The Benzo[b]thiepin Ring System.[1] A 12-π-Electron System

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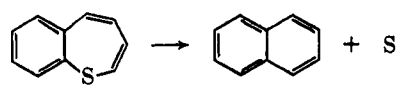
Derivatives of the benzo[b]thiepin ring system have been prepared by primary reactions designed as synchronous fragmentations involving 13 elimination and ring opening of a three-membered ring, as illustrated in 2 → 4. Evidence for the formation of the unstable benzo[b]thiepins 7 and 13 is presented; derivatives of these ethers with potential hydroxyl groups exist entirely in the keto form.

Until very recently[3] derivatives of the benzo[b]-thiepin ring system containing divalent[4] sulfur were unknown; however, sufficient work had been done to suggest that this system is thermally unstable and



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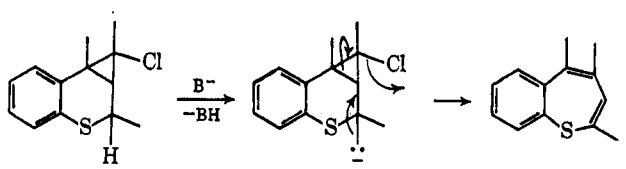
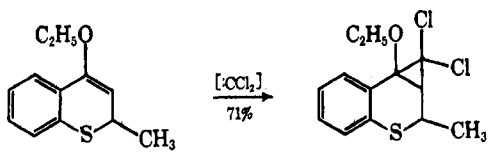
extrudes sulfur to give naphthalene or naphthalene derivatives.[3-8] Previous work also suggested that this system might be sensitive to acids.[5,6] We concluded, therefore, that an E2 elimination reaction with concerted ring expansion, as illustrated in 2–4, represented a promising route to the benzo[b]thiepin system since such reactions should occur at moderate to low temperatures in nonacidic media. We have



2 3 4

now shown that the reaction of 7b-ethoxy-1,1-dichloro-2-methylcyclopropa[c][1]benzothiopyran (6) with sodium methoxide (or sodium ethoxide) in dimethyl sulfoxide leads to derivatives of benzo[b]thiepin, presumably by elimination reactions of the type illustrated above. The results of this study constitute the subject of this report.

7b-Ethoxy-1,1-dichloro-2-methylcyclopropa[c][1]benzothiopyran (6) was prepared in 71% yield[9] by addition of the elements of dichlorocarbene to 4-ethoxy-2-methyl-2H-1-benzothiopyran (5). The reaction of 6 with sodium methoxide in dimethyl sulfoxide was



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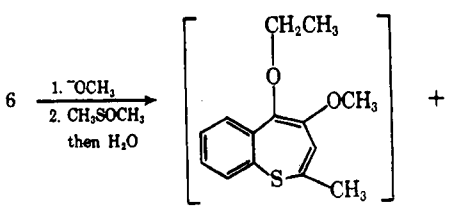

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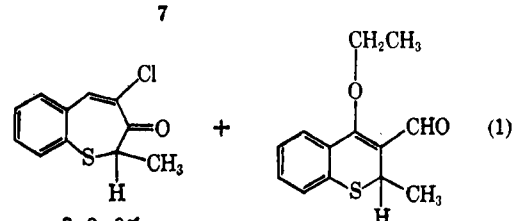
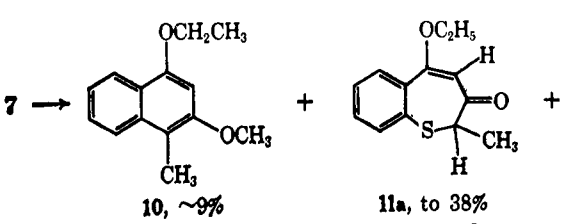
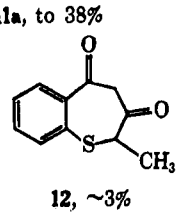


8, 2–9% 9, ~13% (1)

rapid at 20°, and the course of reaction is as shown in eq 1 and 2. The benzo[b]thiepin 7, the aldehyde 9,



10, ~9% 11a, to 38%



12, ~3% (2)

and a chloro ketone, assumed to be 8, appeared to be primary reaction products; however, 7 is unstable and was subsequently converted into the naphthalene 10 by extrusion of sulfur, and into the ketones 11a and 12 by hydrolysis. The reaction of 6 was studied with 1–2.2 equiv of sodium methoxide. Similar results were obtained when sodium ethoxide was employed as the base; however, in this case the unstable benzo[b]thiepin 13 gave 1,3-diethoxy-4-methylnaphthalene (14) and 11a, instead of 1-ethoxy-3-methoxy-4-methylnaphthalene (10), 11a, and 12. While complete resolution of the rather complex mixture of products was undoubtedly not achieved, the approximate yield or

(1) Supported by U. S. Army Research Office (Durham) (DA-ARO-D-31-124-G-848).

(2) From the Ph.D. Thesis of D. G. Weetman, The University of Minnesota, Minneapolis, Minn., 1968.

(3) H. Hofman and H. Westernacher, *Angew. Chem. Intern. Ed. Engl.*, **5**, 958 (1966); **6**, 255 (1967).

(4) Benzo[b]thiepin 1,1-dioxide is stable and its properties have been studied: V. J. Traynelis and R. F. Love, *J. Org. Chem.*, **26**, 2728 (1961).

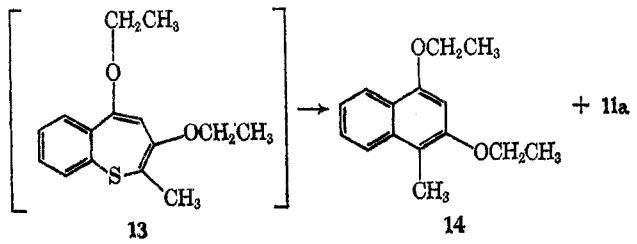
(5) V. J. Traynelis and J. R. Livingston, *ibid.*, **29**, 1092 (1964).

(6) W. E. Parham and R. Koncos, *J. Amer. Chem. Soc.*, **83**, 4034 (1961).

(7) W. E. Parham and M. D. Bhavsar, *J. Org. Chem.*, **29**, 1575 (1964).

(8) (a) 3-Benzothiepin-2,4-dicarboxylic acid has been reported; this isomeric thiepin system loses sulfur in boiling ethanol to give 2,3-naphthalenedicarboxylic acid [G. B. Scott, *J. Amer. Chem. Soc.*, **75**, 6332 (1953)]. (b) K. Dimroth and G. Lenke, *Chem. Ber.*, **89**, 2608 (1953). (c) K. Dimroth and G. Lenke, *Angew. Chem.*, **68**, 519 (1956).

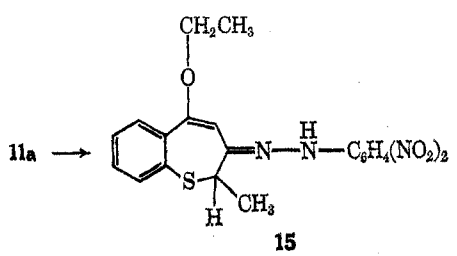
(9) The ethoxy group in **5** promotes addition of CCl_2 and thereby minimized insertion which occurs with cyclic β,γ-unsaturated cyclic sulfides (*cf.* ref 6).



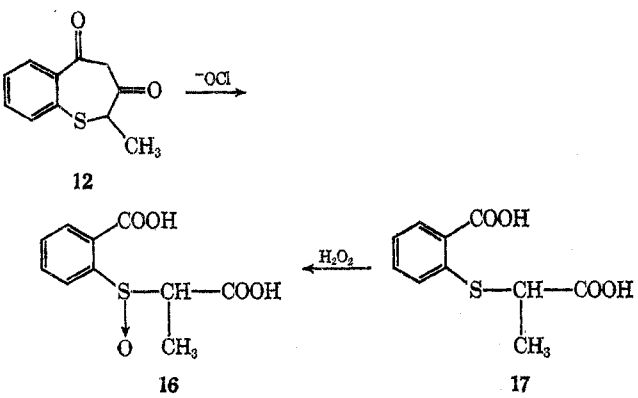
range of yields of the products isolated is indicated by the numbers in parentheses in the above equations. Considerable tarry product was formed in all such reactions. The naphthalenes **10** or **14** could be detected (nmr) in the crude product obtained by removal of solvent under vacuum; however, these products appeared to be formed by thermal decomposition of a primary reaction product (**7** or **13**) and were isolated in highest yield by distillation of the crude product rather than by chromatography of the crude product.

While the benzothiepin **7** was not isolated, its presence was signaled by (a) the formation of the naphthalene **10** in increased amounts when the crude product was heated, and (b) by nmr studies of the crude product taken prior to and subsequent to exposure of the product to water. These nmr studies showed the disappearance of the vinyl proton absorption at τ 4.47 (assigned to the H-4 of **7**) with a large increase in absorption due to that assigned to the 4 proton of **11a**, subsequent to exposure of the sample to water.

Structure of Products.—The ketone **11a** was obtained pure and was further characterized by its conversion into the 2,4-dinitrophenylhydrazone **15**. The structure

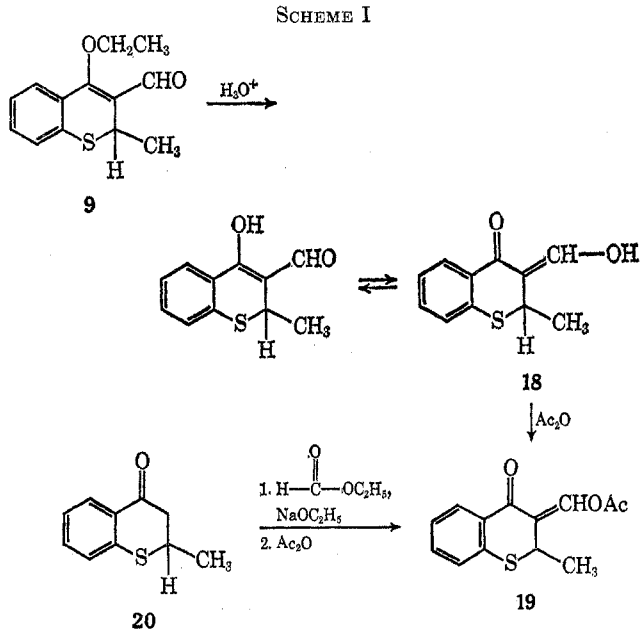


of **11a** was assigned on the basis of composition, spectra (nmr, infrared, and ultraviolet), and its hydrolysis to **12**. The diketone **12**, also obtained directly from **6**, was unstable and rapidly turned red in air. While satisfactory carbon and hydrogen analysis were not obtained for a sample of **12**, the spectra (nmr, infrared, and ultraviolet) were consistent with the assigned structure, and mass spectral analysis confirmed the molecular weight of 206. Additional chemical evidence for the structures of **11a** and **12** were obtained by their degradation to α-(O-carboxyphenylsulfinyl)-propionic acid (**16**) by oxidation of **12** with aqueous sodium hypochlorite. The sample of **16** was identical with an authentic sample, prepared independently by oxidation of **17**.

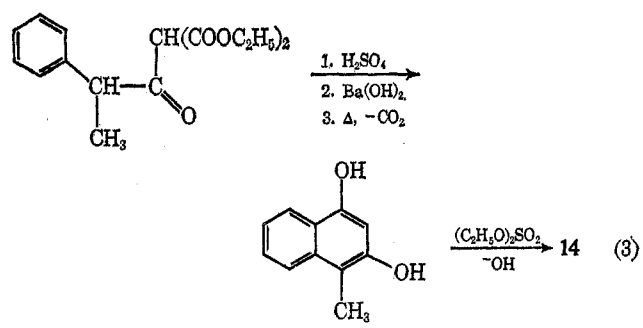


The structure of 4-ethoxy-2-methyl-2H-1-benzothiapyran-3-al (**9**) was assigned on the basis of spectral analysis (see Experimental Section); the structure was confirmed by its conversion into 3-acetoxymethylene-2-methylthiochroman-4-one (**19**). The derived sample of **19** was identical with an authentic sample of **19** prepared by an independent route from **20**. These transformations are summarized by Scheme I.

SCHEME I



The structures of 1-ethoxy-3-methoxy-4-methylnaphthalene (**10**) and 1,3-diethoxy-4-methylnaphthalene (**14**) were originally assigned on the basis of spectral analysis and composition. The nmr spectra suggested the 1,3 orientation (uncoupled H-2), and the structures were confirmed by the independent synthesis of **14** as illustrated in eq 3.

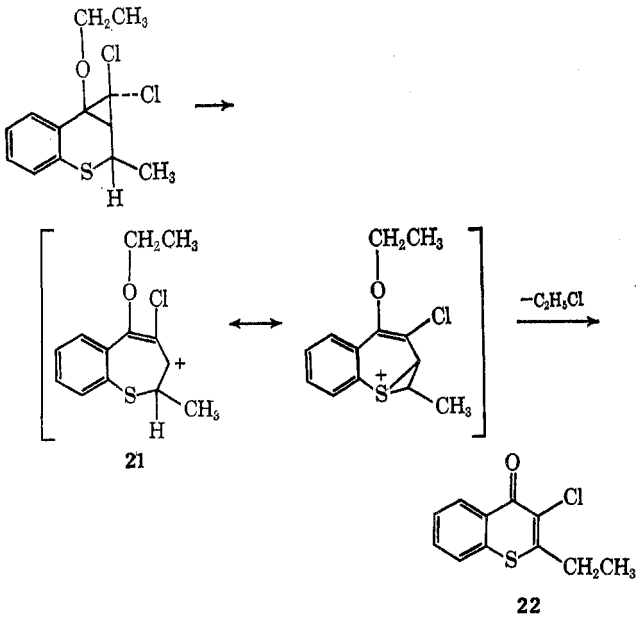


(3)

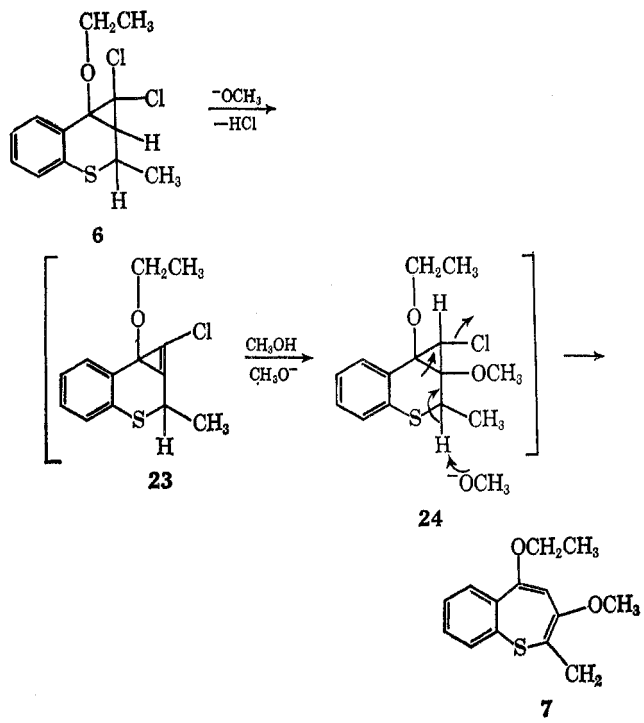
The structural assignment of the chloro ketone as 4-chloro-2-methyl-2,3-dihydro-1-benzothiepin-3-one (**8**) is tentative since the assignment was made only on the basis of composition and spectral analysis. The nmr spectrum appeared to be quite definitive, however, and showed a single proton coupled to a methyl group (position 2), and five protons from τ 3.07 to 1.83.

Mechanism.—The cyclopropane **6** was recovered

SCHEME II



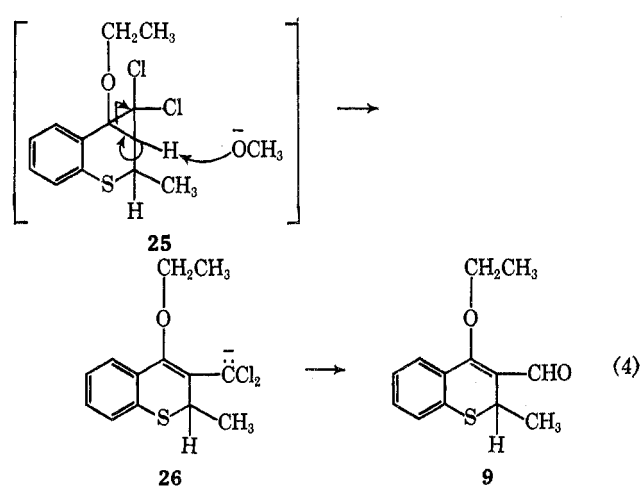
SCHEME III



in high yield from solutions of **6** in dimethyl sulfoxide containing lithium chloride (~3 mol/mol of **6**), which suggested that the reactions leading to the products discussed above were formed by a prior E2 rather than an E1 elimination process. Confirmation of this conclusion was obtained by studies of the reaction of **6** in hot pyridine. This reaction probably occurs by an E1 elimination[7] process and the reaction follows an entirely different course (Scheme II). The principle product, other than tar, was **22**. This chloro ketone was assumed to be formed from the ion **21** by a process similar to that described[7] for a related reaction leading to 3-chloro-2-methylthiochromone. The structure of **22** was confirmed by independent synthesis (see Experimental Section).

5-Ethoxy-3-methoxy-2-methylbenzo[*b*]thiepin (**7**) and the diethoxy analog **13**, are thought to arise as shown in Scheme III. The elimination of hydrogen chloride from **6** to give **23**, and the subsequent addition of methanol (or ethanol) to give **24**, is expected in view of the extensive studies by Shields and Gardner[10] of the reaction of 7,7-dichlorobicyclo[4.1.0]heptane with potassium isopropoxide in dimethyl sulfoxide. The reaction of **24** → **7** is sufficiently reasonable to have prompted this study, and is analogous to other synchronous fragmentation reactions.[11] The extrusion of sulfur from **7** to give **10** or from **13** to give **14** is consistent with results of other studies of the benzo[*b*]thiepin[3,5,6] system, and the hydrolysis of the vinyl ether function at C-3 rather than at C-5 in **7** or **13** to give 5-ethoxy-2-methyl-2,3-dihydro-1-benzothiepin-3-one (**11a**) is expected.[12]

The formation of 4-ethoxy-2-methyl-2H-1-benzothiopyran-3-al (**9**) is thought to occur by an elimination process as shown in eq 4. Elimination reactions involving displacement of C–Cl_2, as shown in **25**, have previously been noted.[13] A number of alternative



(4)

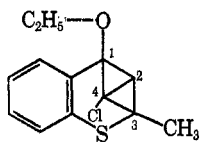
paths for the conversion of **26** into **9**, including the intermediate conversion of the C–Cl_2 group into $-CHCl_2$ or $-CH(OCH_3)_2$, appear reasonable.

A similar elimination mechanism (Scheme IV) is suggested for the formation of the chloro ketone **8**. The elimination of ethoxy rather than halogen, as shown in **27**, appears unusual and no evidence for **30** other than the formation of **8** was obtained; however, the reactions are analogous to those of Shields and Gardner[10]

(10) T. C. Shields and P. D. Gardner, *J. Amer. Chem. Soc.*, **89**, 5425 (1967).

(11) *Cf.* C. A. Grob, H. R. Kiefer, H. Lutz, and H. Wilkens, *Tetrahedron Lett.*, **39**, 2901 (1964).

(12) An alternative mechanism for conversion of **6** into **7** involves formation of the intermediate bicyclobutane A, a process somewhat analogous to



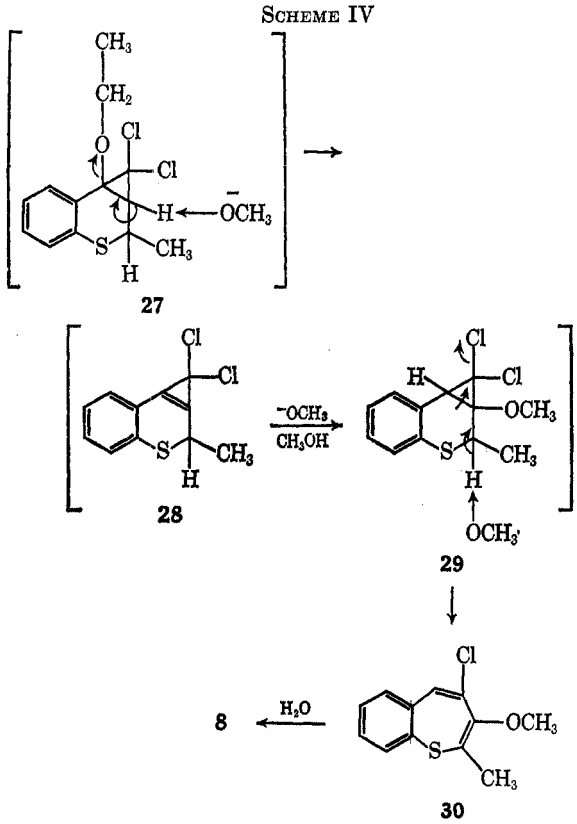
A

bicyclobutane formation described by O. L. Chapman, 12th National Organic Chemistry Symposium, Vt., 134, 1967, p 134.

Formation of **7** could then involve attack of alkoxide at position 4 followed by eliminations involving the sequential breaking of bonds 4–1, 2–3, and C–Cl.

(13) *Cf.* (a) W. E. Parham and J. F. Dooley, *J. Amer. Chem. Soc.*, **89**, 985 (1967); W. E. Parham and J. F. Dooley, *J. Org. Chem.*, **33**, 1476 (1968).

SCHEME IV

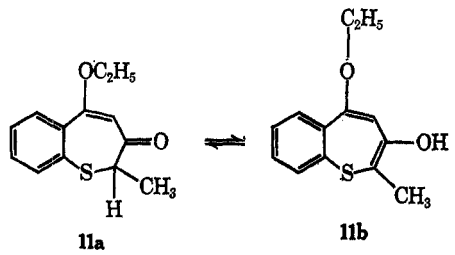


and the elimination reactions discussed above. This scheme is obviously more tenuous, particularly since the structure of **8** cannot be considered as unequivocal.

Discussion

The rather unusual elimination reactions described above have provided a spectrum of derivatives of benzo[*b*]thiepin, which permit a more accurate definition of the consequence of steric and conjugative effects in this system.

The thermal instability of **7** and **13** leading to naphthalenes, and the facile hydrolysis of **7** and **13** to 5-ethoxy-2-methyl-2,3-dihydro-1-benzothiepin-3-one (**11a**) indicate quite clearly that the gain of energy due to resonance in this 12-π-electron system is offset by the added strain imposed. This effect of strain and resonance is also exemplified by the structures of **11a** and **12**.



The ketone **11a** does not give a test for enol with ferric chloride and there is no spectral evidence for **11b** or the corresponding dienolic form of **12**. Examination of models of **11a** shows that the heterocyclic ring is nonplanar and rigid; considerable strain is observed in the enolic form **11b**. This conclusion is supported by the observed properties of the available benzo[*b*]thiepins, and is consistent with the observations reported by Hofman and Westernacher.[3]

Experimental Section

2-Methylthiochroman-4-one was prepared from β-(phenylmercapto)-*n*-butyric acid[7,14] by a procedure similar to that described for thiochroman-4-one.[7] The ketone was obtained as a pale yellow liquid: bp 125–127° (2 mm); n^{26}D 1.6088; 72% yield; $\lambda_{max}^{95\%\ EtOH}$ 241 (ϵ 23840), 263 (ϵ 5100), 348 (ϵ 2935); $\nu_{C=O}$ 1680 cm^{-1} [lit.[14] bp 146–147° (19 mm), n^{20}D 1.6125].

4-Ethoxy-2-methyl-2H-1-benzothiopyran (5).—The procedure used was essentially identical with that described[7] for 4-ethoxy-2H-1-benzothiopyran. From 2-methylthiochroman-4-one (200 g, 1.12 mol) there was obtained 229 g of **5**: 98% yield; bp 110–112° (0.05 mm); n^{23}D 1.6092; yellow liquid; $\lambda_{max}^{95\%\ EtOH}$ 223 mμ (ϵ 17,510), 254 (13,200), and 318 (1560); nmr (10% in $CDCl_3$), τ 8.72 (t, 3, J = 7 Hz, OCH_2CH_3), 8.69 (d, 3, J = 7 Hz, 2-CH_3), 6.24 (q, 3, J = 7 Hz, OCH_2CH_3 and H-2), 4.90 (d, 1, J = 7 Hz, H-3), and 3.07–2.46 and 2.46–2.00 (2 m, 3 and 1, aromatic H).

Anal. Calcd for $C_{12}H_{14}OS$: C, 69.86; H, 6.84; S, 15.54. Found: C, 69.59; H, 6.87; S, 15.43.

7b-Ethoxy-1,1-dichloro-2-methylcyclopropa[*c*][1]benzothiopyran (6).—The procedure used was essentially identical with that described[7] for the preparation of 7b-ethoxy-1,1-dichlorocyclopropa[*c*][1]benzothiopyran. From 61.8 g (0.30 mol) of **5** there was obtained 61.8 g (71% yield) of redistilled product, bp 120–124° (0.025 mm), n^{25}D 1.5740. The cyclopropane **6** crystallized and was recrystallized, essentially without loss, to give white crystals: mp 44°; $\lambda_{max}^{95\%\ EtOH}$ 211 mμ (ϵ 11,670), 225 (12,660), 261 (5620), and 291 (1407); nmr (10% in $CDCl_3$), τ 8.88 (t, 3 J = 7 Hz, OCH_2CH_3), 8.44 (d, 3, J = 7 Hz, 2-CH_3), 7.96 (d, 1, J = 7 Hz, H-3), 6.93–6.15 (m, 3, H-2 and OCH_2CH_3), 2.97–2.67 and 2.56–2.29 (2 m, 3 and 1, aromatic H).

Anal. Calcd for $C_{13}H_{14}OCl_2S$: C, 53.98; H, 4.88; Cl, 24.52; S, 11.09. Found: C, 53.72; H, 4.81; Cl, 25.04; S, 11.26.

Reaction of 7b-Ethoxy-1,1-dichloro-2-methylcyclopropa[*c*][1]-benzothiopyran (6) with Strong Base.—Many reactions of this type were conducted under a variety of conditions, and all of the products of reaction were not isolated from a single run.

A.—In a typical experiment **6** (5.00 g, 0.0173 mol) in dry dimethyl sulfoxide (15 ml) was added to a slurry of freshly prepared sodium methoxide–DMSO (0.985 g, 0.182 mol) contained in a nitrogen-filled 50-ml flask equipped with a nitrogen inlet and outlet tube, dropping funnel, magnetic stirrer, and water bath (20–25°). Addition of the cyclopropane required 7 min, and the resulting black system was allowed to stir for 70 min. In procedure A the contents of the flask were poured into water (100 ml) and ether (100 ml), and the resulting mixture was stirred for 10 min (in an alternate procedure, B, the reaction product was filtered and dimethyl sulfoxide was removed by low-temperature distillation). The combined ether extract was dried ($MgSO_4$) and concentrated, and the residual heavy black oil (4.51 g) was chromatographed on silica gel (85 g, 100–200 mesh). Eluent sample sizes were usually 250 ml and a typical chromatogram involved the following fractions: 1–4 (petroleum ether (PE), bp 60–80°); 5–8 (10% benzene–petroleum ether); 9–12 (20% benzene–PE); 13–16 (30% benzene–PE); 17–20 (40% benzene–PE); 21–23 (50% benzene–PE); 24–28 (60% benzene–PE); 29–32 (70% benzene–PE); 33–35 (90% benzene–PE); 36–39 (chloroform); 40–43 (diethyl ether).

Isolation of Recovered 6.—Fractions 5–8 (1.48 g) were redistilled in a Babcock distillation apparatus to give recovered **6**: 1.15 g, 22.8%; bp 90–130° (0.05 mm); n^{26}D 1.5745; ir identical with that of authentic **6**.

Isolation of 5-Ethoxy-2-methyl-2,3-dihydro-1-benzothiepin-3-one (11a).—Fractions 30–34 (0.62 g, mp 98–100°, 15% yield) were recrystallized from ethanol to give white crystals which were identified as **11a**: 0.31 g, 7.8%, mp 101–102°; $\lambda_{max}^{95\%\ EtOH}$ 220 mμ (ϵ 21,350), 246 (8800), 266 (6110), and 296 (1077); $\nu_{C=O}$ 1640 cm^{-1}; nmr (10% CCl_4), τ 8.68 (d, 3, J = 7 Hz, 2-CH_3), 8.52 (t, 3, J = 7 Hz, OCH_2CH_3), 6.82 (q, 1, J = 7 Hz, H-2), 5.97 (q, 2, J = 7 Hz, CH_2CH_3), 4.21 (s, 1, H-4), and 2.93–2.00 (m, 4, aromatic H).

(14) J. C. Petropoulos, M. A. McCall, and D. S. Tarbell, *J. Amer. Chem. Soc.*, **75**, 1130 (1953).

Anal. Calcd for $C_{13}H_{14}O_2S$: C, 66.63; H, 6.02; S, 13.69. Found: C, 66.54; H, 6.06; S, 13.87.

Note.—When the reaction was conducted with 2.2 equiv of sodium methoxide and the reaction was stirred for only 10 min at 20°, the yield of **11a** was considerably higher (25%, mp 71–97°; 14.5%, mp 101°). Similar results were obtained when *sodium ethoxide* was used as base; with 2.5 equiv of ethoxide, a reaction time of 10 min, and use of alumina for chromatography, the yield of **11a** was 38% crude (mp 94–100°; 16.7% yield, mp 101°).

Reaction of **11a** with 2,4-dinitrophenylhydrazine reagent gave an immediate red precipitate of the **2,4-dinitrophenylhydrazone of 5-ethoxy-2-methyl-2,3-dihydro-1-benzothiepin-3-one**: *15*, mp 199.5–201°, from ethyl acetate–95% ethanol; nmr (10% in $CDCl_3$), τ 8.45 (t superimposed on d (three lines), 6, J = 7 Hz, 2-CH_3 and OCH_2CH_3), 6.17–5.55 (m, 3, **H**-2 and OCH_2CH_3), 4.12 (s, 1, **H**-4), 2.85–0.75 (m, 7, aromatic **H**), and τ 1.30 (broad, 1, **NH**).

Anal. Calcd for $C_{19}H_{18}N_4O_5S$: C, 55.06; H, 4.38; N, 13.52. Found: C, 54.99; H, 4.31; N, 13.29.

Isolation of 4-Chloro-2-methyl-2,3-dihydro-1-benzothiepin-3-one (8).—Fractions 10–14 (0.39 g, red oil) were combined and distilled in a Babcock distillation apparatus to give 0.35 g [8.9% yield, bp 100–180° (0.05 mm), but not accurately determined] of product which was tentatively assigned the structure 4-chloro-2-methyl-2,3-dihydro-1-benzothiepin-3-one: $\lambda_{max}^{95\%\ EtOH}$ 372 mμ (ε 4930), 264 (12,570), and 247 (18,500); $\nu_{C=O}$ 1658 cm^{-1}; nmr (10% in CCl_4), τ 8.48 (d, 3, J = 7 Hz, 2-CH_3), 5.53 (q, 1, J = 7 Hz, **H**-2), 3.07–2.58 and 2.07–1.83 (2 m, 4 and 1, **H**-5 and aromatic **H**). The yellow oil was unstable and turned red in air.

Anal. Calcd for $C_{11}H_9OSCl$: C, 58.79; H, 4.04; Cl, 15.78; S, 14.27. Found: C, 59.10; H, 4.17; Cl, 15.19; S, 14.43.

The yield of **8** was lower (~2–3.5%) in two experiments in which 2 equiv of base was employed.

Isolation of 4-Ethoxy-2-methyl-2H-1-benzothiopyran-3-al (9).—Fractions 21–28 (0.642 g, red oil) were combined and distilled in a Babcock distillation apparatus to give **9** as a clear yellow oil: 0.528 g, 13% yield; bp ~85–160° (0.05 mm); $\lambda_{max}^{95\%\ EtOH}$ 370 mμ (ε 1573), 307 (11,030), 264 (13,330), 251 (14,980), and 212 (10,750); $\nu_{C=O}$ 1655 cm^{-1}; nmr (CCl_4), τ 8.91–8.48 (d superimposed on t (four lines), 6, J = 7 Hz, 2-CH_3 and OCH_2CH_3), 6.50–5.70 (m, 3, OCH_2CH_3 and **H**-2), 3.00–2.30 (m, 4, aromatic **H**), and 0.1 (s, 1, **CHO**). The OCH_2CH_3 and 2-CH_3 absorption were resolved in benzene solution (triplet, centered at τ 8.99, and doublet, centered at τ 8.88, J = 7 Hz for each, respectively). The aldehyde turned red slowly in air.

Anal. Calcd for $C_{13}H_{14}O_2S$: C, 66.63; H, 6.02; S, 13.69. Found: C, 66.46; H, 5.93; S, 13.70.

Isolation of 1-Ethoxy-3-methoxy-4-methylnaphthalene (10).—The reaction of **6** with sodium methoxide (2 equiv) was carried out as described above except that procedure B (see above) was used for processing. The crude product was not added to water, but filtered and concentrated under vacuum to remove dimethyl sulfoxide. The oil was distilled and the solid, thus obtained, was recrystallized several times from 95% ethanol (activated charcoal was used to effect decolorization). 1-Ethoxy-3-methoxy-4-methylnaphthalene was obtained as a white crystalline solid: 8.9% yield; mp 71–72°; $\lambda_{max}^{95\%\ EtOH}$ 330 mμ (ε 3280), 303 (5820), 293 (5480), 239 (48,800), and 212 (29,000); mass spectrum showed parent mass 216 (calcd 216); nmr ($CDCl_3$), τ 8.56 (t, 3, J = 7 Hz, OCH_2CH_3), 7.58 (s, 3, 4-CH_3), 6.20 (s, 3, OCH_3), 5.49 (q, 2, J = 7 Hz, OCH_2CH_3), 3.47 (s, 1, **H**-2), and 2.92–2.42, 2.33–2.08 and 1.90–1.65 (3 m, 2, 1 and 1, aromatic **H**).

Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.74; H, 7.46. Found: C, 77.93; H, 7.66.

In a similar experiment **6** was treated with sodium ethoxide (2.5 equiv, 90-min reaction time, procedure B) and the product was chromatographed over silica gel. The column was developed with 20% benzene–petroleum ether (bp 60–80°) and 250-ml fractions were collected. **1,3-Diethoxy-4-methylnaphthalene** (6.72% yield, mp 86° from 95% ethanol) was isolated from fractions 8–20 of the chromatogram. 1,3-Diethoxy-4-methylnaphthalene has two melting points, and the product, mp 86°, melted at 79.5–80° after standing several months. When the material, mp 80°, was melted and seeded with product, mp 86°, the melt solidified and melted at 86°. This product was identical (melting point and mixture melting point) with authentic 1,3-diethoxy-4-methylnaphthalene which showed identical melting characteristics.

Isolation of 2-Methyl-2,3,4,5-tetrahydro-1-benzothiepin-3,5-dione (12).—This unstable diketone was obtained from a reaction similar to the one described above (procedure A) in which 2.2 equiv of sodium methoxide was used. The concentrate (0.10 g) obtained from the mother liquor from the recrystallization of **11a** (obtained from fractions 37–48, 50 and 60% benzene–petroleum ether as eluent) were combined with the oil (0.54 g) from fractions 30–36 (50% benzene as eluent), and the mixture was rechromatographed over silica gel (10 g). An unstable yellow oil (0.11 g, 3% yield) was obtained which rapidly turned red in air.

Anal. Calcd for $C_{11}H_{10}O_2S$: C, 64.05, H, 4.89; S, 15.54. Found: C, 64.99; H, 5.39; S, 14.63.

The poor analysis was attributed primarily to the instability of this product which was assigned structure **12** on the basis of its spectra (ir and nmr), its synthesis from **11a**, and its degradation to **16**: nmr of diketone (CCl_4), τ 8.61 (d, 3, J = Hz, 2-CH_3), 6.56 (q, 1, J = 7 Hz, **H**-2), **H**-4 (an AB system, two doublets, centered at 6.18 with J = 14 Hz and at 5.48, J = 14 Hz, wt 2), and 2.90–2.00 (m, 4, aromatic **H**); uv, $\lambda_{max}^{95\%\ EtOH}$ 324 mμ (ε 3850) and 203 (14,500); ir, $\nu_{C=O}$ at 1710 and 1670 cm^{-1}; the mass spectrum confirmed the molecular weight of 206.

B.—In another experiment **6** (1 equiv), sodium methoxide (2.1 equiv), and dry dimethyl sulfoxide (15 ml, distilled from calcium hydride) were stirred, as described in A, for 30 min. The mixture was filtered and heated at 85° (~0.5 mm) to remove dimethyl sulfoxide. The nmr spectrum of the residual black oil showed four absorptions in the vinyl hydrogen region: a broad singlet of minor intensity at τ 4.22 (assigned to the 4 proton of 5-ethoxy-2-methyl-2,3-dihydro-1-benzothiepin-3-one, supported by $\nu_{C=O}$ 1640 cm^{-1}), broad singlet at 3.48 (assigned to 2 proton of 1-ethoxy-3-methoxy-4-methylnaphthalene, supported by characteristic absorption at 7.60 and 6.17 for CH_3 and OCH_3 of **10**), a singlet of moderate intensity at 4.47 (assigned to H-4 of **7**), and a singlet of moderate intensity 3.73 which was not assigned. A doublet centered at 8.55 (J = 7 Hz) was characteristic of 2-CH_3 of 4-chloro-2-methyl-2,3-dihydro-1-benzothiepin-3-one (**8**).

An aliquot of the product in ether was stirred with an equal volume of water for 10 min and the ether layer was dried and concentrated. The nmr spectrum of the product (CCl_4) in the vinyl H region was essentially identical with that of the unhydrolyzed sample except (a) absorption at τ 4.47 assigned to **7** was absent and (b) the intensity of absorption at 4.22 assigned to **11a** was three times greater than in the unhydrolyzed sample.

Degradation of 5-Ethoxy-2-methyl-2,3-dihydro-1-benzothiepin-3-one (11a). Conversion into 2-Methyl-2,3,4,5-tetrahydro-1-benzothiepin-3,5-dione (12).—A solution of **11a** (0.50 g, 0.0021 mol), acetone (10 ml), hydrochloric acid (12 *N*, 10 drops), and water (3.3 ml) were stirred under nitrogen at the reflux temperature. Studies of aliquots showed that after 6 hr the vinyl ether **11a** was absent (no absorption at ν 1210 cm^{-1}) and that the concentration of **12** was at a maximum ($\nu_{C=O}$ 1710 cm^{-1}). The mixture was concentrated (rotary evaporator) and the organic product was chromatographed over silica gel (15 g, 100–200 mesh); 200-ml fractions were collected; and the order of solvent use was as described above for the reaction of **6** with strong base. A red oil (0.120 g) was collected (with 20% benzene–petroleum ether) which was redistilled (Babcock apparatus) to give 0.1 g [22% yield, bp 85° (0.05 mm)] of **12** as a pale yellow oil. The material was identical (ir and nmr) with the sample described above which was obtained directly from **6**.

Conversion into α-(O-Carboxyphenylsulfinyl)propionic Acid (16).—The hydrolysis of **11a** (1.56 g, 0.0064 mol) was carried out essentially as described above. The reaction mixture, after 6 hr at the reflux temperature, was poured into a beaker and sufficient 5% sodium hydroxide was added to adjust the pH of the solution to **7** (universal indicator paper). Acetone was then removed (rotatory evaporator). Water (50 ml) was added to the suspension of red oil in water, and potassium hydroxide (0.70 g) was added to dissolve the oil. The alkaline solution was added dropwise to a solution of 6% aqueous sodium hypochlorite (47 g, Purex bleach, 0.038 mol) and the resulting solution was allowed to stir for 16 hr. The solution was made strongly acidic by addition of 5% hydrochloric acid, and was treated with sodium sulfite (5 g) to remove excess hypochlorite. The solution was extracted with ether (three 100-ml portions) and the ether solution was dried ($MgSO_4$) and concentrated to give a brown oil (0.94 g) which partly solidified. Treatment of the oil with ether gave 0.16 g of white solid (mp 164° dec with gas evolution) and 0.79 g of brown oil. The aqueous acidic solution was concentrated to one-third its volume and was reprocessed to give an additional 0.2 g of solid (mp 158° dec) and 0.06 g of oil.

The oil was not processed further. The white solid (0.36 g,

22% yield of slightly impure **16**) was dissolved in methanol and water (at cloud point) and the solution was filtered and cooled. The yield of **16** was 0.27 g (mp 163–165° dec, 16.7%). It had mp 165–166° dec after further recrystallization and 161° after careful drying. The material was identical with authentic **16** (ir and mixed decomposition point) prepared (38% yield) by oxidation of α-(O-carboxyphenylmercapto)propionic acid[15,16] with hydrogen peroxide in acetic acid–methanol.

Anal. Calcd for $C_{10}H_{10}O_5S$: C, 49.58; H, 4.16. Found: C, 49.69; H, 4.33.

Conversion of 9 into 19.—A solution prepared from **9** (0.117 g, 0.477 mmol), water (10 ml) acetone (25 ml) and hydrochloric acid (12 *N*, 8 drops) was heated under nitrogen for 48 hr. Acetone was removed (rotatory evaporator) from the cooled mixture and the residue was extracted with ether to give 0.173 g of red oil. The mixture was distilled without fractionation in a Babcock apparatus to give 0.11 g of yellow oil. The infrared and nmr spectra showed that the material was principally 3-hydroxymethylene-2-methylthiochroman-4-one (**18**). The product was chromatographed over silica gel (10 g, 100–200 mesh) and the red oil (0.06 g), eluted with 20% benzene–80% petroleum ether (bp 60–80°), was heated at 100° for 5 min with acetic anhydride containing triethylamine (1 drop). The mixture was allowed to stand 24 hr and was concentrated (at 0.1 mm) and the orange solid was collected and recrystallized from petroleum ether (bp 60–80°) to give yellow-orange crystals (0.01 g, mp 77–79°). The infrared and nmr spectra of the product were essentially identical with those of authentic 3-acetoxymethylene-2-methylthiochroman-4-one (**19**), mp 84°, mmp 79–83°.

3-Acetoxymethylene-2-methylthiochroman-4-one (19).—**3-Hydroxymethylene-2-methylthiochroman-4-one** (**18**) [bp 105–115° (0.025 mm); $n^{25.5}D$ 1.6631; nmr (CCl_4), τ 8.58 (d, 3, *J* = 7 Hz, 2-CH_3), 6.21 (q, 1, *J* = 7 Hz, H-2), 3.10–2.63 and 2.23–1.90 (2 m, 3 and 1, aromatic H), 1.54 (s, 1, CHO), −4.05 to −5.28 (broad s, 1, OH); $\lambda_{max}^{95\%\ EtOH}$ 323 mμ (ε 7750), 268 (shoulder, 6550), and 250 (16,850); $\nu_{C=O}$ 1630 cm^{-1}] was prepared (71% yield) from 2-methylthiochroman-4-one by a procedure essentially identical with that described[17] for the preparation of 2-hydroxymethylenecyclohexanone, and was acetylated, as described in the preceding experiment, to give authentic 3-acetoxymethylene-2-methylthiochroman-4-one: 65% yield, yellow crystals, mp 84–86°; $\nu_{C=O}$ 1660 and 1765 cm^{-1}; nmr (CCl_4), τ 8.48 (d, 3, *J* = 7 Hz, 2-CH_3), 7.78 (s, 3, $OCOCH_3$), 5.63 (q, 1, *J* = 7 Hz, H-2), 3.05–1.82 (2 m, 3 and 1, aromatic H), 1.92 (s, 1, =CHOAc); $\lambda_{max}^{95\%\ EtOH}$ 370 mμ (ε 2920), 278 (11,960), and 248 (19,110).

Anal. Calcd for $C_{13}H_{12}O_3S$: C, 62.88; H, 4.87; S, 12.92. Found: C, 62.68; H, 5.01; S, 13.11.

Authentic 1,3-Diethoxy-4-methylnaphthalene.—The synthesis was patterned after that described[18] for the preparation of naphthoresorcinol.

Ethyl 1,3-Dihydroxy-4-methyl-2-naphthoate.—Crude ethyl hydratropoyl malonate (204 g), prepared by condensation[18] of hydratropoyl chloride (102 g) with diethyl malonate, was treated[18] with sulfuric acid to give ethyl 1,3-dihydroxy-4-methyl-2-naphthoate: 41 g, 29% yield based on hydratropoyl chloride; mp 91–93°; $\nu_{C=O}$ 1640 cm^{-1}, ν_{OH} 3800 cm^{-1}; nmr (CCl_4), τ 8.55 (t, 3, *J* = 7 Hz, OCH_2CH_3), 7.73 (s, 3, 4-CH_3), 5.55 (q, 2, *J* = 7 Hz, OCH_2CH_3), 3.05–1.70 (m, 4, aromatic H), and 0.92 and −1.12 (broad s, one each, OH).

Anal. Calcd for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 68.12; H, 5.97.

1,3-Diethoxy-4-methylnaphthalene (**14**).—Ethyl 1,3-dihydroxy-4-methyl-2-naphthoate (21 g, 0.085 mol) was hydrolyzed[18] with barium hydroxide (22 g) to give 14.4 g (77.5% yield) of crude 1,3-dihydroxy-4-methyl-2-naphthoic acid (mp 134–138° dec with gas evolution). Since considerable loss was encountered in purification of 1,3-dihydroxy-2-naphthoic acid, the crude acid was decarboxylated[16] to give impure 4-methylnaphthoresorcinol (6 g, mp 52–65°, 40% yield). The crude product was dissolved in boiling water (200 ml) containing sodium hydrosulfite (0.5 g) and activated charcoal (0.3 g). The mixture was filtered, saturated with sodium chloride, and cooled to give 3.8 g (25% yield) of product (mp 52–62°). This material was unstable and was, for example, converted into a black tar upon standing in air for 12 hr; consequently it was used immediately, without further purification, in the next step.

Crude 1,3-dihydroxy-4-methylnaphthoresorcinol (3.8 g) was ethylated in 10% aqueous sodium hydroxide (20 ml), under nitrogen at 5°, by action of diethyl sulfate (7 g). The resulting solution was allowed to warm to room temperature and was heated at the reflux temperature for 24 hr. The oil, obtained from the mixture, was crystallized from methanol to give pure **14** (mp 80.5 and 86°, 5–8% yield based on ethyl 1,3-dihydroxy-4-methyl-2-naphthoate).

Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.14; H, 7.65.

Reaction of 6 with Pyridine.—A solution of **6** (5.22 g, 0.018 mol) in pyridine (60 ml) was heated under nitrogen at the reflux temperature. Studies of aliquots showed a maximum yield of product ($\nu_{C=O}$ 1630 cm^{-1}) after 13 days at the reflux temperature. Attempts in subsequent experiments to obtain higher yields of product by using hot collidine or quinoline were unsuccessful. The material was concentrated by vacuum distillation, and the black residue (5 g) was chromatographed on silica gel (100 g); 250-ml fractions were collected, and the solvents were varied: 1–8, petroleum ether (bp 60–80°); 9–16, 20% benzene–petroleum ether; 17–25, 40% benzene; 26–42, 60% benzene; 43–56, 70% benzene; 57–73, 80% benzene; and 74–86, benzene. Fractions 9–27 contained recovered **6** (mp 41–44°, 27.7% recovery), and fractions 41–77 crude **22** (2.4 g, red solid, mp 73–78°, 58.5% yield). This material was recrystallized from 95% ethanol to give pure 3-chloro-2-ethylthiochromanone (**22**) [0.96 g, 23.6% yield, white solid; mp 79.5–81°; $\nu_{C=O}$ 1620 cm^{-1}; $\lambda_{max}^{95\%\ EtOH}$ 344 mμ (ε 10,880), 291 (2610), 281 (3120), 256 (22,600), 250 (22,700), 227 (10,720), and 216 (9800); nmr (CCl_4), τ 8.63 (t, 3, *J* = 8 Hz, OCH_2CH_3), 7.15 (q, 2, *J* = 8 Hz, OCH_2CH_3), and 2.46–2.39 and 1.77–1.50 (2 m, three and one, aromatic H)] which was identical (ir, nmr, melting point and mixture melting point) with an authentic sample.

2-Ethylthiochroman-4-one.—β-(Phenylmercapto)-*n*-pentanoic acid [bp 143–147° (0.05 mm), $n^{25}D$ 1.5560, 85% yield] was prepared from thiophenol and 2-pentenoic acid[19] by a procedure similar to that described for the preparation of β(phenylmercapto)-*n*-butyric acid.[14] This product (59.6 g, 0.284 mol) was treated with polyphosphoric acid (180 g) by a procedure similar to that described for the preparation of[7] 2-methylthiochroman-4-one. The yield of ketone [bp 116–119° (0.025 mm); $n^{26}D$ 1.6002; $\nu_{C=O}$ 1675 cm^{-1}; $\lambda_{max}^{95\%\ EtOH}$ 346 mμ (ε 2960), 262 (7550), and 241 (24,500)] was 64% (35 g).

Anal. Calcd for $C_{11}H_{12}OS$: C, 68.71; H, 6.29; S, 16.68. Found: C, 68.49; H, 6.08; S, 17.08.

Authentic 3-chloro-2-ethylthiochromone (mp 79.5–81°) was prepared in 24.3% yield by chlorination of 2-ethylthiochroman-4-one by a procedure essentially identical with that described[7] for 3-chloro-2-methylthiochromone.

Anal. Calcd for $C_{11}H_9OSCl$: C, 58.79; H, 4.04; Cl, 15.78; S, 14.02. Found: C, 58.91; H, 3.86; Cl, 15.30; S, 14.38.

Registry No.—**5**, 17954-45-9; **6**, 17954-46-0; **8**, 17954-47-1; **9**, 17954-48-2; **10**, 17954-49-3; **11a**, 17954-50-6; **12**, 17954-51-7; **14**, 17954-52-8; **15**, 17954-53-9; **16**, 17954-54-0; **18**, 17954-55-1; **19**, 17954-56-2; **22**, 17954-57-3; 2-methylthiochroman-4-one, 826-86-8; ethyl 1,3-dihydroxy-4-methyl-2-naphthoate, 17954-59-5; 2-ethylthiochroman-4-one, 17954-60-8; 3-chloro-2-ethylthiochromone, 17954-57-3.

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