Furan Derivatives. Part **13** [1]. Synthesis of Thiopyrano[4,3,2-*cd*]benzofuran

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Thiopyrano[4,3,2-*cd*]benzofuran **9** possessing benzofuran and methylenethiopyran structures in the molecule was synthesized starting from 1-chloro-4-methoxy-2-nitrobenzene **11**. Some reactions (formylation, protonation and catalytic hydrogenation) on **9** were examined. The 2-position of **9** was highly reactive toward electrophilic reagents and the furan ring was readily reduced by catalytic hydrogenation with palladium-charcoal. Thiopyrano[4,3,2-*cd*]benzofuran **9** has both properties of methylenethiopyran and benzofuran.

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Introduction.

Tropone **1** [2] and heptafulvene **2** [3] have been widely investigated as nonbenzenoid aromatic compounds. Heptafulvene itself is unstable and the carbon-carbon double bonds have olefinic character rather than aromatic character, however, its derivatives which have electron-withdrawing substituents such as cyano and carbonyl groups at the exo double bond show some aromatic character [4]. On the other hand, pyran-4-one **3** [5] and thiopyran-4-one **4** [5e,6] are iso-π-electronic with tropone. However, compounds **3** and **4** do not show typical carbonyl properties, because contribution of pyrilium or thiopyrilium structure is large [5a,5g,6b,6d]. Similarly, methylenepyran **5** and methylenethiopyran **6** are iso-π-electronic with heptafulvene **2**. While fundamental molecules of methylenepyran and methylenethiopyran are not known there are several derivatives of **5** [5h,7] and **6** [6e-f, 8]. Recently, we reported synthesis and properties of cyclohepta[*cd*]benzofuran **7** possessing benzofuran and heptafulvene structures in one molecule [9]. The results suggest that cyclohepta[*cd*]benzofuran has both properties of benzofuran and heptafulvene. Furthermore, we synthesized furo[4,3,2-*de*][1]benzopyran **8** [10] which is iso-π-electronic with cyclohepta[*cd*]benzofuran **7**. Compound **8** shows both properties of benzofuran and methylenepyran. In this paper, we report synthesis and properties of thiopyrano[4,3,2-*cd*]benzofuran **9** possessing benzofuran and methylenethiopyran structures in the molecule. Thiopyrano[4,3,2-*cd*]benzofuran is a rare heterocycle and compound **10** [11] is known as a derivative.

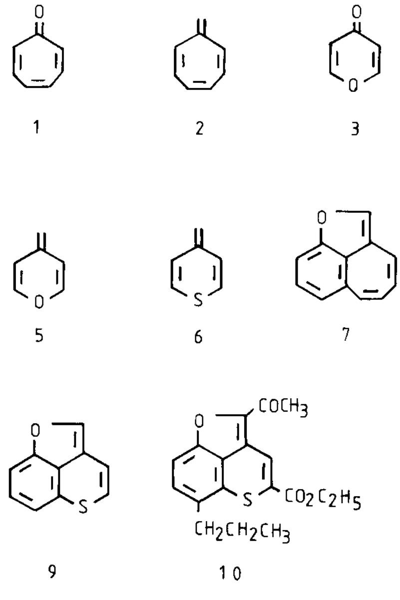


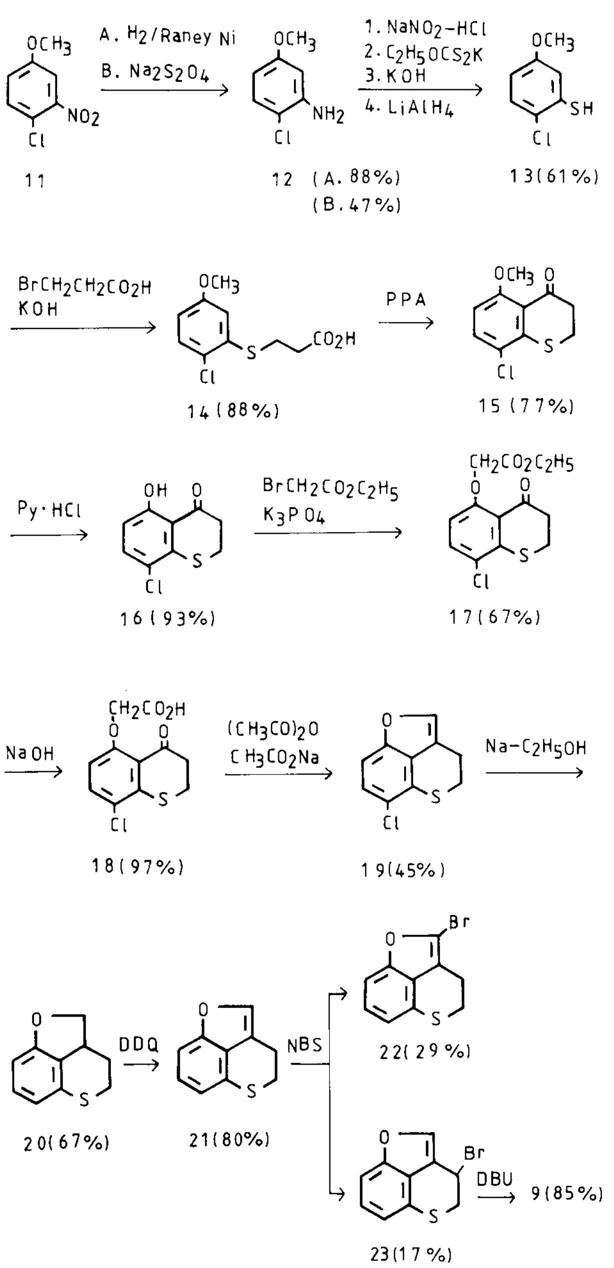
Figure 1

Results and Discussion.

In the synthesis of thiopyrano[4,3,2-*cd*]benzofuran **9** we planned initial preparation of benzothiopyran-4-one moiety and the following condensation of a furan ring at the peri-positions. The synthetic pathway is summarized in Scheme 1.

1-Chloro-4-methoxy-2-nitrobenzene **11** was used as a starting material to introduce a mercapto group into the benzene ring. Catalytic hydrogenation of **11** with Raney nickel gave 2-chloro-5-methoxyaniline **12** [12] in 88% yield. However, this method was not effective for reduction of a large amount of **11** because a long reaction time is necessary for complete reduction. Next, we used sodium hydrosulfite as a reducing agent [13]. Refluxing of **11** with sodium hydrosulfite in aqueous methanol afforded **12** in 47% yield. The yield was not necessarily good, however, the product was pure and used directly in the following reaction. This method is effective to obtain a large amount

Scheme 1



of **12**. To introduce a mercapto group the aniline **12** was converted to the diazonium salt with sodium nitrite and hydrochloric acid, and reacted with potassium *O*-ethyl dithiocarbonate to give dithiocarbonate ester [14]. Hydrolysis of the ester with a aqueous potassium hydroxide solution gave bis(2-chloro-5-methoxyphenyl)disulfide [14], which was reduced to 2-chloro-5-methoxybenzenethiol **13** with lithium aluminum hydride [15]. The yield of **13** based on **12** was 61%. The structure of **13** was determined from the ir and nmr spectra. The ir spectrum showed a peak due to a mercapto group at 2580 cm^{-1} and the ^{1}H nmr spectrum gave an absorption (s, 1H) of a mercapto group at 3.92 ppm.

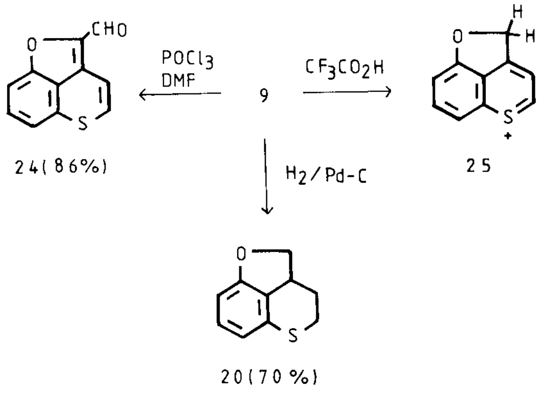
To synthesize benzothiopyran-4-one moiety, thiol **13** was reacted with 3-bromopropanoic acid to give 3-(2-chloro-5-methoxyphenylthio)propanoic acid **14** in 88% yield [16]. There are two reagents (polyphosphoric acid [17] and sulfuric acid [18]) to cyclize **14** into benzothiopyran-4-one **15**. In this case polyphosphoric acid was used as a dehydrating agent. Reaction of **14** with a large amount of polyphosphoric acid gave 8-chloro-5-methoxy-2,3-dihydro-4*H*-1-benzothiopyran-4-one **15** in 77% yield. Using a small amount of polyphosphoric acid reduced the yield of **15**. In this step we attempted to eliminate the chlorine atom of **15** which was no longer necessary in the following reactions. Catalytic hydrogenation of **15** with palladium-charcoal could not remove the chlorine atom. By use of Raney nickel as a catalyst 2′-methoxypropiophenone was obtained. Therefore, we had to eliminate the chlorine atom in the later steps. Compound **15** was readily demethylated by heating with pyridinium chloride to give 8-chloro-5-hydroxy-2,3-dihydro-4*H*-1-benzothiopyran-4-one **16** in 93% yield [9,19].

In the next step furan-ring formation is necessary for synthesis of thiopyrano[4,3,2-*cd*]benzofuran **9**. When compound **16** was reacted with ethyl bromoacetate in the presence of tripotassium phosphate, ethyl (8-chloro-4-oxo-2,3-dihydro-4*H*-1-benzothiopyran-5-yloxy)acetate **17** was obtained in 67% yield. The ester **17** was hydrolyzed with sodium hydroxide to (8-chloro-4-oxo-2,3-dihydro-4*H*-1-benzothiopyran-5-yloxy)acetic acid **18** in 97% yield. By refluxing **18** with sodium acetate in acetic anhydride, 6-chloro-3,4-dihydrothiopyrano[4,3,2-*cd*]benzofuran **19** was obtained in 45% yield. The structure of **19** was confirmed by the ir and nmr spectra. The ir spectrum of **19** gave no absorption due to a carbonyl group and ^{1}H nmr spectrum showed a peak (s, 1H) due to a furan-ring hydrogen at 7.40 ppm. The ^{13}C nmr spectrum of **19** was in agreement with its structure. Some attempts to remove the chlorine atom from **19** were carried out. Catalytic hydrogenation with palladium-charcoal or reduction with tributyltin hydride and 2,2′-azobis(isobutyronitrile) (AIBN) [20] could not remove the chlorine atom from **19**. However, the chlorine atom was eliminated by reduction with sodium-ethanol to give 2,2a,3,4-tetrahydrothiopyrano[4,3,2-*cd*]benzofuran **20** in 67% yield. In this step the fundamental skeleton of thiopyrano[4,3,2-*cd*]benzofuran was prepared.

Finally, we carried reactions out to introduce two carbon-carbon double bonds into the molecule of **20**. Dehydrogenation of **20** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) [21] proceeded smoothly to afford 3,4-dihydrothiopyrano[4,3,2-*cd*]benzofuran **21** in 80% yield, however, the second double bond could not be introduced in the thiopyran ring. Dehydrogenation of **21** using triphenylcarbenim perchlorate [22] was unsuccessful. Therefore, selective bromination of **21** at the allylic position was carried out to prepare a double bond in the thiopyran ring [10,23]. When tetrachloromethane solution (1.3 x 10^{-1} *M*/l) of **21** was refluxed with *N*-bromosuccinimide (NBS), the 2-bromo compound **22** was obtained in 60% yield and the desired 3-bromo compound **23** was obtained in a trace amount. When highly diluted tetrachloromethane solution (1.3 x 10^{-2} *M*/l) of **21** was treated with *N*-bromosuccinimide under fluorescent lamps, the 2-bromo and 3-bromo compounds were isolated in 29 and 17% yields respectively. Unfortunately, further examination of the reaction conditions could not raise the yield of the 3-bromo compound **23**. The 2-bromo compound **22** could be used repeatedly as it was easily converted to **21** by catalytic hydrogenation with palladium-charcoal.

When compound **23** was heated with 1,8-diazabicyclo-[5.4.0]-7-undecene (DBU) [24] the desired thiopyrano[4,3,2-*cd*]benzofuran **9** was obtained in 85% yield. The structure of **9** was confirmed by the nmr spectra. The ^{1}H nmr spectrum of **9** showed two peaks due to the thiopyran-ring hydrogens at 6.05 (d, J = 9.7 Hz, 1H) and 6.45 ppm (d, J = 9.7 Hz, 1H), and an absorption due to a furan-ring hydrogen at 7.18 ppm (s, 1H). The ^{13}C nmr spectrum of **9** was in agreement with its structure. Thus, the chemical shifts (6.05 and 6.45 ppm) of thiopyran-ring hydrogens in **9** appear at olefinic region rather than aromatic region, showing no strong ring current in the pyran ring. These chemical shifts are similar to those (6.2-6.9 ppm) of thiopyran-ring hydrogens in methylenethiopyran derivatives [8d,8j]. In contrast, the chemical shifts of thiopyran-ring hydrogens (7.09 and 7.89 ppm) in thiopyran-4-one **4** show presence of ring current [5g,6d]. Furthermore, the chemical shift of the furan-ring hydrogen (7.17 ppm) in **9** appears at the normal region of benzofurans. Thiopyrano[4,3,2-*cd*]benzofuran **9** is colorless crystals of mp 32-33° and prone to decompose into a greenish material, especially, it decomposes easily in a bright place. However, compound **9** is storable in a freezer (-20°) under a nitrogen atmosphere.

Scheme 2



Some reactions on thiopyrano[4,3,2-*cd*]benzofuran **9** were examined and compared with those of cyclohepta-[*cd*]benzofuran **7**, furo[4,3,2-*de*][1]benzopyran **8**, benzofuran and methylenethiopyran derivatives. However, a variety of reactions could not be carried out because of poor overall yield and instability of **9**. The results are shown in Scheme 2.

Initially, formylation which is a typical reaction of benzofurans was carried out. Reaction of **9** with phosphorus oxychloride and dimethylformamide proceeded smoothly within 30 minutes at room temperature to give 2-formylthiopyrano[4,3,2-*cd*]benzofuran **24** (86%) [9,10,25]. The result suggests that the 2-position of **9** is highly reactive as well as cyclohepta[*cd*]benzofuran **7** and furo[4,3,2-*de*][1]-benzopyran **8** toward the electrophilic reagent since formylation of benzofurans needs refluxing conditions. The high reactivity at the 2-position in **9** is attributed to contribution of thiopyrilium structure.

When trifluoroacetic acid was added to a deuteriochloroform solution of **9**, the color turned immediately deep purple. The ^{1}H nmr spectrum showed a peak due to the methylene hydrogens of the furan-ring at 6.25 ppm (s, 2H) and the two peaks due to thiopyran-ring hydrogens at 8.46 (d, J = 8.8 Hz, 1H) and 9.77 ppm (d, J = 8.8 Hz, 1H). The chemical shifts of the thiopyran-ring hydrogens appeared at a much lower magnetic field (2.4-3.3 ppm) than those of the parent molecule of **9**, showing production of a thiopyrylium ion **25**. The protonation is attributed to formation of a stable thiopyrylium ion [26]. In contrast, 3-ethylbenzofuran do not give such a cation under the same conditions. The property is similar to that of methylenethiopyran derivatives [27], cyclohepta[*cd*]benzofuran [9] and furo[4,3,2-*de*][1]benzopyran **8** [10].

Next, hydrogenation was examined on **9**. Upon catalytic hydrogenation with palladium-charcoal, **9** absorbed two equivalents of hydrogen to give 2,2a,3,4-tetrahydrothiopyrano[4,3,2-*cd*]benzofuran **20** in 70% yield, showing facile reduction of the carbon-carbon double bond in the furan ring of **9**. Usually, the furan ring of benzofurans is not so easy to reduce.

As mentioned above, the ^{1}H nmr spectrum and reactions of **9** suggest that thiopyrano[4,3,2-*cd*]benzofuran has both properties of methylenethiopyran and benzofuran.

EXPERIMENTAL

The melting points are uncorrected. Column chromatography was performed on silica gel (Wakogel C-200). Unless otherwise stated anhydrous sodium sulfate was employed as the drying agent. Ether refers to diethyl ether. Polyphosphoric acid (PPA) was prepared by heating a mixture of phosphorus pentoxide (525 g) and 85% phosphoric acid (670 g) at 140-150° for 5 hours. The ir spectra were determined on a Hitachi Model 270-30 IR spectrometer. The ^{1}H and ^{13}C nmr spectra were determined at 90

MHz and 22.49 MHz on a JEOL-FX 90Q FT NMR spectrometer, using tetramethylsilane as the internal standard.

2-Chloro-5-methoxyaniline **12**.

Method A. Reduction of **11** with Raney Nickel.

A mixture of commercially available **11** (20.0 g, 106 mmoles), Raney nickel (0.30 g) and ethanol (200 ml) was shaken at room temperature under hydrogen atmosphere (1 atmosphere). Raney nickel (0.07 g) was added every two hours because activity of the catalyst decreased gradually. For complete reduction about 24 hours were necessary. After removal of the catalyst by filtration the ethanol was evaporated. The resulting oil was distilled to give **12** (14.8 g, 88%) as a colorless oil, bp 140° at 3.0 Torr (lit [12] 140° at 18 Torr); ir (neat): 3475, 3380 (NH_2) cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.70 (s, 3H, OCH_3), 3.98 (broad s, 2H, NH_2), 6.14-6.24 (m, 2H, Ar-H_2), 7.00-7.10 (m, 1H, Ar-H); ^{13}C nmr (deuteriochloroform): δ 55.3 (q), 101.4 (d), 104.9 (d), 111.3 (s), 129.8 (d), 143.8 (s), 159.4 (s).

Anal. Calcd. for C_7H_8ClNO: C, 53.34; H, 5.12; N, 8.89. Found: C, 53.45; H, 5.24; N, 8.97.

Method B. Reduction of **11** with Sodium Hydrosulfite.

A mixture of **11** (25.0 g, 133 mmoles), sodium hydrosulfite (83.6 g, 480 mmoles) and aqueous methanol (400 ml, methanol:water = 3:1) was refluxed for 3 hours. After removal of insoluble materials by filtration the methanol was evaporated. To the residue a 10*M* aqueous potassium hydroxide solution was added and the resulting aniline was extracted with ether. The extract was washed, dried and evaporated to give **12** (9.90 g, 47%). This compound was pure enough to use in the following reaction.

2-Chloro-5-methoxybenzenethiol **13**.

Compound **12** (20.0 g, 126 mmoles) was dissolved in 6*M* hydrochloric acid (210 ml) and diazotized by adding a 3*M* aqueous solution (48 ml) of sodium nitrite under cooling with ice-water. The diazonium solution was dropped into potassium *O*-ethyl dithiocarbonate (100 g, 623 mmoles) in water (100 ml) which was kept at 70° with stirring. After addition the solution was further stirred at 70° for 1 hour and extracted with ether. The extract was washed, dried and evaporated. The resulting dithiocarbonate ester was dissolved in ethanol (100 ml) and hydrolyzed by adding a 4*M* aqueous potassium hydroxide solution (100 ml) and heating at 70° for 2 hours with stirring. The solution was acidified with 6*M* hydrochloric acid and the resulting products were extracted with ether. The extract was washed, dried and evaporated. The residue was chromatographed and eluted with benzene (50)-hexane (50) to give disulfide. The disulfide in dry ether (80 ml) was added during 30 minutes into an ethereal solution (50 ml) of lithium aluminum hydride (1.1 g, 29.2 mmoles) under cooling with ice-water and with stirring. The mixture was refluxed for 1 hour and then decomposed with an excess of 6*M* sulfuric acid. The resulting product was extracted with ether. The extract was washed, dried and evaporated. The residue was chromatographed and eluted with benzene (50)-hexane (50) to give **13** (13.7 g, 61%) as a pale yellow oil [14b]; ir (neat): 2570 (SH) cm^{-1}; ^1H nmr (deuteriochloroform): δ 3.75 (s, 3H, OCH_3), 3.92 (s, 1H, SH), 6.62 (dd, J = 2.9 and 8.8 Hz, 1H, Ar-H), 6.86 (d, J = 2.9 Hz, 1H, Ar-H), 7.23 (d, J = 8.8 Hz, 1H, Ar-H); ^{13}C nmr (deuteriochloroform): δ 55.5 (q), 112.7 (d), 114.8 (d), 123.4 (s), 130.1 (d), 132.4 (s), 158.3 (s).

Anal. Calcd. for C_7H_7ClOS: C, 48.14; H, 4.04. Found: C, 47.87; H, 4.12.

3-(2-Chloro-5-methoxyphenylthio)propanoic Acid **14**.

3-Bromopropanoic acid (17.6 g, 115.0 mmoles) was dissolved in a 2*M* aqueous potassium hydroxide solution (60 ml) which was deoxygenated by bubbling nitrogen gas. Compound **13** (20.0 g, 114.5 mmoles) in a deoxygenated 2*M* aqueous potassium hydroxide solution (50 ml) was added to the bromopropanoic acid solution under a nitrogen atmosphere and the mixture was stirred for 2 hours at 50°. The solution was acidified with 6*M* hydrochloric acid and the resulting products were extracted with ether. The extract was washed three times with a 1*M* aqueous potassium carbonate solution. The alkaline solution was acidified with 6*M* hydrochloric acid and the resulting precipitates were extracted with ether. The extract was washed, dried and evaporated to give **14** (24.9 g, 88%). It formed colorless crystals from ether, mp 72-73°; ir (potassium bromide): 1710 (CO_2H) cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.72 (t, J = 6.7 Hz, 2H, SCH_2CH_2CO), 3.17 (t, J = 6.7 Hz, 2H, SCH_2CH_2CO), 3.77 (s, 3H, OCH_3), 6.66 (dd, J = 2.9 and 8.8 Hz, 1H, Ar-H), 6.86 (d, J = 2.9 Hz, 1H, Ar-H), 7.25 (d, J = 8.8 Hz, 1H, Ar-H), 10.49 (broad s, 1H, CO_2H); ^{13}C nmr (deuteriochloroform): δ 27.6 (t), 33.8 (t), 55.6 (q), 112.9 (d), 115.7 (d), 126.0 (s), 130.4 (d), 135.3 (s), 158.6 (s), 177.6 (s).

Anal. Calcd. for $C_{10}H_{11}ClO_3S$: C, 48.68; H, 4.49. Found: C, 48.82; H, 4.70.

8-Chloro-5-methoxy-2,3-dihydo-4*H*-1-benzothiopyran-4-one **15**.

A mixture of **14** (10.0 g, 40.5 mmoles) and polyphosphoric acid (1000 g) was heated at 80° for 2 hours with stirring. The mixture was poured into ice-water and extracted with benzene. The extract was washed with a 1*M* aqueous potassium carbonate solution, then with water, dried and evaporated to give **15** (7.10 g, 77%). It formed colorless crystals from ethanol, mp 88-89°; ir (potassium bromide): 1690 (Ar-CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.86-3.02 (m, 2H, SCH_2CH_2CO), 3.12-3.30 (m, 2H, SCH_2CH_2CO), 3.87 (s, 3H, OCH_3), 6.67 (d, J = 8.9 Hz, 1H, Ar-H), 7.37 (d, J = 8.9 Hz, 1H, Ar-H); ^{13}C nmr (deuteriochloroform): δ 26.0 (t), 40.4 (t), 56.4 (q), 109.3 (d), 122.7 (s), 133.5 (d), 142.8 (s), 159.7 (s), 193.0 (s).

Anal. Calcd. for $C_{10}H_9ClO_2S$: C, 52.52; H, 3.97. Found: C, 52.43; H, 4.21.

8-Chloro-5-hydroxy-2,3-dihydro-4*H*-1-benzothiopyran-4-one **16**.

A mixture of **15** (20.0 g, 87.4 mmoles) and pyridinium chloride (100 g, 865 mmoles) was heated at 200° for 1.5 hours with occasional stirring. After cooling the mixture was poured into ice-water and extracted with ether. The extract was washed, dried and evaporated to give **16** (17.5 g, 93%). It formed yellow crystals from ethanol, mp 70-72°; ir (potassium bromide): 1635 (Ar-CO) cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.91-3.07 (m, 2H, SCH_2CH_2CO), 3.14-3.33 (m, 2H, SCH_2CH_2CO), 6.64 (d, J = 8.9 Hz, 1H, Ar-H), 7.34 (d, J = 8.9 Hz, 1H, Ar-H), 12.76 (s, 1H, OH); ^{13}C nmr (deuteriochloroform): δ 25.2 (t), 38.7 (t), 115.1 (d), 116.2 (s), 120.6 (s), 136.4 (d), 141.4 (s), 163.3 (s), 200.6 (s).

Anal. Calcd. for $C_9H_7ClO_2S$: C, 50.35; H, 3.29. Found: C, 50.05; H, 3.36.

Ethyl (8-Chloro-4-oxo-2,3-dihydro-4*H*-1-benzopyran-5-yloxy)acetate **17**.

A mixture of **16** (5.00 g, 23.2 mmoles), ethyl bromoacetate (12.0 g, 71.8 mmoles), tripotassium phosphate (20.0 g, 94.2 mmoles) and dimethyl sulfoxide (78 ml) was stirred at room temperature for 20 minutes. After removal of tripotassium phosphate by filtration the filtrate was poured into water and extracted with ether. The extract was washed, dried and evaporated. The residue was chromatographed and eluted with benzene (70)-ether (30) to give **17** (4.70 g, 67%). It formed colorless crystals from ethanol, mp 93-94°; ir (potassium bromide): 1735 ($CO_2CH_2CH_3$), 1680 (Ar-CO) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.29 (t, J = 7.1 Hz, 3H, $OCH_2C\mathit{H}_3$), 2.88-3.04 (m, 2H, $SCH_2C\mathit{H}_2CO$), 3.16-3.32 (m, 2H, $SC\mathit{H}_2CH_2CO$), 4.26 (q, J = 7.1 Hz, 2H, $OC\mathit{H}_2CH_3$), 4.68 (s, 2H, OCH_2CO_2), 6.61 (d, J = 7.0 Hz, 1H, Ar-H), 7.36 (d, J = 7.0 Hz, 1H, Ar-H); ^{13}C nmr (deuteriochloroform): δ 14.1 (q), 25.9 (t), 40.1 (t), 61.3 (t), 67.1 (t), 112.1 (d), 123.8 (s), 124.3 (s), 133.3 (d), 143.0 (s), 157.9 (s), 168.2 (s), 192.7 (s).

Anal. Calcd. for $C_{13}H_{13}ClO_4S$: C, 51.91; H, 4.36. Found: C, 51.87; H, 4.56.

(8-Chloro-4-oxo-2,3-dihydro-4*H*-1-benzothiopyran-5-yloxy)acetic Acid **18**.

Compound **17** (3.50 g, 11.6 mmoles) was dissolved in ethanol (24 ml) and hydrolyzed by adding a 1*M* aqueous sodium hydroxide solution (30 ml) and heating at 50° for 3 hours with stirring. The solution was acidified with 6*M* hydrochloric acid and the resulting precipitates were extracted with ether. The extract was washed, dried and evaporated to give **18** (3.10 g, 97%). It formed colorless crystals from acetone, mp 160-162°; ir (potassium bromide): 1780, 1760 (CO_2H), 1650 (Ar-CO) cm^{-1}; ^{1}H nmr (deuterioacetone): δ 2.92-3.08 (m, 2H, $SCH_2C\mathit{H}_2CO$), 3.28-3.46 (m, 2H, $SC\mathit{H}_2CH_2CO$), 4.83 (s, 2H, OCH_2CO_2), 6.96 (d, J = 8.8 Hz, 1H, Ar-H), 7.57 (d, J = 8.8 Hz, 1H, Ar-H); ^{13}C nmr (deuteriodimethyl sulfoxide): δ 25.3 (t), 39.9 (t), 65.9 (t), 111.8 (d), 122.3 (s), 122.9 (s), 133.3 (d), 142.1 (s), 157.7 (s), 169.5 (s), 192.4 (s).

Anal. Calcd. for $C_{11}H_9ClO_4S$: C, 48.45; H, 3.33. Found: C, 48.33; H, 3.61.

6-Chloro-3,4-dihydrothiopyrano[4,3,2-*cd*]benzofuran **19**.

A mixture of **18** (5.40 g, 19.8 mmoles), sodium acetate (22.8 g, 277 mmoles) and acetic anhydride (75 ml) was refluxed at 150° for 3 hours. The mixture was poured into ice-water, stirred for 10 minutes to decompose excess of acetic anhydride and extracted with ether. The extract was washed with a 1*M* aqueous potassium carbonate solution, then with water, dried and evaporated. The residue was chromatographed and eluted with benzene (30)-hexane (70) to give **19** (1.88 g, 45%). It formed colorless crystals from benzene-hexane, mp 90-91°; ir (potassium bromide): 855 (furan-H) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 3.00-3.28 (m, 4H, SCH_2CH_2CO), 7.12 (d, J = 8.6 Hz, 1H, Ar-H), 7.21 (d, J = 8.6 Hz, 1H, Ar-H), 7.40 (s, 1H, furan-H); ^{13}C nmr (deuteriochloroform): δ 21.3 (t), 29.1 (t), 108.2 (d), 115.0 (s), 123.0 (s), 125.3 (d), 125.3 (s), 127.3 (s), 139.9 (d), 151.8 (s).

Anal. Calcd. for $C_{10}H_7ClOS$: C, 57.01; H, 3.35. Found: C, 56.90; H, 3.48.

2,2a,3,4-Tetrahydrothiopyrano[4,3,2-*cd*]benzofuran **20**.

An ethanolic solution (60 ml) of **19** (3.00 g, 14.2 mmoles) was kept under reflux. Small pieces of sodium were added to the solution until a precipitate of sodium ethoxide appeared. The solution was extracted with ether. The extract was washed, dried and evaporated. The residue was chromatographed and eluted with benzene (50)-hexane (50) to give **20** (1.70 g, 67%). It formed colorless crystals from benzene-hexane, mp 83-84°; ^{1}H nmr (deuteriochloroform): δ 1.32-1.76 (m, 1H, $SCH_2C\mathit{H}_2CH$), 2.24-2.52 (m, 1H, $SCH_2C\mathit{H}_2CH$), 2.96-3.50 (m, 3H, $SC\mathit{H}_2CH_2C\mathit{H}$), 4.00 (dd, J = 8.4 and 11.7 Hz, 1H, OCH_2), 4.79 (dd, J = 8.4 and 8.4 Hz, 1H, OCH_2), 6.48 (d, J = 7.9 Hz, 1H, Ar-H), 6.61 (d, J = 7.9 Hz, 1H, Ar-H), 7.00 (dd, J = 7.9 and 7.9 Hz, 1H, Ar-H); ^{13}C nmr (deuteriochloroform): δ 25.1 (t), 28.1 (t), 38.3 (d), 78.2 (t), 105.0 (d), 116.8 (d), 122.9 (s), 128.8 (d), 131.0 (s), 159.2 (s).

Anal. Calcd. for $C_{10}H_{10}OS$: C, 67.38; H, 5.66. Found: C, 67.47; H, 5.75.

3,4-Dihydrothiopyrano[4,3,2-*cd*]benzofuran **21**.

A mixture of **20** (1.00 g, 5.61 mmoles), DDQ (1.30 g, 5.72 mmoles) and benzene (19 ml) was refluxed for 10 hours. After removal of insoluble materials by filtration the filtrate was evaporated. The residue was chromatographed and eluted with benzene (25)-hexane (75) to give **21** (0.80 g, 80%). It formed colorless crystals from ether, mp 38-39°; ir (potassium bromide): 875 (furan-H) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 2.90-3.12 (m, 4H, SCH_2CH_2), 6.94-7.18 (m, 3H, Ar-H_3), 7.31 (s, 1H, furan-H); ^{13}C nmr (deuteriochloroform): δ 21.9 (t), 28.9 (t), 107.4 (d), 114.9 (s), 118.6 (d), 123.8 (s), 124.9 (d), 128.4 (s), 138.7 (d), 153.4 (s).

Anal. Calcd. for $C_{10}H_8OS$: C, 68.15; H, 4.58. Found: C, 67.93; H, 4.38.

2-Bromo-3,4-dihydrothiopyrano[4,3,2-*cd*]benzofuran **22** and 3-Bromo-3,4-dihydrothiopyrano[4,3,2-*cd*]benzofuran **23**.

A mixture of **21** (0.25 g, 1.41 mmoles), NBS (0.26 g, 1.46 mmoles), benzoyl peroxide (0.035 g, 0.144 mmole) and tetrachloromethane (110 ml) was refluxed under fluorescent lamps for 2 hours in oil bath (bath temperature of 95°). After cooling the solution was washed with a 0.3*M* aqueous sodium sulfite solution, then with water, dried and evaporated. The residue was chromatographed and eluted with benzene (20)-hexane (80). The first fraction gave **22** (0.105 g, 29%). It formed colorless crystals from hexane, mp 61-62°; ^{1}H nmr (deuteriochloroform): δ 2.86-3.00 (m, 2H, $SCH_2C\mathit{H}_2$), 3.06-3.20 (m, 2H, $SC\mathit{H}_2CH_2$), 6.90-7.20 (m, 3H, Ar-H_3); ^{13}C nmr (deuteriochloroform): δ 22.2 (t), 28.6 (t), 107.1 (d), 115.0 (s), 119.3 (d), 122.5 (s), 124.9 (s), 124.9 (d), 127.5 (s), 154.3 (s).

Anal. Calcd. for $C_{10}H_7BrOS$: C, 47.07; H, 2.77. Found: C, 46.82; H, 3.01.

The second fraction afforded **23** (0.062 g, 17%) as a colorless oil; ^{1}H nmr (deuteriochloroform): δ 3.20-3.52 (m, 2H, $SC\mathit{H}_2CHBr$), 5.42 (ddd, J = 1.3, 4.7, and 7.3 Hz, 1H, $SCH_2C\mathit{H}Br$), 6.99-7.24 (m, 3H, Ar-H_3), 7.59 (d, J = 1.3 Hz, 1H, furan-H); ^{13}C nmr (deuteriochloroform): δ 37.7 (d), 37.7 (t), 108.0 (d), 118.3 (s), 119.1 (d), 122.6 (s), 125.5 (d), 126.6 (s), 142.1 (d), 153.3 (s).

Anal. Calcd. for $C_{10}H_7BrOS$: C, 47.07; H, 2.77. Found: C, 46.89; H, 2.90.

Thiopyrano[4,3,2-*cd*]benzofuran **9**.

A mixture of **23** (0.028 g, 0.109 mmole), DBU (0.031 g, 0.203 mmole) and benzene (1.0 ml) was heated at 60° for 40 minutes with stirring. After removal of insoluble materials by filtration the filtrate was directly chromatographed and eluted with benzene (20)-hexane (80). The solvent of the fraction was replaced with ethanol by repeating addition of ethanol and evaporation at room temperature, because direct evaporation of the benzene-hexane solution of **9** afforded decomposed products. Complete evaporation of the ethanol gave **9** (0.016 g, 85%) as colorless crystals, mp 32-33°. Recrystallization of **9** from solvents was difficult.

^{1}H nmr (deuteriochloroform): δ 6.05 (d, J = 9.7 Hz, 1H, SCH=C*H*), 6.45 (d, J = 9.7 Hz, 1H, SC*H*=CH), 6.65-7.24 (m, 3H, Ar-H_3), 7.18 (s, 1H, furan-H); ^{13}C nmr (deuteriochloroform): δ 108.3 (d), 114.2 (d), 115.7 (d), 116.5 (s), 122.1 (d), 124.8 (s), 126.8 (d), 127.2 (s), 135.7 (d), 154.1 (s).

Anal. Calcd. for $C_{10}H_6OS$: C, 68.94; H, 3.47. Found: C, 68.78; H, 3.52.

Formylation of **9** with Phosphorus Oxychloride and Dimethylformamide.

Compound **9** (0.018 g, 0.103 mmole) in dimethylformamide (1.0 ml) was added to phosphorus oxychloride (0.061 g, 0.397 mmole) in dimethylformamide (0.1 ml) and the solution was stirred for 1 hour at room temperature. The tlc analysis showed the formylation finished after 30 minutes. The solution was poured into a 3% sodium hydrogen carbonate solution and left for one day. The resulting precipitate was extracted with ether. The extract was washed, dried and evaporated. The residue was chromatographed and eluted with benzene (90)-ether (**X**) to give 2-formylthiopyrano[4,3,2-*cd*]benzofuran **24** (0.018 g, 86%). It formed yellow crystals from acetone, mp 153-155°; ir (potassium bromide): 1645 (CHO) cm^{-1}; ^{1}H nmr (deuteriodimethyl sulfoxide): δ 7.12-7.58 (m, 5H, Ar-H_3 and SCH=CH), 9.83 (s, 1H, CHO).

Anal. Calcd. for $C_{11}H_6O_2S$: C, 65.33; H, 2.99. Found: C, 65.21; H, 3.10.

Protonation of **9** with Trifluoroacetic Acid.

Trifluoroacetic acid (0.05 ml) was added to a deuteriochloroform solution (0.12 ml) of **9** (0.010 g, 0.0574 mmole) in nmr sample tube. The solution immediately turned a deep purple color and the nmr spectrum showed production of the thiopyrylium ion **25**. ^{1}H nmr (deuteriochloroform): δ 6.25 (s, 2H, OCH_2), 7.62 (d, J = 8.2 Hz, 1H, Ar–H), 8.07 (d, J = 8.2 Hz, 1H, Ar–H), 8.41 (dd, J = 8.2 and 8.2 Hz, 1H, Ar–H), 8.46 (d, J = 8.8 Hz, 1H, SCH=C*H*), 9.78 (d, J = 8.8 Hz, 1H, SC*H*=CH).

Catalytic Hydrogenation of **9** with Palladium-Charcoal.

A mixture of **9** (0.028 g, 0.160 mmole), 10% palladium-charcoal (0.050 g) and ethanol (5.0 ml) was shaken for 2 hours at room temperature under hydrogen atmosphere (1 atmosphere). After removal of the catalyst by filtration the ethanol was evaporated. The residue was chromatographed and eluted with benzene (30)-hexane (70) to give **20** (0.020 g, 70%). This compound was identical with a sample prepared by reduction of **19** using sodium and ethanol in the ir and nmr spectra.

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