A Facile Synthesis of 1-Alkylthio and Acylthio-2,3-dihydro-1*H*-naphtho[2,1-*b*]thiopyrans and 4-Alkylthio and Acylthio-3,4-dihydro-2*H*-naphtho[1,2-*b*]thiopyrans

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The reaction of 3-(2-naphthylthio)propionaldehyde (**3**) and its (1-naphthylthio)isomer (**7**) with a variety of thiols and thio acids in the presence of sulfuric acid at room temperature afforded 1-alkylthio and acylthio-2,3-dihydro-1*H*-naphtho[2,1-*b*]thiopyrans **5** and 4-alkylthio and acylthio-3,4-dihydro-2*H*-naphtho[1,2-*b*]thiopyrans **9** in excellent yield.

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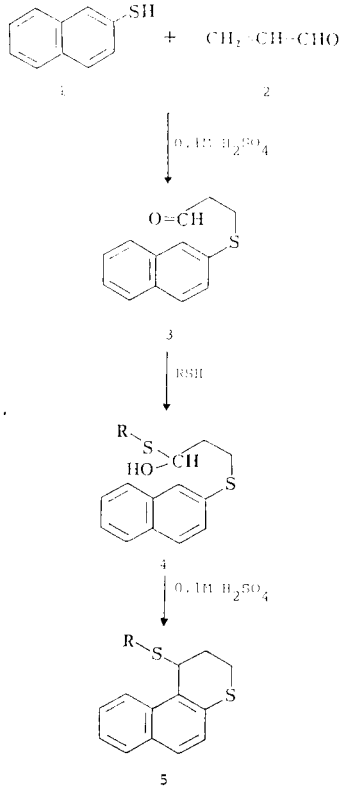
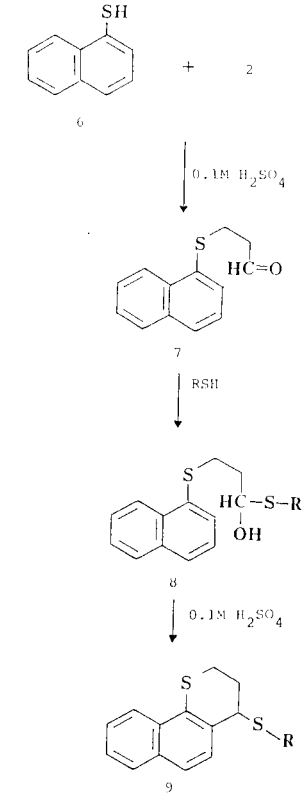
Fused thiopyrans are useful in a variety of fields as drugs and dyes intermediates [1]. However, the detailed studies on the fused thiopyrans are scarcely found.

Dihydronaphthothiopyrans are generally synthesized through the ring-closure reaction of carboxyl or carbonyl function at the β-position of the alkyl chain of naphthylalkyl sulfides in the presence of a large excess of protic acid [2-5] or Lewis acid [6] catalysts. The use of acid catalysts for this reaction may simultaneously cause side reactions including rearrangement and/or isomerization,

Scheme 1



Scheme 2

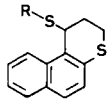


so the yields of the thiopyrans are less favorable. Separation of the products is also laborious. Alternatively, condensed ring dihydrothiopyrans can be obtained by Thio-Claisen rearrangement of aryl-allyl sulfides [7-9] but this reaction needs a high temperature and thiophene ring compounds are formed as by-products.

We have recently reported [10] that naphthothiopyrans are synthesized by the ring-closure reaction of 3-(2-naphthylthio)propionaldehyde (**3**) which was obtained by the addition reaction of 2-naphthalenethiol (**1**) with 2-propenal

Table 1

Preparation of 1-Alkylthio and Acylthio-2,3-dihydro-1*H*-naphtho[2,1-*b*]thiopyrans



Compound No.	R	Yield (%)	MP (°C) (Solvent)	Molecular Formula	Analysis (%) Calcd. C	Calcd. H	Calcd. S	Found C	Found H	Found S
5a	n-C_4H_9	95	43-45 (PE)	$C_{17}H_{20}S_2$	70.78	6.99	22.23	70.79	7.05	22.20
5b	C_6H_5	96	127-129 (PE)	$C_{19}H_{16}S_2$	73.98	5.23	20.79	74.26	5.14	21.04
5c	$C_6H_5CH_2$	95	127-129 (PE)	$C_{20}H_{18}S_2$	74.49	5.63	19.88	74.77	5.69	20.09
5d	1-$C_{10}H_7$	94	134-136 (acetone)	$C_{23}H_{18}S_2$	77.05	5.06	17.87	77.18	5.17	17.75
5e	2-$C_{10}H_7$	95	125-126 (acetone)	$C_{23}H_{18}S_2$	77.05	5.06	17.87	76.98	4.94	17.57
5f	CH_3CO	90	127-128 (n-hexane)	$C_{15}H_{14}OS_2$	65.66	5.14	23.37	65.84	5.17	23.43
5g	C_6H_5CO	91	107-109 (n-hexane)	$C_{20}H_{16}OS_2$	71.40	4.79	19.06	71.55	4.81	19.12

Yield of isolated product. PE = Petroleum ether (bp 60-70°).

Table 2

^{1}H-NMR Spectral Data of Compounds **5a-g**

Compound	^{1}H-NMR (δ) [a]
5a	0.91 (t, 3H, J = 6.3 Hz, CH_3), 1.23-1.78 (m, 4H, CH_2 x 2), 2.21 (dddd, 1H, J = 14.2, 14.7, 3.4, 3.4 Hz, CH_2), 2.44-2.72 (overlapping q, 3H, J = 6.3 Hz, CH_2, dddd, J = 14.2, 3.4, 3.4, 3.4 Hz, CH_2), 2.89 (dddd, 1H, J = 12.7, 3.4, 3.4, 1.0 Hz, CH_2), 3.89 (ddd, 1H, J = 12.7, 12.7, 3.4 Hz, CH_2), 4.81 (br 1H, CH), 7.06-8.16 (m, 6H, ArH)
5b	2.19 (dddd, 1H, J = 14.2, 12.7, 3.4, 3.4 Hz, CH_2), 2.50 (dddd, 1H, J = 14.2, 3.4, 3.4, 3.4 Hz, CH_2), 2.82 (dddd, 1H, J = 12.7, 3.4, 3.4, 1.0 Hz, CH_2), 3.99 (ddd, 1H, J = 12.7, 12.7, 3.4 Hz, CH_2), 5.25 (br 1H, CH), 7.09-8.27 (m, 11H, ArH)
5c	2.12 (dddd, 1H, J = 14.2, 12.7, 3.4, 3.4 Hz, CH_2), 2.52 (dddd, 1H, J = 14.2, 3.4, 3.4, 3.4 Hz, CH_2), 2.84 (dddd, 1H, J = 12.7, 3.4, 3.4, 1.0 Hz, CH_2), 3.71-3.75 (br 2H, S-CH_2), 3.88 (ddd, 1H, J = 12.7, 12.7, 3.4 Hz, CH_2), 4.56 (br 1H, CH), 7.06-7.69 (m, 11H, ArH)
5d	2.14 (dddd, 1H, J = 14.2, 12.7, 3.4, 3.4 Hz, CH_2), 2.42 (dddd, 1H, J = 14.2, 3.4, 3.4, 3.4 Hz, CH_2), 2.84 (dddd, 1H, J = 12.7, 3.4, 3.4, 1.0 Hz, CH_2), 4.03 (ddd, 1H, J = 12.7, 12.7, 3.4 Hz, CH_2), 5.36 (br 1H, CH), 7.13-8.46 (m, 13H, ArH)
5e	2.20 (dddd, 1H, J = 14.2, 12.7, 3.4, 3.4 Hz, CH_2), 2.55 (dddd, 1H, J = 14.2, 3.4, 3.4, 3.4 Hz, CH_2), 2.83 (dddd, 1H, J = 12.7, 3.4, 3.4, 1.0 Hz, CH_2), 4.00 (ddd, 1H, J = 12.7, 12.7, 3.4 Hz, CH_2), 5.37 (br 1H, CH), 7.10-8.33 (m, 13H, ArH)
5f	2.36-2.44 (m, 4H, CH_3, CH_2), 2.56 (dddd, 1H, J = 14.3, 3.5, 3.5, 3.2 Hz, CH_2), 2.96 (dddd, 1H, J = 12.9, 3.5, 3.5, 1.2 Hz, CH_2), 3.53 (ddd, 1H, J = 12.9, 12.9, 3.2 Hz, CH_2), 5.67 (br 1H, CH), 7.11-7.78 (m, 6H, ArH)
5g	2.29-2.83 (m, 2H, CH_2), 2.98 (dddd, 1H, J = 12.5, 3.6, 3.6, 1.2 Hz, CH_2), 3.70 (ddd, 1H, J = 12.5, 12.5, 3.6 Hz, CH_2), 5.89 (br 1H, CH), 7.03-8.08 (m, 11H, ArH)

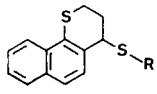
[a] All compounds were measured in deuteriochloroform.

(**2**) in the presence of a relatively small amount of sulfuric acid in dry ether.

Subsequently, we have investigated ring-closure reaction of **3** and its **7** isomer which was obtained by the addition reaction of 1-naphthalenethiol (**6**) with **2**. The reaction of **3** and **7** in the presence of concentrated sulfuric acid at room temperature afforded a mixture of naphthothiopyrans. Furthermore, the reaction of **3** and **7** with equimolecular amount of nucleophiles such as thiols **a-e**, thio acids **f,g** in the presence of sulfuric acid in benzene at room temperature, the ring-closure reaction of 3-(2-naphthylthio)propionaldehyde hemithioacetal (**4**) and its (1-naphthylthio) isomer **8** proceeded *via* the addition of nucleophiles to the formyl carbon to give the corresponding 1-substituted-2,3-dihydro-1*H*-naphtho[2,1-*b*]thiopyrans **5a-g** and 4-substituted-3,4-dihydro-2*H*-naphtho[1,2-*b*]thiopyrans **9a-g** in excellent yields (Table 1-4).

Table 3

Preparation of 4-Alkylthio and Acylthio-3,4-dihydro-2*H*-naphtho[1,2-*b*]thiopyrans



Compound No.	R	Yield (%)	MP (°C) (Solvent)	Molecular Formula	Analysis (%) Calcd. C	Calcd. H	Calcd. S	Found C	Found H	Found S
9a	n-C_4H_9	90	liquid	$C_{17}H_{20}S_2$	70.78	6.99	22.23	71.01	6.95	22.18
9b	C_6H_5	92	84-86 (PE)	$C_{19}H_{16}S_2$	73.98	5.23	20.79	74.20	5.14	20.68
9c	$C_6H_5CH_2$	90	69-71 (PE)	$C_{20}H_{18}S_2$	74.49	5.63	19.88	74.72	5.75	20.01
9d	1-$C_{10}H_7$	90	138-139 (acetone)	$C_{23}H_{18}S_2$	77.05	5.06	17.87	77.13	5.00	17.60
9e	2-$C_{10}H_7$	90	115-117 (acetone/PE)	$C_{23}H_{18}S_2$	77.05	5.06	17.87	76.95	5.01	17.95
9f	CH_3CO	80	89-91 (PE)	$C_{15}H_{14}OS_2$	65.66	5.14	23.37	65.79	5.17	23.40
9g	C_6H_5CO	90	92-94 (acetone)	$C_{20}H_{16}OS_2$	71.40	4.79	19.06	71.51	4.92	19.13

Yield of isolated product. PE = Petroleum ether (bp 60-70).

Table 4

^{1}H-NMR Spectral Data of Compounds **9a-g**

Compound	^{1}H-NMR (δ) [a]
9a	0.88 (t, 3H, J = 7.7 Hz, CH_3), 1.37 (q, t, 2H, J = 7.7, 7.7 Hz, CH_2), 1.55 (t, d, 2H, J = 7.7, 7.7 Hz, CH_2), 2.16 (dddd, 1H, J = 14.2, 12.6, 3.3, 3.3 Hz, CH_2), 2.37 (dddd, 1H, J = 14.2, 4.4, 3.3, 3.3 Hz, CH_2), 2.50 (m, 2H, S-CH_2), 2.92 (dddd, 1H, J = 12.6, 4.4, 3.3, 1.1 Hz, CH_2), 3.64 (ddd, 1H, J = 12.6, 12.6, 3.3 Hz, CH_2), 4.15 (br 1H, CH), 7.01-8.08 (m, 6H, ArH)
9b	2.22 (dddd, 1H, J = 14.3, 12.6, 3.3, 3.3 Hz, CH_2), 2.42 (dddd, 1H, J = 14.3, 4.4, 3.3, 3.3 Hz, CH_2), 2.99 (dddd, 1H, J = 12.6, 4.4, 3.3, 1.1 Hz, CH_2), 3.08 (ddd, 1H, J = 12.6, 12.6, 3.3 Hz, CH_2), 4.70 (ddd, 1H, J = 3.3, 3.3, 1.1 Hz, CH), 7.27-8.11 (m, 11H, ArH)
9c	2.20 (dddd, 1H, J = 14.2, 12.2, 3.4, 3.4 Hz, CH_2), 2.48 (dddd, 1H, J = 14.2, 4.4, 3.4, 3.4 Hz, CH_2), 3.02 (dddd, 1H, J = 12.2, 4.4, 3.4, 1.0 Hz, CH_2), 3.70 (ddd, 1H, J = 12.2, 12.2, 3.4 Hz, CH_2), 3.78-3.80 (br 2H, S-CH_2), 4.11 (ddd, 1H, J = 3.4, 3.4, 1.0 Hz, CH), 7.05-8.11 (m, 11H, ArH)
9d	2.13 (dddd, 1H, J = 14.2, 12.7, 2.9, 2.9 Hz, CH_2), 2.30 (dddd, 1H, J = 14.2, 4.4, 2.9, 2.9 Hz, CH_2), 2.98 (dddd, 1H, J = 12.7, 4.4, 2.9, 1.0 Hz, CH_2), 3.93 (ddd, 1H, J = 12.7, 12.7, 2.9 Hz, CH_2), 4.72 (ddd, 1H, J = 2.9, 2.9, 1.0 Hz, CH), 7.39-8.69 (m, 13H, ArH)
9e	2.25 (dddd, 1H, J = 14.2, 12.7, 2.9, 2.9 Hz, CH_2), 2.46 (dddd, 1H, J = 14.2, 3.9, 2.9, 2.9 Hz, CH_2), 3.00 (dddd, 1H, J = 12.7, 3.9, 2.9, 1.0 Hz, CH_2), 3.85 (ddd, 1H, J = 12.7, 12.7, 2.9 Hz, CH_2), 4.85 (br 1H, CH), 7.43-8.13 (m, 13H, ArH)
9f	2.36 (s, 3H, CH_3), 2.41 (dddd, 1H, J = 14.3, 12.6, 3.3, 3.3 Hz, CH_2), 2.49 (dddd, 1H, J = 14.3, 4.7, 3.3, 3.3 Hz, CH_2), 3.08 (dddd, 1H, J = 12.6, 4.7, 3.3, 1.4 Hz, CH_2), 3.37 (ddd, 1H, J = 12.6, 12.6, 3.3 Hz, CH_2), 5.16 (ddd, 1H, J = 3.3, 3.3, 1.4 Hz, CH), 7.22-8.08 (m, 6H, ArH)
9g	2.50 (dddd, 1H, J = 14.3, 12.6, 3.3, 3.3 Hz, CH_2), 2.62 (dddd, 1H, J = 14.3, 4.4, 3.3, 3.3 Hz, CH_2, 3.12 (dddd, 1H, J = 12.6, 4.4, 3.3, 1.1 Hz, CH_2), 3.48 (ddd, 1H, J = 12.6, 12.6, 3.3 Hz, CH_2), 5.39 (ddd, 1H, J = 3.3, 3.3, 1.1 Hz, CH), 7.30-8.11 (m, 11H, ArH)

[a] All compounds were measured in deuteriochloroform.

In order to verify the reaction path on the ring-closure reaction, we are noted to the reaction of **3** and thiol. The reaction of **3** (1 mole) with **1** (1 mole) in ether give 1,3-bis-(2-naphthylthio)-1-propanol (**4e**) in a quantitative yield. The reaction of **4e** in the presence of sulfuric acid (0.1 mole) in dry ether at room temperature readily formed 1-(2-naphthylthio)-2,3-dihydro-1*H*-napththo[2,1-*b*]thiopyran (**5e**). These results suggest that the cyclodehydration takes place on the hemithioacetal **4** formed during the addition reaction of thiols (thio acids) with formyl group on **3** and **7**. On the other hand, the reaction of **3** and with ethanol give the corresponding diethylacetal. This diethyl acetal did not occur for the ring-closure reaction in the presence of sulfuric acid. It seems likely that the facility in the formation of naphthothiopyrans is dependent on the

stability [12] of the intermediate hemithioacetals. Analytical and spectroscopic data (^{1}H-nmr and ms) of all products are in agreement with the described structures.

In conclusion, the present work provides convenient methods which are applicable to the preparation of a variety of 1-alkylthio and acylthio-2,3-dihydro-1*H*-naphtho[2,1-*b*]thiopyrans (**5**) and 4-alkylthio and acylthio-3,4-dihydro-2*H*-naphtho[1,2-*b*]thiopyrans (**9**).

EXPERIMENTAL

Melting points were determined with a Yanaco micromelting point apparatus and uncorrected. The ir spectra were recorded on a Shimadzu IR-435 spectrometer using potassium bromide pellets. The ^{1}H-nmr spectra were obtained in deuteriochloroform using a JEOL JNM-GX400 spectrometer. Chemical shifts are reported in ppm from TMS used as internal standard and are given in δ units. The following abbreviations were used to designate the multiplicity of individual signals: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad and J = coupling constant (Hertz). The ms spectra were recorded on a Hitachi M-80B mass spectrometer. Elemental analyses were performed on a Perkin-Elmer 240C elemental analyzer.

3-(2-Naphthylthio)propionaldehyde (**3**). Typical Procedure.

2-Propenal (**2**) (2.8 g, 50 mmoles) in dry ether (30 ml) was added dropwise to solution of 2-naphthalenethiol (**1**) (8.0 g, 50 mmoles) and sulfuric acid (0.5 g, 5 mmoles) in dry ether (60 ml), and the mixture was stirred at 30° for 2 hours. The reaction mixture was washed with water, and the organic layer dried with sodiumsulfate, was evaporated under reduced pressure. The residual product was recrystallized from petroleum ether (bp 60°) to give **3** as white solid (10.3 g, 95%), mp 26-28°; ms: m/z 216 (M^+); ir (capillary): ν = 1722 cm^{-1} (C=O); ^{1}H-nmr (deuteriochloroform): 2.69 (t, d, 2H, J = 6.8, 1.4 Hz, CH_2), 3.24 (t, 2H, J = 6.8 Hz, CH_2), 7.35-7.83 (m, 7H, ArH), 9.72 (t, 1H, J = 1.4 Hz, CHO).

Anal. Calcd. for $C_{13}H_{12}OS$: C, 72.19; H, 5.59; S, 14.82. Found: C, 72.43; H, 5.39; S, 14.88.

3-(1-Naphthylthio)propionaldehyde (**7**).

Compound **7** was prepared by a procedure similar to that described for **3**, colorless liquid (petroleum ether, 95%); ms: m/z 216 (M^+); ir (capillary): ν = 1720 cm^{-1} (C=O); ^{1}H-nmr (deuteriochloroform): 2.72 (t, d, 2H, J = 6.8, 1.5 Hz, CH_2), 3.21 (t, 2H, J = 6.8 Hz, CH_2), 7.24-8.44 (m, 7H, ArH), 9.71 (t, 1H, J = 1.5 Hz, CHO).

Anal. Calcd. for $C_{13}H_{12}OS$: C, 72.19; H, 5.59; S, 14.82. Found: C, 72.06; H, 5.61; S, 14.79.

1-Alkylthio and Acylthio-2,3-dihydro-1*H*-naphtho[2,1-*b*]thiopyrans **5a-g**. General Procedure.

To a solution of 3-(2-naphthylthio)propionaldehyde (**3**) (5.4 g, 25 mmoles) and thiol or thio acid (**a-g**, 25 mmoles) in benzene (100 ml) was added sulfuric acid (2.6 g, 25 mmoles), and the mixture was stirred at 30° for 2 hours. The reaction mixture was washed with water, and the organic layer dried with sodium sulfate, and was evaporated under reduced pressure. The residual product was recrystallized from petroleum ether (bp 60-70°) or acetone to give **5a-g** (Tables 1 and 2).

4-Alkylthio and Acylthio-3,4-dihydro-2*H*-naphtho[1,2-*b*]thiopyrans **9a-g**. General Procedure.

To a solution of 3-(1-naphthylthio)propionaldehyde (**7**) (5.4 g, 25 mmoles) and thiol or thio acid (**a-g**, 25 mmoles) in benzene was (100 ml) was added sulfuric acid (2.6 g, 25 mmoles), and the mixture was stirred at 30° for 2 hours. The reaction mixture was washed with water, and the organic layer dried with sodium sulfate, and was evaporated under reduced pressure. The residual product was recrystallized from petroleum ether (bp 60-70°) or acetone to give **9a-g** (Tables 3 and 4).

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