An Effective Synthesis of Fused Cyclic Thiopyrans and Pyrans by Molybdenum(VI) Sulfide Catalyzed Reduction of the Corresponding Thiopyranones and Pyranones

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The synthesis of fused cyclic dihydrothiopyrans **2a-c** from dihydrothiopyranones **1a-c** and thiopyrans **2d-f** from thiopyranones **1d-f** by catalytic reduction over molybdenum(VI) sulfide (MoS_3) has been studied. The hydrogenolysis of the carbonyl group of **1a-f** over MoS_3 catalyst proceeded selectively to give the corresponding **2a-f** in high yields. Neither alcohols nor olefins were not detected in the products. The method was also applied successfully to the synthesis of dihydropyran **2h** and pyran **2g** from dihydropyranone **1h** and pyranone **1g**.

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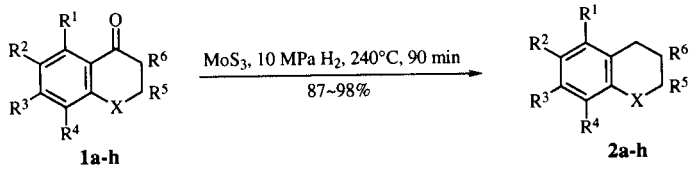
Fused cyclic dihydrothiopyrans may be obtained by the ring closure of 3-arylthio-1-propene [1], but this process requires a high temperature, and is accompanied by the thio-Claisen rearrangement to form undesired thiophenes [2a,b]. Dihydrothiopyrans or thiopyrans can also be obtained from the corresponding thiopyranones by Clemmensen reduction [3] or by the reaction with a reducing reagent such as diborane [4a-b]. The starting thiopyranones are easily prepared by the ring closure of 3-arylthiopropionic acid or 3-arylthioacrylic acid [5].

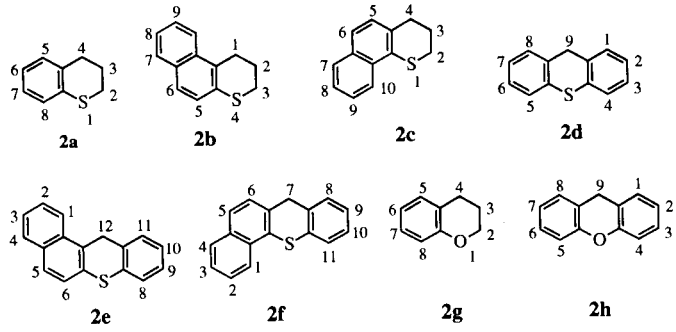
However, for a large scale synthesis of these thiopyrans the catalytic reduction of the corresponding thiopyranones is undoubtedly more advantageous than those using stoichiometric reducing reagents, although the catalytic reduction has rarely been used for the synthesis. This is because the reaction proceeded with saturation of the aromatic ring and cleavage of the heterocyclic ring simultaneously under violent reaction conditions required for the reduction of the sulfur-containing compounds [6]. As an exceptional example, Campbell *et al* [7] hydrogenated 2,2-dimethylthiochroman-4-one using 25% by its weight of 5% palladium on carbon in ethyl acetate-sulfuric acid and obtained 2,2-dimethylthiochroman in 82% yield. These authors stated that the success of the selective hydrogenation of this compound is an unusual result and is attributed to the steric hindrance of the *gem*-dimethyl groups of the chomanone which may block the catalyst-poisoning sulfur atom.

Previously, we have reported the hydrogenation of organic sulfur compounds over a molybdenum(VI) sulfide (MoS_3) catalyst [8a-b,9]. As this catalyst has inertness to sulfur poisoning, the hydrogenation of sulfur-containing compounds proceeded smoothly under the usual



1a-h **2a-h**

a, X = S, $R^1 = R^2 = R^3 = R^4$ = H, $R^5 = R^6 = CH_2$
b, X = S, $R^1 = R^2$ = benz, $R^3 = R^4$ = H, $R^5 = R^6 = CH_2$
c, X = S, $R^1 = R^2$ = H, $R^3 = R^4$ = benz, $R^5 = R^6 = CH_2$
d, X = S, $R^1 = R^2 = R^3 = R^4$ = H, $R^5 = R^6$ = benz
e, X = S, $R^1 = R^2$ = benz, $R^3 = R^4$ = H, $R^5 = R^6$ = benz
f, X = S, $R^1 = R^2$ = H, $R^3 = R^4$ = benz, $R^5 = R^6$ = benz
g, X = O, $R^1 = R^2 = R^3 = R^4$ = H, $R^5 = R^6 = CH_2$
h, X = O, $R^1 = R^2 = R^3 = R^4$ = H, $R^5 = R^6$ = benz



2a **2b** **2c** **2d** **2e** **2f** **2g** **2h**

Figure 1.

conditions. Furthermore, the hydrogenation of an octanethioic acid over the MoS_3 catalyst proceeded to form an octanethiol by cleavage of the C-O linkage of the carbonyl group of the thio acid [10]. On the other hand, the hydrogenation of the aromatic ring did not proceed over the MoS_3 catalyst [11].

On the basis of the previous experience described above, we have studied the selective synthesis of thiopyrans by the catalytic hydrogenation of the corresponding thiopyranones using the MoS_3 catalyst under a non-violent reaction condition.

The results show that the MoS_3 catalyst can achieve the transformation of the carbonyl group of thiopyranones into the corresponding methylene group to afford thiopyrans in high yields.

The hydrogenation of condensed aromatic dihydrobenzothiopyranones **1a-1c** and thiopyranones **1d-1f** over MoS_3 catalyst proceeded smoothly at 240° and 10 MPa H_2 to afford the corresponding dihydrothiopyrans **2a-2c** and thiopyrans **2d-2f** in high yields without forming thiopyranols or being accompanied by the hydrogenation of the aromatic ring. Chromanone **1g** and xanthone **1h** were also reduced in a similar manner to give chroman **2g** and xanthene **2h**, respectively.

All the products were easily separated from the reaction mixtures and purified. The structural identification of the products was confirmed made by means of ^{1}H-nmr spectroscopy and mass spectroscopy.

It is considered that the hydrogenation of the carbonyl group of 2,3-dihydro-1*H*-naphtho[2,1-*b*]thiopyran-1-one (**1b**) and 12*H*-benz[a]thioxanthen-12-one (**1e**) may suffer decrease in reactivity and selectivity because of a hindered structure.

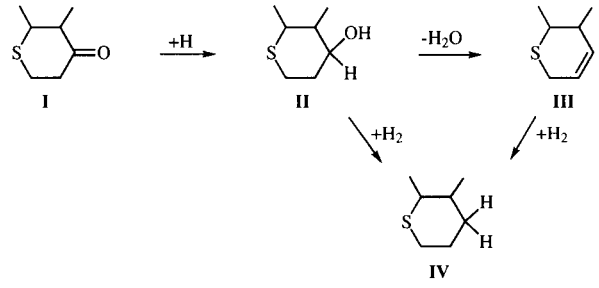
The hydrogenation of **1b** over MoS_3 catalyst, however, proceeded smoothly, the same as the other compounds to give 2,3-dihydro-1*H*-naphtho[2,1-*b*]thiopyran (**2b**) as the only product without forming the corresponding alcohol and olefin. The corresponding alcohol and olefin were not found in the product even in a conversion of about 30% in the hydrogenation of **1b**.

The hydrogenation of **1b** over 5% palladium on carbon catalyst instead of MoS_3 catalyst proceeded to give **2b** in only an 18% yield and the main product was the hydrodesulfurized compound. Even hydrogenation over 5% palladium sulfide on carbon catalyst, which is more resistant to sulfur poisoning, gave only a 51% yield of **2b**.

Consequently, the MoS_3 catalyst has been found effective for the hydrogenolysis from fused cyclic carbonyl compounds containing sulfur or oxygen atoms to the corresponding methylene compounds.

In general, the hydrogenolysis of aromatic carbonyl compounds occurs *via* benzyl type alcohols which are readily susceptible to the loss of the hydroxyl group [12]. The hydrogenolysis is facilitated by polar solvents and by acid [13a-b].

In our study, the corresponding alcohol and/or olefin were not found in the course of the catalytic reaction. Even with the use of octane as a nonpolar solvent, the hydrogenation of dihydrothiopyranones and thiopyranones over MoS_3 catalyst gave only dihydrothiopyrans and thiopyrans.



Scheme 1. Reaction pathways for the hydrogenolysis of thiopyranone over molybdenum(VI) sulfide.

The reaction pathways of the hydrogenolysis may briefly be described as shown in Scheme 1.

The carbonyl compound **I** is first hydrogenated to the corresponding alcohol **II**. Then alcohol **II** is transformed into the methylene compound **IV**. It is considered that the transformation of **II** into **IV** may proceed in two ways [14]:

1) The alcohol **II** is dehydrated to an olefinic type compound **III** which is hydrogenated to give **IV**.

2) The alcohol **II** is hydrogenated directly to give **IV**.

Although in the cases of **1a, 1b, 1c,** and **1g** the dehydration to form **III** may be possible, with **1d, 1e, 1f,** and with **1h** the formation of **III** is not possible and **IV** must be formed directly from **II** by hydrogenolysis. The fact that neither **III** nor **II** was detected and the product was only **2b** at a low conversion of 30% in the hydrogenation of **1b** suggests that with **1a, 1b, 1c,** and **1g**, as in the cases of **1d, 1e, 1f,** and **1h**, the carbonyl group is hydrogenolyzed without forming **III** probably *via* **II** which is converted to **IV** as soon as formed.

The present method has the following advantages: the reaction proceeds highly selectively, separation of the products is easy, and the reaction can be performed with a wide range of fused cyclic dihydrothiopyrans, thiopyrans and pyrans.

EXPERIMENTAL

Melting points were determined using a Yanagimoto melting apparatus and are not corrected. The ^{1}H-nmr spectra were obtained with a JEOL JNM-GX400 spectrometer in the indicated solvents. Chemical shifts and coupling constants were measured in ppm (δ) and J (Hz) with respect to TMS. The mass spectra were obtained on a Hitachi M-80B spectrometer. Elemental analyses were performed on a Perkin-Elmer 240C elemental analyzer.

2,3-Dihydro-1*H*-naphtho[2,1-*b*]thiopyran-1-one (**1b**) [15], 2,3-dihydro-4*H*-naphtho[1,2-*b*]thiopyran-4-one (**1c**) [16], 12*H*-benz[*a*]thioxanthen-12-one (**1e**) [17] and 7*H*-benz[*c*]thioxanthen-7-one (**1f**) [17] were made by literature methods.

Preparation of Thiopyrans or Dihydrothiopyrans **2a-f**.

General Procedures.

Thiopyranones or dihydrothiopyranones **1a-f**: (5 mmoles), MoS_3 catalyst (10 mmoles) and octane (10 ml) were placed in a 100 ml magnetically stirring type of autoclave, and subsequently hydrogen was admitted to an initial pressure of 10 MPa after several flushings. The autoclave was then heated to 240°. Stirring was started about 10 minutes after an establishment of thermal equilibrium, and continued until the pressure ceased to fall. After cooling the autoclave under running water, the liquid phase was separated from the catalyst by filtration. The reaction was complete in 90 minutes by means of gas chromatography monitoring. The filtrate was evaporated under reduced pressure and distillation or recrystallization of the resulting residue afforded thiopyrans and dihydrothiopyrans **2a-f** in high yield.

Thiochromane (**2a**).

This compound was obtained as colorless liquid, 95% yield; ms: (70 eV) m/z [M+] Found: 150.0491; Calcd. for $C_9H_{10}S$: 150.0502; ^{1}H-nmr (deuteriochloroform): δ 2.11 (2H, quin, J = 6.0 Hz, $SCH_2CH_2CH_2$), 2.81 (2H, t, J = 6.0 Hz, $SCH_2CH_2CH_2$), 3.02 (2H, t, J = 6.0 Hz, $SCH_2CH_2CH_2$), 6.94-7.10 (4H, m, Arom).

Anal. Calcd. for $C_9H_{10}S$: C, 72.00; H, 6.66; S, 21.33. Found: C, 72.05; H, 6.68; S, 21.30.

2,3-Dihydro-1*H*-naphtho[2,1-*b*]thiopyran (**2b**).

This compound was obtained as colorless needles (hexane), 96% yield, mp 96.5-97.0°; ms: (70 eV) m/z [M+] Found: 200.0662; Calcd. for $C_{13}H_{12}S$; 200.0659; ^{1}H-nmr (deuteriochloroform): δ 2.32 (2H, quin, J = 6.3 Hz, $SCH_2CH_2CH_2$), 3.07 (2H, t, J = 6.3 Hz, $SCH_2CH_2CH_2$), 3.18 (2H, t, J = 6.3 Hz, $SCH_2CH_2CH_2$), 7.16 (1H, d, J = 8.5 Hz, 5-H), 7.38 (1H, ddd, J = 7.9, 6.8, 1.1 Hz, 8-H), 7.48 (1H, ddd, J = 8.2, 6.8, 1.1 Hz, 9-H), 7.55 (1H, dd, J = 7.9, 1.1 Hz, 7-H), 7.89 (1H, dd, J = 8.2, 1.1 Hz, 10-H).

Anal. Calcd. for $C_{13}H_{12}S$: C, 78.00; H, 6.00; S, 16.00. Found: C, 78.05; H, 5.89; S, 15.97.

2,3-Dihydro-4*H*-naphtho[1,2-*b*]thiopyran (**2c**).

This compound was obtained as colorless liquid, 88% yield, ms: (70 eV) m/z [M+] Found: 200.0629; Calcd. for $C_{13}H_{12}S$: 200.0659; ^{1}H-nmr (deuteriochloroform): δ 2.21 (2H, quin, J = 6.0 Hz, $SCH_2CH_2CH_2$), 2.99 (2H, t, J = 6.0 Hz, $SCH_2CH_2CH_2$), 3.15 (2H, t, J = 6.0 Hz, $SCH_2CH_2CH_2$), 7.13 (1H, d, J = 8.2 Hz, 5-H), 7.43 (1H, ddd, J = 8.2, 7.9, 1.3 Hz, 8-H), 7.45 (1H, ddd, J = 8.2, 8.2, 1.3 Hz, 9-H), 7.48 (1H, d, J = 8.2 Hz, 6-H), 7.75 (1H, dd, J = 7.9, 1.3 Hz, 7-H), 8.08 (1H, dd, J = 8.2, 1.3 Hz, 10-H).

Anal. Calcd. for $C_{13}H_{12}S$: C, 78.00; H, 6.00; S, 16.00. Found: C, 77.98; H, 6.03; S, 15.95.

Thioxanthene (**2d**).

This compound was obtained as colorless needles (cyclohexane), 97% yield, mp 134.0-134.5°; ms: (70 eV) m/z [M+] Found: 198.0513; Calcd. for $C_{13}H_{10}S$: 198.0502; ^{1}H-nmr (deuteriochloroform): δ 3.86 (2H, s, 9-H), 7.18 (2H, ddd, J = 7.4, 7.4, 1.9 Hz, 2-H and 7-H), 7.21 (2H, ddd, J = 7.4, 7.4, 1.9 Hz, 3-H and 6-H), 7.32 (2H, dd, J = 7.4, 1.9 Hz, 4-H and 5-H), 7.44 (2H, dd, J = 7.4, 1.9 Hz, 1-H and 8-H).

Anal. Calcd. for $C_{13}H_{10}S$: C, 78.79; H, 5.05; S, 16.16. Found: C, 78.76; H, 5.13; S, 16.19.

Benz[*a*]thioxanthene (**2e**).

This compound was obtained as colorless needles (toluene), 87% yield, mp 109.0-109.5°; ms: (70 eV) m/z [M+] Found: 248.0648; Calcd. for $C_{17}H_{12}S$: 248.0659; ^{1}H-nmr (deuteriochloroform): δ 4.29 (2H, s, CH_2), 7.21 (1H, ddd, J = 7.4, 7.4, 1.6 Hz, 10-H), 7.24 (1H, ddd, J = 7.4, 7.4, 1.6 Hz, 9-H), 7.44 (1H, dd, J = 7.4, 1.6 Hz, 8-H), 7.46 (1H, ddd, J = 8.2, 8.2, 1.3 Hz, 3-H), 7.48 (1H, dd, J = 7.4, 1.6 Hz, 11-H), 7.52 (1H, d, J = 8.5 Hz, 6-H), 7.58 (1H, ddd, J = 8.2, 8.2, 1.3 Hz, 2-H), 7.69 (1H, d, J = 8.5 Hz, 5-H), 7.84 (1H, dd, J = 8.2, 1.3 Hz, 4-H), 8.25 (1H, dd, J = 8.2, 1.3 Hz, 1-H).

Anal. Calcd. for $C_{17}H_{12}S$: C, 82.26; H, 4.84; S, 12.90. Found: C, 82.24; H, 4.89; S, 12.89.

Benz[*c*]thioxanthene (**2f**).

This compound was obtained as colorless needles (toluene), 92% yield, mp 88.5-89.5°; ms: (70 eV) m/z [M+] Found: 248.0650; Calcd. for $C_{17}H_{12}S$: 248.0659; ^{1}H-nmr (deuteriochloroform): δ 4.02 (2H, s, CH_2), 7.21 (1H, ddd, J = 7.4, 7.4, 1.6 Hz, 10-H), 7.25 (1H, ddd, J = 7.4, 7.4, 1.6 Hz, 9-H), 7.37 (1H, dd, J = 7.4, 1.6 Hz, 11-H), 7.44 (1H, d, J = 8.2 Hz, 6-H), 7.47 (1H, ddd, J = 8.2, 8.2, 1.3 Hz, 3-H), 7.55 (1H, dd, J = 7.4, 1.6 Hz, 8-H), 7.56 (1H, ddd, J = 8.2, 8.2, 1.3 Hz, 2-H), 7.72 (1H, d, J = 8.2 Hz, 5-H), 7.83 (1H, dd, J = 8.2, 1.3 Hz, 4-H), 8.30 (1H, dd, J = 8.2, 1.3 Hz, 1-H).

Anal. Calcd. for $C_{17}H_{12}S$: C, 82.26; H, 4.84; S, 12.90. Found: C, 82.19; H, 4.99; S, 12.96.

Preparation of the Fused Pyrans **2g,h**.

General Procedures.

In a similar manner, fused pyranones **1g,h** were reduced to form corresponding pyrans **2g,h**.

Chromane (**2g**).

This compound was obtained as colorless liquid, 94% yield; ms: (70 eV) m/z [M+] Found: 134.0737; Calcd. for $C_9H_{10}O$: 134.0731; ^{1}H-nmr (deuteriochloroform): δ 2.00 (2H, quin, J = 6.6 Hz, 3-H), 2.79 (2H, t, J = 6.6 Hz, 4-H), 4.18 (2H, t, J = 6.6 Hz, 2-H), 6.78 (1H, dd, J = 8.2, 1.1 Hz, 5-H), 6.82 (1H, ddd, J = 7.4, 7.4, 1.1 Hz, 7-H), 7.03 (1H, dd, J = 7.4, 1.6 Hz, 8-H), 7.07 (1H, ddd, J = 8.2 , 7.4, 1.6 Hz, 6-H).

Anal. Calcd. for $C_9H_{10}O$: C, 80.60; H, 7.46. Found: C, 80.55; H, 7.51.

Xanthene (**2h**).

This compound was obtained as colorless needles (cyclohexane), 98% yield, mp 98.0-99.0°; ms: (70 eV) m/z [M+] Found: 182.0724; Calcd. for $C_{13}H_{10}O$: 182.0731; ^{1}H-nmr (deuteriochloroform): δ 4.06 (2H, s, 9-H), 7.00-7.05 (4H, m, 1-H, 3-H, 6-H and 8-H), 7.16-7.21 (4H, m, 2-H, 4-H, 5-H and 7-H).

Anal. Calcd. for $C_{13}H_{10}O$: C, 85.71; H, 5.49. Found: C, 85.73; H, 5.42.

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