9 (2C), 122.0 (2C), 128.2 (2C), 135.9 (2C), 157.2 (2C), 182.3 (2C); MS (EI) *m*/*z* (%) 444 (60, M), 380 (5, M − S_2), 365 (10, M − CH_3S_2), 324 (16, $C_{15}H_{16}O_2S_3$), 260 (20, $C_{15}H_{16}O_2S$), 161 (100), 86 (98, C_4H_6S). Anal. Calcd for $C_{22}H_{20}O_4S_3$ (444.59): C, 59.43, H, 4.53, S, 21.64. Found: C, 59.46, H, 4.47, S, 21.31.

***trans*-2,2,2″,2″-Tetraethyldispiro[chroman-3,3′-[1,2,4]-trithiolane-5′,3″-chroman]-4,4″-dione (*trans*-14b):** colorless crystals; mp 214−17 °C; IR $\nu_{C=O}$ 1700 cm^{-1}; ^{1}H NMR (500 MHz) δ 0.91−1.01 (6H, m, 2 × CH_3), 1.22−1.35 (6H, m, 2 × CH_3), 1.80−2.15 (2H, m, CH_3CH_2), 2.57−2.68 (4H, m, 2 × CH_3CH_2), 6.98 (2H, dd, 2 ArH), 7.02−7.10 (2H, m, 2 ArH), 7.48−7.55 (2H, m, 2 ArH), 7.98 (2H, dd, 2 ArH); ^{13}C NMR (125 MHz) δ 8.9 (2C), 9.4 (2C), 27.4 (2C), 28.1 (2C), 88.1 (2C), 92.9 (2C), 117.9 (2C), 119.4 (2C), 121.8 (2C), 128.0 (2C), 135.7 (2C), 157.1 (2C), 182.5 (2C); MS (EI) *m*/*z* (%) 500 (50, M), 436 (8, M − S_2), 407 (8, M − C_2H_5S), 380 (5, $C_{19}H_{24}O_2S_3$), 316 (3, $C_{19}H_{24}O_2S$), 162 (100), 114 (61, $C_6H_{10}S$). Anal. Calcd for $C_{26}H_{28}O_4S_3$ (500.70): C, 62.37; H, 5.64; S, 19.21. Found: C, 62.39; H, 5.69; S, 19.19.

***trans*-2,2″-Diethyl-2,2″-dimethyldispiro[chroman-3,3′-[1,2,4]trithiolane-5′,3″-chroman]-4,4″-dione (*trans*-14c):** colorless crystals; mp 216−219 °C; IR $\nu_{C=O}$ 1700 cm^{-1}; ^{1}H NMR (500 MHz) δ 0.90−0.95 (3H, m, CH_3CH_2), 1.18−1.20 (3H, m, CH_3CH_2), 1.53−1.62 (4H, m, CH_3 + CH_aH$_b$), 2.06−2.15 (4H, m, CH_3 + CH$_a$H$_b$), 2.52−2.69 (2H, m, CH_3CH_2), 6.98 (2H, dd, 2 ArH), 7.06−7.10 (2H, m, 2 ArH), 7.49−7.52 (2H, m, 2 ArH), 7.99 (2H, dd, 2 ArH); ^{13}C NMR (125 MHz) δ 7.5, 7.8, 20.6, 20.7, 28.9, 29.8, 85.9 (2C), 86.4 (2C), 117.9, 118.0, 119.1, 119.4, 121.9, 122.0, 128.1, 128.2, 135.9 (2C), 156.8, 157.1, 182.3 (2C); MS (EI) *m*/*z* (%) 472 (20, M), 408 (2, M − S_2), 379 (6, M − $C_2H_5S_2$), 352 (4, $C_{17}H_{20}O_2S_3$), 288 (4, $C_{17}H_{20}O_2S$), 100 (100, C_5H_8S). Anal. Calcd for $C_{24}H_{24}O_4S_3$ (472.65): C, 60.99, H, 5.12, S, 20.35. Found: C, 61.16, H, 5.12, S, 20.12.

***trans*-Tetraspiro[cyclopentane-1,2′-chroman-3′,3″-[1,2,4]-trithiolane-5″,3‴-chroman-2‴,1⁗-cyclopentane]-4′,4‴-dione (*trans*-14d):** colorless crystals; mp 219−222 °C; IR $\nu_{C=O}$ 1701 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.65−2.40 (14H, m, 7 CH_2), 3.35−3.61 (2H, m, CH_2), 6.92 (2H, dd, 2 ArH), 7.08−7.10 (2H, m, 2 ArH), 7.45−7.51 (2H, m, 2 ArH), 8.00 (2H, dd, 2 ArH); ^{13}C NMR (125 MHz) δ 25.0 (2C), 25.3 (2C), 35.7 (2C), 38.4 (2C), 90.7 (2C), 95.4 (2C), 118.3 (2C), 119.3 (2C), 122.0 (2C), 128.5 (2C), 135.8 (2C), 157.9 (2C), 182.6 (2C); MS (EI) *m*/*z* (%) 496 (35, M), 432 (8, M − S_2), 376 (16, $C_{19}H_{20}O_2S_3$), 312 (21, $C_{19}H_{20}O_2S$), 112 (100, C_6H_8S). Anal. Calcd for $C_{26}H_{24}O_4S_3$ (496.67): C, 62.88, H, 4.87, S, 19.37. Found: C, 62.98, H, 4.81, S, 19.24.

***cis*-2,2,2″,2″-Tetramethyldispiro[chroman-3,3′-[1,2,4,5]-tetrathiane-6′,3″-chroman]-4,4″-dione (*cis*-15a):** colorless crystals; mp 236−240 °C; IR $\nu_{C=O}$ 1688 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.50 (6H, s, 2 Me), 1.65 (3H, s, Me), 1.88 (3H, s, Me), 6.87−7.09 (4H, m, ArH), 7.46−7.52 (2H, m, ArH), 7.85 (1H, dd, ArH), 7.99 (1H, dd, ArH); ^{13}C NMR (125 MHz) δ 21.9, 23.8, 24.9, 25.5, 63.3 (2C), 80.5, 86.1, 117.9, 118.1, 118.8, 119.4, 121.4, 122.0, 127.5, 128.0, 136.1, 136.3, 157.1, 158.5, 184.7, 188.3; MS (EI) *m*/*z* (%) 444 (13, M − S), 365 (5, M − CH_3S_3), 324 (6, $C_{15}H_{16}O_2S_4$), 260 (5, $C_{14}H_{12}O_3S$), 86 (100, C_4H_6S); MS (CI) *m*/*z* (%) 494 (3, M + NH_4^+), 477 (8, M + H^+), 207 (100, $C_{11}H_{11}O_2S$). Anal. Calcd for $C_{22}H_{20}O_4S_4$ (476.66): C, 55.44, H, 4.23, S, 26.91. Found: C, 57.12, H, 4.36, S, 23.69. Repeated attempts to obtain better elemental analyses failed. However, on the strength of the spectroscopic data and the X-ray structure determination, we have no doubts as to the identity of *cis*-**15a**.

***cis*-Tetraspiro[cyclopentane-1,2′-chroman-3′,3″-[1,2,4,5]-tetrathiane-6″,3‴-chroman-2‴,1⁗-cyclopentane]-4′,4‴-dione (*cis*-15d):** colorless crystals; mp 255−260 °C; IR $\nu_{C=O}$ 1693 cm^{-1}; ^{1}H NMR (250 MHz) δ 1.75−2.71 (16H, m, 8 CH_2), 6.88 (2H, dd, 2 ArH), 7.03−7.10 (2H, m, 2 ArH), 7.45−7.54 (2H, m, 2 ArH), 7.98 (2H, dd, 2 ArH); ^{13}C NMR (125 MHz) δ 24.3 (2C), 24.6 (2C), 33.8 (2C), 34.2 (2C), 71.9 (2C), 96.9 (2C), 118.1 (2C), 119.8 (2C), 122.0 (2C), 128.3 (2C), 135.9 (2C), 157.5 (2C), 184.5 (2C); MS (CI) *m*/*z* (%) 529 (1, M + H^+), 497 (w, M + H^+ − S), 465 (0.2, M + H^+ − S_2), 235 (100). Anal. Calcd for $C_{26}H_{24}O_4S_4$ (528.74): C, 59.06, H, 4.58, S, 24.26. Found: C, 59.25, H, 4.55, S, 24.07.

2,2,7′,7′-Tetraethylspiro[chroman-3,2′-2*H*-chromeno-[3,4-*g*][1,3,4,5,6]oxatetrathiocin]-4-one (16b): yellow crystals; mp 127−130 °C; IR $\nu_{C=O}$ 1704 cm^{-1}; ^{1}H NMR (250 MHz) δ 0.99 (6H, m, 2 CH_3), 1.09−1.19 (6H, m, 2 CH_3), 1.72−2.32 (8H, m, 4 CH_2), 6.75−7.91 (8H, m, 8 ArH); ^{13}C NMR (125 MHz) δ 8.1, 8.6, 8.9, 9.2, 22.8, 27.1, 31.9, 32.4, 85.9, 87.4, 91.9, 105.0, 118.3, 118.3, 120.1, 120.5, 120.7, 121.8, 127.8, 129.7, 135.7, 135.9, 144.6, 153.8, 157.0, 181.8; MS (EI) *m*/*z* (%) 500 (0.7, M − S), 436 (0.1, M − S_3), 380 (4, $C_{19}H_{24}O_2S_3$), 162 (100). Anal. Calcd for $C_{26}H_{28}O_4S_4$ (532.77): C, 58.62; H, 5.29; S, 24.07. Found: C, 59.01; H, 5.33; S, 23.45.

2,7′-Diethyl-2,7′-dimethylspiro[chroman-3,2′-2*H*-chromeno[3,4-*g*][1,3,4,5,6]oxatetrathiocin]-4-one (16c). This compound was obtained as a mixture of diastereomers: yellow crystals; mp 132−135 °C; IR $\nu_{C=O}$ 1697 cm^{-1}; ^{1}H NMR (250 MHz) δ 0.98−1.22 (6H, m, 2 CH_3CH_2), 1.60−1.75 (6H, m, 2 Me), 1.81−2.33 (4H, m, 2 CH_3CH_2), 6.79−7.30 (6H, m, 6 ArH), 7.49−7.52 (1H, m, ArH), 7.40 (1H, dd, ArH); MS (CI) *m*/*z* (%) 505 (2, M + H^+), 473 (100, M + H^+ − S), 472 (12, M − S), 409 (1, M + H^+ − S_3), 238 (5, $C_{12}H_{12}O_2S$ + NH_4^+), 221 (67). Anal. Calcd for $C_{24}H_{24}O_4S_4$ (504.67): C, 57.11; H, 4.79; S, 25.41. Found: C, 57.09; H, 4.85; S, 25.19.

Trispiro[cyclopentane-1,2′-chroman-3′,2″-2*H*-chromeno-[3,4-*g*][1,3,4,5,6]oxatetrathiocin-7″,1‴-cyclopentan]-4′-one (16d): yellow crystals; mp 155−157 °C; IR $\nu_{C=O}$ 1715 cm^{-1}; ^{1}H NMR (250 MHz) δ 1.49−2.49 (16H, m, 8 CH_2), 6.75−7.99 (8H, m, ArH); ^{13}C NMR (125 MHz) δ 23.7, 23.9, 24.1, 24.3, 33.2, 34.1, 35.8, 36.4, 88.8, 89.8, 94.4, 105.6, 117.0, 118.1, 119.6, 120.2, 120.6, 121.0, 122.0, 128.2, 130.0, 135.8, 144.7, 152.4, 157.8, 184.4; MS (CI) *m*/*z* (%) 529 (4, M + H^+), 497 (100, M + H^+ − S). Anal. Calcd for $C_{26}H_{24}O_4S_4$ (528.74): C, 59.06, H, 4.58, S, 24.26. Found: C, 59.13, H, 4.43, S, 24.27.

Dispiro[cyclopentane-1,2′-chroman-3′,7″-[1,2,3,4,5,6]-hexathiepan]-4′-one (17d): colorless crystals; mp 160−162 °C; IR $\nu_{C=O}$ 1680 cm^{-1}; ^{1}H NMR (500 MHz) δ 1.69−2.35 (8H, m, 4 CH_2), 6.88 (1H, dd, ArH), 7.04−7.11 (1H, m, ArH), 7.47−7.56 (1H, m, ArH), 7.92 (1H, dd, ArH); ^{13}C NMR (125 MHz) δ 24.3, 24.6, 35.5, 36.6, 96.4, 96.6, 118.5, 119.4, 122.1, 128.5, 136.6, 157.6, 184.3; MS (CI) *m*/*z* (%) 410 (1, M + NH_4^+), 393 (3, M + H^+), 235 (100). Anal. Calcd for $C_{13}H_{12}O_2S_6$ (392.63): C, 39.77, H, 3.08, S, 48.99. Found: C, 40.32, H, 3.11, S, 48.36.

Acknowledgment. A grant from the Egyptian Government under the Channel Systems to F.A.G.E.-E. is gratefully acknowledged. This work was also supported by the Danish Research Councils (SNF). Technical support by Mrs. Jytte Grove-Rasmussen, Department of Organic Chemistry, Technical University of Denmark, is highly appreciated.

Supporting Information Available: Tables of complete crystallographic data (38 pages). This material is contained in libraries of microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO981534+