Reductive Opening of Thiophthalan: A New Route To Functionalized Sulfur-Containing Compounds†

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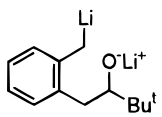
Introduction

Sulfur-containing compounds are important in organic chemistry in both theoretical and physical applications.[1] In the case of sulfur-bearing carbanion derivatives, only the α-substituted intermediates have been widely used because of their stability and ready preparation by direct deprotonation.[2] Little chemistry has been reported for other sulfur-containing carbanions, due to their difficult synthesis and instability.[3] On the other hand, and in keeping with our continued interest in functionalized organolithium intermediates and their applications in organic synthesis,[4] we have recently developed a new and potent lithiation methodology[5] using a catalytic amount of arene [usually naphthalene or 4,4′-di-*tert*-butylbiphenyl (DTBB)] as an electron carrier, which has allowed us to prepare very reactive lithiated intermediates. Thus, we could have prepared alkyllithium compounds from nonhalogenated precursors[6] (mesylates,[6a] sulfates,[6b,c] phosphates,[6d] nitriles,[6e] thioethers,[5] phenylsulfones,[6f,g] phenylsulfoxides,[6g] as well as allylic and benzylic alcohols or their silylated derivatives[6h]), very reactive oxygenated and nitrogenated functionalized organolithium compounds through chlorine−lithium exchange[7] or through reductive opening of saturated heterocycles[8] (aziridines,[8a,b] azetidines,[8c] tetrahydrofuran,[8d] dioxolanes,[8e,f] phthalan,[8g] and isochroman[8h]) and polylithiated synthons from polychlorinated precursors.[9] A recent communication on the reductive cleavage of thiochroman[10] prompts this report on the application of the above mentioned arene-catalyzed lithiation procedure to the reductive opening of thiophthalan. Thereby, a wide range of functionalized sulfur-containing molecules have become accessible through the corresponding sulfurated organolithium intermediates.

Results and Discussion

After 30 min, the reaction between thiophthalan (**1**; easily prepared from α,α′-dibromo-*o*-xylene and sodium sulfide[11]) and an excess of lithium powder (1:18 molar ratio) and a catalytic amount of DTBB (1:0.1 molar ratio, 5 mol %) in THF at −78 °C led to a solution of dianion intermediate **2**, which when treated with different electrophiles [H_2O, D_2O, Pr^iCHO, Bu^tCHO, PhCHO, $(CH_2)_4$-CO, PhCOMe] at the same temperature for 15 min and after hydrolysis with water, yielded the expected functionalized thiols **3a**−**h**. When using carbon dioxide as the electrophilic reagent, thiolactone **3i** was directly obtained after workup (Scheme 1 and Table 1).

The reaction shown in Scheme 1 has to be performed at low temperature in order to prepare products **3**. As was already observed in the reductive opening of phthalan,[8g] when the temperature was allowed to rise to 20 °C, a second benzylic lithiation took place. Therefore after reaction with pivalaldehyde under the reaction conditions shown above, and after warming the reaction mixture to room temperature, the new dianion intermediate **4** was formed, which reacted with water or deuterium oxide, giving products **5**. This process was not studied in depth because the resulting products of type **5** are the same as those already prepared from phthalan.[8g]



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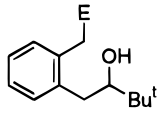


5a : E = H (74%)
5b : E = D (56%)

Of the products **3**, we find those corresponding to carbonyl compound derivatives **3c**−**h** especially interesting, because they can be converted into sulfur-containing heterocycles. Thus, treatment of compounds **3e**−**h** with 85% phosphoric acid in refluxing toluene gave the expected thioisochromans **6e**−**h**. Only for the isobutyraldehyde or pivalaldehyde derivatives **3c** and **3d** did we obtain products resulting from rearrangement processes. While compound **3c** yielded not only the expected product **6c**, but also the seven-membered ring **7c**, in the case of starting compound **3d** only the rearranged thioisochroman derivative **6′d** was isolated (Scheme 2 and Table 2). The preparation of compounds **6** represents a two-step homologation of the starting precursor thiophthalan (**1**).

† This paper is dedicated to Professor Robert B. Bates for his fundamental contributions to carbanion chemistry.

(1) For a monography, see: *Organic Sulfur Chemistry*; Bernardi, F.; Csizmadia, I. G.; Mangini, A., Eds.; Elsevier: Amsterdam, 1985.

(2) See, for instance: Bates, R. B.; Ogle, C. A. *Carbanion Chemistry*; Springer Verlag: Berlin, 1983; p 17.

(3) (a) Screttas, C. G.; Micha-Screttas, M. *J. Org. Chem.* **1978**, *43*, 1064. (b) Screttas, C. G.; Micha-Screttas, M. *J. Org. Chem.* **1979**, *44*, 713. (c) Almena, J.; Foubelo, F.; Yus, M. *Tetrahedron* **1995**, *51*, 11883.

(4) For a review on functionalized organolithium compounds, see: Nájera, C.; Yus, M. *Trends Org. Chem.* **1991**, *2*, 155.

(5) Yus, M.; Ramón, D. J. *J. Chem. Soc., Chem. Commun.* **1991**, 398.

(6) (a) Guijarro, D.; Mancheño, B.; Yus, M. *Tetrahedron* **1992**, *48*, 4593. (b) Guijarro, D.; Mancheño, B.; Yus, M. *Tetrahedron Lett.* **1992**, *33*, 5597. (c) Guijarro, D.; Guillena, G.; Mancheño, B.; Yus, M. *Tetrahedron* **1994**, *50*, 3427. (d) Guijarro, D.; Mancheño, B.; Yus, M. *Tetrahedron* **1994**, *50*, 8551. (e) Guijarro, D.; Yus, M. *Tetrahedron* **1994**, *50*, 3447. (f) Guijarro, D.; Yus, M. *Tetrahedron Lett.* **1994**, *35*, 2965. (g) Alonso, E.; Guijarro, D.; Yus, M. *Tetrahedron* **1995**, *51*, 2699. (h) Alonso, E.; Guijarro, D.; Yus, M. *Tetrahedron* **1995**, *51*, 11457.

(7) (a) Yus, M.; Ramón, D. J. *J. Org. Chem.* **1992**, *57*, 750. (b) Guijarro, A.; Ramón, D. J.; Yus, M. *Tetrahedron* **1993**, *49*, 469. (c) Gil, J. F.; Ramón, D. J.; Yus, M. *Tetrahedron* **1993**, *49*, 4923. (d) Guijarro, A.; Yus, M. *Tetrahedron Lett.* **1993**, *34*, 3487. (e) Ramón, D. J.; Yus, M. *Tetrahedron* **1993**, *49*, 10103. (f) Ramón, D. J.; Yus, M. *Tetrahedron* **1993**, *49*, 7115. (g) Bachki, A.; Foubelo, F.; Yus, M. *Tetrahedron Lett.* **1994**, *35*, 7643.

(8) (a) Almena, J.; Foubelo, F.; Yus, M. *Tetrahedron Lett.* **1993**, *34*, 1649. (b) Almena, J.; Foubelo, F.; Yus, M. *J. Org. Chem.* **1994**, *59*, 3210. (c) Almena, J.; Foubelo, F.; Yus, M. *Tetrahedron* **1994**, *50*, 5775. (d) Ramón, D. J.; Yus, M. *Tetrahedron* **1992**, *48*, 3585. (e) Gil, J. F.; Ramón, D. J.; Yus, M. *Tetrahedron* **1993**, *49*, 9535. (f) Gil, J. F.; Ramón, D. J.; Yus, M. *Tetrahedron* **1994**, *50*, 3437. (g) Almena, J.; Foubelo, F.; Yus, M. *Tetrahedron* **1995**, *51*, 3351. (h) Almena, J.; Foubelo, F.; Yus, M. *Tetrahedron* **1995**, *51*, 3365.

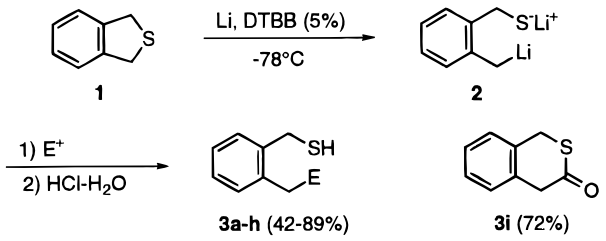
(9) (a) Ramón, D. J.; Yus, M. *Tetrahedron Lett.* **1992**, *33*, 2217. (b) Guijarro, A.; Yus, M. *Tetrahedron Lett.* **1993**, *34*, 2011. (c) Gomez, C.; Ramón, D. J.; Yus, M. *Tetrahedron* **1993**, *49*, 4117. (d) Guijarro, A.; Yus, M. *Tetrahedron Lett.* **1994**, *35*, 253. (e) Guijarro, A.; Yus, M. *Tetrahedron* **1994**, *50*, 7857. (f) Guijarro, A.; Yus, M. *Tetrahedron* **1994**, *50*, 13269. (g) Guijarro, A.; Yus, M. *Tetrahedron* **1995**, *51*, 231. (h) Huerta, F. F.; Gómez, C.; Guijarro, A.; Yus, M. *Tetrahedron* **1995**, *51*, 3375.

(10) Cohen, T.; Chen F.; Kulinski, T.; Florio, S.; Capriati, V. *Tetrahedron Lett.* **1995**, *36*, 4459.

(11) (a) King, G.; Higgins, S. J. *J. Chem. Soc., Chem. Commun.* **1994**, 825. (b) Harpp, D. N.; MacDonald, J. G. *Tetrahedron Lett.* **1984**, *25*, 703.

0022-3263/96/1961-1859$12.00/0

Scheme 1



[E^+= H_2O, D_2O, Pr^iCHO, Bu^tCHO, PhCHO, $(CH_2)_4CO$, PhCOMe]

Table 1. Preparation of Compounds 3 from Thiophthalan 1

entry	electrophile E^+	product **3**[a] no.	E	yield (%)[b]	R_f[c]
1	H_2O	**3a**	H	89	0.18[d]
2	D_2O	**3b**	D	80[e]	0.18[d]
3	Pr^iCHO	**3c**	Pr^iCHOH	49	0.26
4	Bu^tCHO	**3d**	Bu^tCHOH	62	0.38
5	PhCHO	**3e**	PhCHOH	42	0.21
6	Me_2CO	**3f**	Me_2COH	74	0.14
7	$(CH_2)_4CO$	**3g**	$(CH_2)_4COH$	65	0.23
8	PhCOMe	**3h**	PhC(OH)Me	51	0.27
9	CO_2	**3i**	−	72	0.38[f]

[a] All products **3** were >95% pure (GLC and/or 300 MHz ^{1}H NMR). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting thiophthalan **1**. [c] Silica gel, hexane/ethyl acetate: 5/1. [d] Silica gel, hexane. [e] >90% deuterium from mass spectrum and 75 MHz ^{13}C NMR. [f] Mp 71−72 °C (pentane/dichloromethane).

Scheme 2

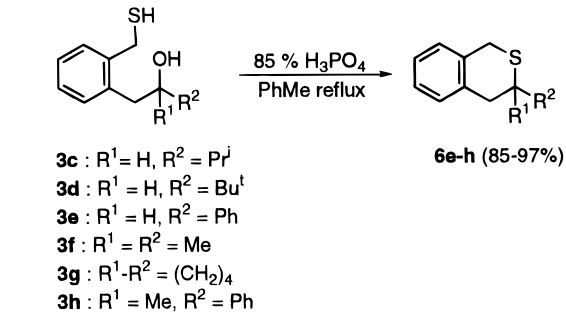


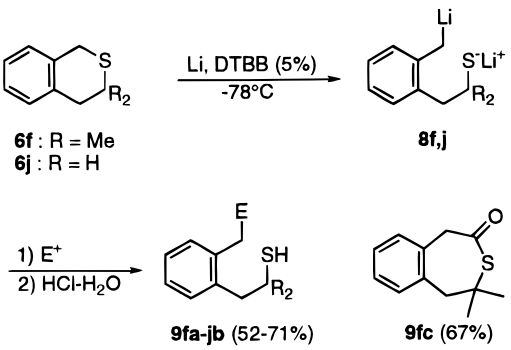
Table 2. Preparation of Compounds 6

entry	starting material	product[a] no.	yield (%)[b]	R_f[c]
1	**3c**	**6c** + **7c**	51 (2:3)	0.17[d] + 0.61
2	**3d**	**6′d**[e]	35	0.38[d]
3	**3e**	**6e**	97	0.60
4	**3f**	**6f**	89	0.66
5	**3g**	**6g**	85	0.22
6	**3h**	**6h**	94	0.67

[a] All products **6** and **7c** were >94% pure (GLC and/or 300 MHz ^{1}H NMR). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **3**. [c] Silica gel, hexane/ethyl acetate: 5/1. [d] Silica gel, hexane. [e] A *ca.* 30% of another product of unknown structure was also isolated.

In the last part of this study we considered the reductive opening of thioisochromans **6f** (prepared as described above) and **6j** (easily prepared from 2-phenylethanethiol and paraformaldehyde in the presence of hydrochloric acid[12]). Applying the procedure shown in Scheme 1 to both of these starting materials, the corresponding dianion intermediates **8** were prepared which, after condensation with different electrophiles [D_2O, Bu^tCHO, Me_2CO, $(CH_2)_4CO$] and final hydrolysis with water, led to the expected products **9fa**−**jb**. After workup, the carbonation of intermediate **8f** yielded thiolactone **9fc** directly (Scheme 3 and Table 3).

Scheme 3



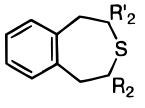
[E^+= D_2O, Bu^tCHO, Me_2CO, $(CH_2)_4CO$]

Table 3. Preparation of Compounds 9

entry	starting material	electrophile E^+	product[a] no.	R	E	yield (%)[b]	R_f[c]
1	**6f**	D_2O	**9fa**	Me	D	71[d]	0.20[e]
2	**6f**	Me_2CO	**9fb**	Me	Me_2COH	52	0.22
3	**6f**	CO_2	**9fc**	Me	−	67	0.43
4	**6j**	Bu^tCHO	**9ja**	H	Bu^tCHOH	57	0.34
5	**6j**	$(CH_2)_4CO$	**9jb**	H	$(CH_2)_4COH$	55	0.17

[a] All products **9** were >95% pure (GLC and/or 300 MHz ^{1}H NMR). [b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **6**. [c] Silica gel, hexane/ethyl acetate: 5/1. [d] >95% deuterium from mass spectrum and 75 MHz ^{13}C NMR. [e] Silica gel, hexane.

In the case of hydroxy thiols **9fb** and **9jb**, cyclization under acidic conditions (see Scheme 2) was carried out, thus isolating seven-membered ring thioethers **10**.



10fb (76%)
10jb (90%)

In conclusion, the chemistry described in this paper offers an easy and versatile approach to a wide range of sulfur-containing acyclic and cyclic compounds.

Experimental Section

General. For general information see reference 8. Starting material **1**[11] and **6j**[12] were prepared according to the literature procedures. High resolution mass spectra were performed at the corresponding service at the University of Valencia.

Preparation of Compounds 3 from Thiophthalan 1. General Procedure. To a blue suspension of lithium powder (0.125 g, 18.0 g atoms) and a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (0.027 g, 0.10 mmol) in THF (8 mL) at −78 °C was added thiophthalan (**1**; 1 mmol) under argon, and the mixture was stirred for 30 min at the same temperature. The corresponding electrophile (1.5 g mmol; 0.5 mL in the case of

(12) Böhme, H.; Tils, L.; Unterhalt, P. *Chem. Ber.* **1964**, *19*, 179.

H_2O or D_2O; CO_2 was bubbled for 1 h) was added. The mixture was stirred at the same temperature for 15 min and was hydrolyzed at −78 °C with water. The resulting mixture was extracted with ethyl acetate. The organic layer was dried over anhyd Na_2SO_4 and evaporated (15 mmHg). The residue was then purified by column chromatography (silica gel; hexane/ethyl acetate) to yield pure products **3a**−**h**. When the electrophile was CO_2, after having hydrolyzed the mixture with water at −78 °C it was basified with 2.5 M NaOH and extracted with ethyl acetate. The aqueous layer was then acidified with 3 M HCl and extracted with ethyl acetate. The organic layer was dried over anhyd Na_2SO_4 and evaporated (15 mmHg). The resulting residue was purified by column chromatography (silica gel; hexane/ethyl acetate) to yield pure compounds **3**. Yields and R_f values are included in Table 1; analytical and spectroscopic data as well as literature references follow.

2-Methylbenzylmercaptan (3a):[13] IR (film) 2560 cm^{-1}; ^1H NMR δ 1.62 (t, J = 7.3 Hz, 1H), 2.37 (s, 3H), 3.69 (d, J = 7.3 Hz, 2H), 7.13−7.21 (m, 4H); ^{13}C NMR δ 18.9, 26.8, 126.3, 127.3, 128.5, 130.5, 135.7, 139.0; MS m/z 138 (M^+, 2%), 45 (100).

2-(Deuteriomethyl)benzylmercaptan (3b): IR (film) 2540 cm^{-1}; ^1H NMR δ 1.64 (t, J = 7.0 Hz, 1H), 2.36−2.38 (m, 2H), 3.73 (d, J = 7.0 Hz, 2H), 7.15−7.24 (m, 4H); ^{13}C NMR δ 18.7 (t, J_{CD} = 19.5 Hz), 26.8, 126.4, 127.3, 128.6, 130.6, 135.7, 139.1; MS m/z 139 (M^+, 47%), 106 (100); HRMS calcd for C_8H_9DS 139.0566, found 139.0570.

1-[2-(Mercaptomethyl)phenyl]-3-methyl-2-butanol (3c):[14] IR (film) 3700−3100, 2520 cm^{-1}; ^1H NMR δ 1.02 (d, J = 6.7 Hz, 6H), 1.69−1.85 (m, 3H), 2.69 (dd, J = 14.0, 10.1 Hz, 1H), 2.90 (dd, J = 14.0, 3.0 Hz, 1H), 3.36−3.84 (m, 3H), 7.16−7.27 (m, 4H); ^{13}C NMR δ 17.5, 18.7, 26.2, 33.7, 36.9, 77.2, 126.9, 127.4, 129.4, 130.6, 137.0, 139.7; MS m/z 176 ($M^+ - H_2S$, 1%), 104 (100).

1-[2-(Mercaptomethyl)phenyl]-3,3-dimethyl-2-butanol (3d):[14] IR (film) 3620−3240, 2540 cm^{-1}; ^1H NMR δ 1.02 (s, 9H), 1.64 (br s, 1H), 1.77 (t, J = 7.0 Hz, 1H), 2.63 (dd, J = 13.8, 10.7 Hz, 1H), 2.95 (dd, J = 13.8, 2.1 Hz, 1H), 3.45 (dd, J = 10.7, 2.1 Hz, 1H), 3.74 (dd, J = 13.1, 7.0 Hz, 1H), 3.81 (dd, J = 13.1, 7.0 Hz, 1H), 7.13−7.28 (m, 4H); ^{13}C NMR δ 25.7, 26.3, 34.5, 35.1, 80.3, 126.9, 127.4, 129.4, 130.7, 137.6, 139.8; MS m/z 224 (M^+, 0.2%), 104 (100).

2-[2-(Mercaptomethyl)phenyl]-1-phenylethanol (3e):[14] IR (film) 3700−3100, 2540 cm^{-1}; ^1H NMR δ 1.72 (t, J = 7.0 Hz, 1H), 2.21 (br s, 1H), 3.05 (dd, J = 14.3, 5.5 Hz, 1H), 3.11 (dd, J = 14.0, 7.9 Hz, 1H), 3.63−3.77 (m, 2H), 4.94 (dd, J = 7.9, 5.5 Hz, 1H), 7.13−7.34 (m, 9H); ^{13}C NMR δ 26.2, 42.3, 75.0, 125.7, 127.2, 127.4, 127.6, 128.4, 129.4, 130.9, 135.8, 139.8, 144.0; MS m/z 226 ($M^+ - H_2O$, 0.5%), 104 (100).

1-[2-(Mercaptomethyl)phenyl]-2-methyl-2-propanol (3f):[14] IR (film) 3600−3100, 2540 cm^{-1}; ^1H NMR δ 1.26 (s, 6H), 1.53 (br s, 1H), 1.71 (t, J = 7.0 Hz, 1H), 2.89 (s, 2H), 3.87 (d, J = 7.0 Hz, 2H), 7.17−7.33 (m, 4H); ^{13}C NMR δ 26.7, 29.7, 45.0, 71.2, 126.8, 127.1, 129.6, 132.1, 135.2, 140.5; MS m/z 147 ($M^+ - H_2S$-CH_3, 1%), 43 (100).

1-{[2-(Mercaptomethyl)phenyl]methyl}cyclopentanol (3g):[14] IR (film) 3600−3120, 2540 cm^{-1}; ^1H NMR δ 1.60−1.82 (m, 10H), 3.01 (s, 2H), 3.88 (d, J = 7.0 Hz, 2H), 7.15−7.31 (m, 4H); ^{13}C NMR δ 23.2, 26.7, 39.6, 42.5, 82.7, 127.0, 127.1, 129.5, 131.6, 135.9, 140.4; MS m/z 204 ($M^+ - H_2O$, 2%), 104 (100).

1-[2-(Mercaptomethyl)phenyl]-2-phenyl-2-propanol (3h):[14] IR (film) 3700−3140, 2540 cm^{-1}; ^1H NMR δ 1.24 (t, J = 7.0 Hz, 1H), 1.62 (s, 3H), 1.92 (br s, 1H), 3.16 (d, J = 3.3 Hz, 2H), 3.61 (d, J = 7.0 Hz, 2H), 6.93−7.38 (m, 9H); ^{13}C NMR δ 26.4, 29.7, 46.2, 74.8, 124.8, 126.7, 126.8, 127.3, 128.1, 129.4, 132.1, 134.3, 140.9, 147.7; MS m/z 240 ($M^+ - H_2O$, 0.2%), 43 (100).

1,4-Dihydro-3*H*-2-thiabenzopyran-3-one (3i):[15] mp 71−72 °C (pentane/CH_2Cl_2); IR (KBr) 1670 cm^{-1}; ^1H NMR δ 3.77 (s, 2H), 4.20 (s, 2H), 7.17−7.33 (m, 4H); ^{13}C NMR δ 34.1, 49.1, 126.5, 127.3, 128.0, 128.6, 133.6, 134.2, 202.8; MS m/z 164 (M^+, 4%), 45 (100).

Preparation of Compounds 5 from Thiophthalan 1. General Procedure. To a blue suspension of lithium powder (0.125 g, 18.0 g atoms) and a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (0.027 g, 0.10 mmol) in THF (8 mL) at −78 °C was added thiophthalan (**1**; 1 mmol) under argon, and the mixture was stirred for 30 min at the same temperature. The corresponding electrophile (1.5 mmol) was added. The mixture was stirred at the same temperature for 15 min, and it was warmed to 20 °C. The mixture was stirred at 20 °C for 1 h, and then it was cooled again at −78 °C and a second electrophile (0.5 mL in the case of H_2O or D_2O) was added. The mixture was hydrolyzed with water at the same temperature. The resulting mixture was extracted with ethyl acetate. The organic layer was dried over anhyd Na_2SO_4 and evaporated (15 mmHg). The residue was then purified by column chromatography (silica gel; hexane/ethyl acetate) to yield pure products **5a**,**b**. Compounds **5a** and **5b** were characterized by comparison of their spectroscopic data with those described in the literature.[8g]

Preparation of Compounds 6 and 7. General Procedure. To a solution of the corresponding mercapto alcohol **3c**-**h** (1 mmol) in toluene (5 mL) was added 85% phosphoric acid (0.4 mL). The reaction mixture was heated at 120 °C for 1 h, and then toluene was removed by distillation and the resulting residue was hydrolyzed with water and extracted with ethyl acetate. The organic layer was dried over anhyd Na_2SO_4 and evaporated (15 mmHg). The resulting residue was purified by column chromatography (silica gel; hexane/ethyl acetate) and/or recrystallized to yield pure products **6c**, **6e**−**h**, **6′d**, and **7c**. Yields and R_f values are included in Table 2; analytical and spectroscopic data as well as literature references follow.

3,4-Dihydro-3-isopropyl-1*H*-2-thianaphthalene (6c): IR (film) 3020, 3000, 730 cm^{-1}; ^1H NMR δ 1.05 (d, J = 6.7 Hz, 6H), 1.75−1.86 (m, 1H), 2.72−3.02 (m, 3H), 3.73 (s, 2H), 7.14−7.17 (m, 4H); ^{13}C NMR δ 18.8, 20.2, 29.8, 33.4, 34.5, 49.1, 126.2, 126.7, 126.8, 129.1, 136.0, 137.6; MS m/z 192 (M^+, 30%), 149 (100); HRMS calcd for $C_{12}H_{16}S$ 192.0973, found 192.1020.

3,4-Dihydro-3-phenyl-1*H*-2-thianaphthalene (6e):[16] IR (film) 3040, 3020, 1590, 1570, 1490, 750, 740, 690 cm^{-1}; ^1H NMR δ 3.22 −3.25 (m, 2H), 3.88 (d, J = 15.1 Hz, 1H), 3.97 (d, J = 15.1 Hz, 1H), 4.21 (dd, J = 8.6, 5.8 Hz, 1H), 7.11−7.38 (m, 9H); ^{13}C NMR δ 30.9, 38.8, 45.2, 126.4, 126.8, 127.3, 127.4, 127.5, 128.5, 129.4, 134.7, 136.9, 142.7; MS m/z 226 (M^+, 32%), 104 (100).

3,4-Dihydro-3,3-dimethyl-1*H*-2-thianaphthalene (6f): IR (film) 3040, 3000, 1570, 1490, 740, cm^{-1}; ^1H NMR δ 1.34 (s, 6H), 2.83 (s, 2H), 3.81 (s, 2H), 7.09−7.22 (m, 4H); ^{13}C NMR δ 29.3, 30.8, 41.7, 45.8, 126.3, 126.5, 127.1, 129.9, 134.1, 136.6; MS m/z 178 (M^+, 42%), 59 (100).

Spiro[cyclopentane-3-(3,4-dihydro-1*H*-2-thianaphthalene)] (6g): IR (film) 3020, 1560, 730 cm^{-1}; ^1H NMR δ 1.67−1.82 (m, 8H), 2.93 (s, 2H), 3.83 (s, 2H), 7.06−7.17 (m, 4H); ^{13}C NMR δ 24.1, 29.6, 40.5, 43.6, 51.7, 126.1, 126.4, 127.4, 129.9, 134.2, 136.9; MS m/z 205 ($M^+ + 1$, 15%), 204 (M^+, 100); HRMS calcd for $C_{13}H_{16}S$ 204.0973, found 204.0988.

3,4-Dihydro-3-methyl-3-phenyl-1*H*-2-thianaphthalene (6h): IR (film) 3040, 3000, 1590, 1570, 1490, 750, 730, 690 cm^{-1}; ^1H NMR δ 1.66 (s, 3H), 3.23 (d, J = 16.2 Hz, 1H), 3.50 (m, 3H), 7.02−7.53 (m, 9H); ^{13}C NMR δ 29.9, 31.2, 43.9, 46.7, 126.1, 126.5, 126.6, 126.7, 127.6, 128.1, 129.9, 133.5, 136.1, 145.9; MS m/z 240 (M^+, 44%), 104 (100); HRMS calcd for $C_{16}H_{16}S$ 240.0973, found 240.0974.

3,4-Dihydro-3-isopropyl-3-methyl-1*H*-2-thianaphthalene (6′d): IR (film) 3040, 3000, 1490, 740 cm^{-1}; ^1H NMR δ 0.98, 1.05 (2d, J = 6.7 Hz, 6H), 1.14 (s, 3H), 1.78 (heptet, J = 6.7 Hz, 1H), 2.68 (d, J = 14.5 Hz, 1H), 2.93 (d, J = 14.5 Hz, 1H), 3.67 (d, J = 14.7 Hz, 1H), 3.73 (d, J = 14.7 Hz, 1H), 7.09−7.23 (m, 4H); ^{13}C NMR δ 17.7, 18.3, 24.4, 29.4, 37.8, 42.0, 51.0, 126.4, 126.5, 126.6, 129.7, 135.8, 137.0; MS m/z 206 (M^+, 18%), 163 (100); HRMS calcd for $C_{13}H_{18}S$ 206.1129, found 206.1134.

3,3-Dimethyl-1,3,4,5-tetrahydro-2-benzothiepin (7c): mp 82−83 °C (pentane/CH_2Cl_2); IR (KBr) 3000, 730 cm^{-1}; ^1H NMR δ 1.40 (s, 6H), 1.80−1.84 (m, 2H), 2.84−2.87 (m, 2H), 3.72 (s, 2H), 7.10−7.13 (m, 4H); ^{13}C NMR δ 29.6, 30.9, 32.3, 42.5, 44.3, 126.5, 126.9, 127.4, 129.8, 141.7, 142.3; MS m/z 193 ($M^+ + 1$,

(13) Cagniant, P.; Cagniant, P. Mme. *Bull. Soc. Chim. Fr.* **1961**, 2225.

(14) For products **3c**−**h**, **9fb**, **9ja**−**jb** was not possible to obtain the corresponding HRMS due to the low intensity of the M^+ signal.

(15) Lemaire, C.; Luxen, A.; Christiaens, L.; Guillaume, M. *J. Heterocycl. Chem.* **1983**, *20*, 811.

(16) Farrington, J. J., Jr., Ph. D. Ann Arbor Univ., 1973; *Chem. Abstr.* **1974**, *81*, 135886m.

10%), 192 (M^+, 76), 143 (100). Anal. Calcd for $C_{12}H_{16}S$: C, 74.94; H, 8.39; S, 16.67. Found: C, 74.51; H, 8.72; S, 16.80.

Preparation of Compounds 9. General Procedure. To a blue suspension of lithium powder (0.125 g, 18.0 g atoms) and a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (0.027 g, 0.10 mmol) in THF (8 mL) at −78 °C was added the corresponding thioisochroman (**6**; 1 mmol) under argon, and the mixture was stirred for 30 min at the same temperature. The corresponding electrophile (1.5 mmol; 0.5 mL in the case of H_2O or D_2O; CO_2 was bubbled for 1 h) was added. The mixture was stirred at the same temperature for 15 min and was hydrolyzed with water at −78 °C. The resulting mixture was extracted with ethyl acetate. The organic layer was dried over anhyd Na_2SO_4 and evaporated (15 mmHg). The residue was then purified by column chromatography (silica gel; hexane/ethyl acetate) to yield pure products **9fa**−**fb** and **9ja**−**jb**. When the electrophile was CO_2, after having hydrolyzed the mixture with water at −78 °C it was basified with 2.5 M NaOH and extracted with ethyl acetate. The aqueous layer was then acidified with 3 M HCl and extracted with ethyl acetate. The organic layer was dried over anhyd Na_2SO_4 and evaporated (15 mmHg). The resulting residue was dissolved in benzene (50 mL), a catalytic amount of *p*-toluenesulfonic acid (0.001 g) was added, the mixture was heated in a 120 °C oil bath temperature (Dean−Stark) for 15 h, the benzene was removed by distillation, and the resulting residue was hydrolyzed with a saturated aqueous solution of Na_2CO_3 and extracted with ethyl acetate. The organic layer was dried over anhyd Na_2SO_4 and evaporated (15 mmHg). The residue was then purified by column chromatography (silica gel; hexane/ethyl acetate) to yield the titled compound **9fc**. Yields and R_f values are included in Table 3; analytical and spectroscopic data follow.

1-[2-(Deuteriomethyl)phenyl]-2-methyl-2-propanethiol (9fa): IR (film) 2540 cm^{-1}; ^1H NMR δ 1.42 (s, 6H), 1.75 (s, 1H), 2.37 (s, 2H), 2.96 (s, 2H), 7.11−7.24 (m, 4H); ^{13}C NMR δ 20.4 (t, J_{CD} = 19.2 Hz), 32.7, 46.0, 47.9, 125.2, 126.6, 130.6, 131.7, 136.3, 137.3; MS *m*/*z* 181 (M^+, 19%), 41 (100); HRMS calcd for $C_{11}H_{15}DS$ 181.1036, found 181.1027.

1-[2-(2-Methyl-2-mercaptopropyl)phenyl]-2-methyl-2-propanol (9fb):[14] IR (film) 3600−3140, 2540 cm^{-1}; ^1H NMR δ 1.20 (s, 6H), 1.38 (s, 6H), 1.59 (br s, 1H), 1.67 (s, 1H), 2.96, 3.07 (2s, 4H), 7.16−7.28 (m, 4H); ^{13}C NMR δ 29.4, 32.7, 45.7, 45.9, 47.6, 71.3, 125.8, 126.3, 131.6, 131.9, 136.9, 137.1; MS *m*/*z* 180 ($M^+ - C_3H_6O$, 20%), 75 (100).

4,5-Dihydro-4,4-dimethyl-3-benzothiepin-2(1*H*)-one (9fc): IR (film) 1650 cm^{-1}; ^1H NMR δ 1.46 (s, 6H), 3.23 (s, 2H), 4.05 (s, 2H), 7.00−7.31 (m, 4H); ^{13}C NMR δ 32.5, 46.6, 51.6, 52.9, 127.6, 127.7, 129.6, 130.7, 132.6, 136.5, 197.6; MS *m*/*z* 206 (M^+, 13%), 131 (100); HRMS calcd for $C_{12}H_{14}OS$ 206.0765, found 206.0768.

1-[2-(2-Mercaptoethyl)phenyl]-3,3-dimethyl-2-butanol (9ja):[14] IR (film) 3700−3240, 2540 cm^{-1}; ^1H NMR δ 1.02 (s, 9H), 1.40 (t, *J* = 7.8 Hz, 1H), 1.49 (br s, 1H), 2.54 (dd, *J* = 13.7, 10.7 Hz, 1H), 2.72−2.99 (m, 5H), 3.41 (dd, *J* = 10.7, 1.9 Hz, 1H), 7.17−7.21 (m, 4H); ^{13}C NMR δ 25.4, 25.8, 34.6, 35.0, 37.1, 80.1, 126.6, 126.7, 129.7, 130.5, 137.8, 138.6; MS *m*/*z* 220 ($M^+ - H_2O$, 0.2%), 105 (100).

1-{[2-(2-Mercaptoethyl)phenyl]methyl}cyclopentanol (9jb):[14] IR (film) 3640−3100, 2540 cm^{-1}; ^1H NMR δ 1.31 (br s, 1H), 1.41 (t, *J* = 7.6 Hz, 1H), 1.59−1.80 (m, 8H), 2.74 (q, *J* = 7.6 Hz, 2H), 2.95 (s, 2H), 3.05 (t, *J* = 7.6 Hz, 2H), 7.15−7.26 (m, 4H); ^{13}C NMR δ 23.1, 25.6, 37.3, 39.4, 42.4, 82.8, 126.3, 126.7, 129.5, 131.4, 136.4, 139.2; MS *m*/*z* 204 ($M^+ - H_2O$, 0.5%), 105 (100).

Preparation of Compounds 10. General Procedure. The same procedure described above for compounds **6** was used in this case but starting from products **9fb** or **9jb**. Yields are shown under structures **10fb** and **10jb**; R_f, analytical and spectroscopic data follow.

1,2,4,5-Tetrahydro-2,2,4,4-tetramethyl-3-benzothiepin (10fb): R_f = 0.28 (hexane); IR (film) 3040, 3000, 1480, 730 cm^{-1}; ^1H NMR δ 1.27 (s, 12H), 3.16 (s, 4H), 7.03−7.25 (m, 4H); ^{13}C NMR δ 32.0, 44.3, 51.0, 126.4, 131.0, 138.7; MS *m*/*z* 220 (M^+, 43%), 131 (100); HRMS calcd for $C_{14}H_{20}S$ 220.1286, found 220.1289.

Spiro[cyclopentane-2-(1,3,4,5-tetrahydro-3-benzothiepin)] (10jb): R_f = 0.13 (hexane); IR (film) 3060, 3020, 1490, 750, 730 cm^{-1}; ^1H NMR δ 1.51−1.74 (m, 8H), 2.60 (t, *J* = 5.3 Hz, 2H), 3.15 (t, *J* = 5.3 Hz, 2H), 3.17 (s, 2H), 6.94−7.06 (m, 4H); ^{13}C NMR δ 24.1, 28.3, 39.7, 40.0, 51.6, 51.7, 126.0, 126.4, 129.5, 131.2, 138.8, 141.5; MS *m*/*z* 218 (M^+, 53%), 118 (100); HRMS calcd for $C_{14}H_{18}S$ requires M, 218.1129, found 218.1130.

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Supporting Information Available: Copies of ^1H (300 MHz) and ^{13}C (75 MHz) NMR spectra of new compounds lacking microanalyses (**3b**, **3c**, **3d**, **3e**, **3f**, **3g**, **3h**, **6c**, **6f**, **6g**, **6h**, **6′d**, **9fa**, **9fb**, **9fc**, **9ja**, **9jb**, **10fb**, **10jb**) (38 pages). This material is contained in libraries on 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.

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