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Synthesis of 2-Alkyl(aryl)thietanes

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Abstract—Thietane and its 2-substituted derivatives were synthesized. A general preparation procedure for the synthesis of thietanes bearing alkyl and aryl substituents in the α-position was developed. Using this procedure, 2-substituted thietanes can be obtained from cheap and easily accessible raw materials in three steps. 2-R-Thietanes (where R = H, CH_3, C_4H_9, C_5H_{11}, C_6H_{13}, C_6H_5) and the corresponding sulfoxides and sulfones were synthesized and examined. Intermediate and by-products of the synthesis were studied.

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INTRODUCTION

Thietanes is a class of organic sulfur compounds that have been little studied. Unlike the chemistry of five- and six-membered substituted saturated monocyclic sulfides, data on four-membered saturated monocyclic sulfides are virtually lacking. The lack of information is most likely due to the chemical and physical properties of these compounds. It is difficult to purify thietanes, because the cycle is unstable in strongly acidic solutions and in the presence of sodium metal, whereas thiolanes and thianes are stable under these conditions. In addition, the handling of thietanes is complicated by their strong and abominable odor.[1]

Light and medium petroleum fractions do not contain thietane or its derivatives; however, substituted sulfide was found in shale oil [2]. Thietanes can serve as useful reagents in organic synthesis and as a reference for studying organic objects (both synthetic and natural) by various techniques (chromatography, NMR, mass spectrometry, etc.).

There are original articles [3–6] and reviews [7, 8] devoted to the chemistry of thietanes, in which the feasibility of the preparation of 2-alkyl- and 2-arylthietanes is mentioned; however, there is no general dedicated method for the synthesis of 2-substituted thietanes. The main purpose of the present work was to develop a method for the large-scale preparation of 2-substituted thietanes.

EXPERIMENTAL

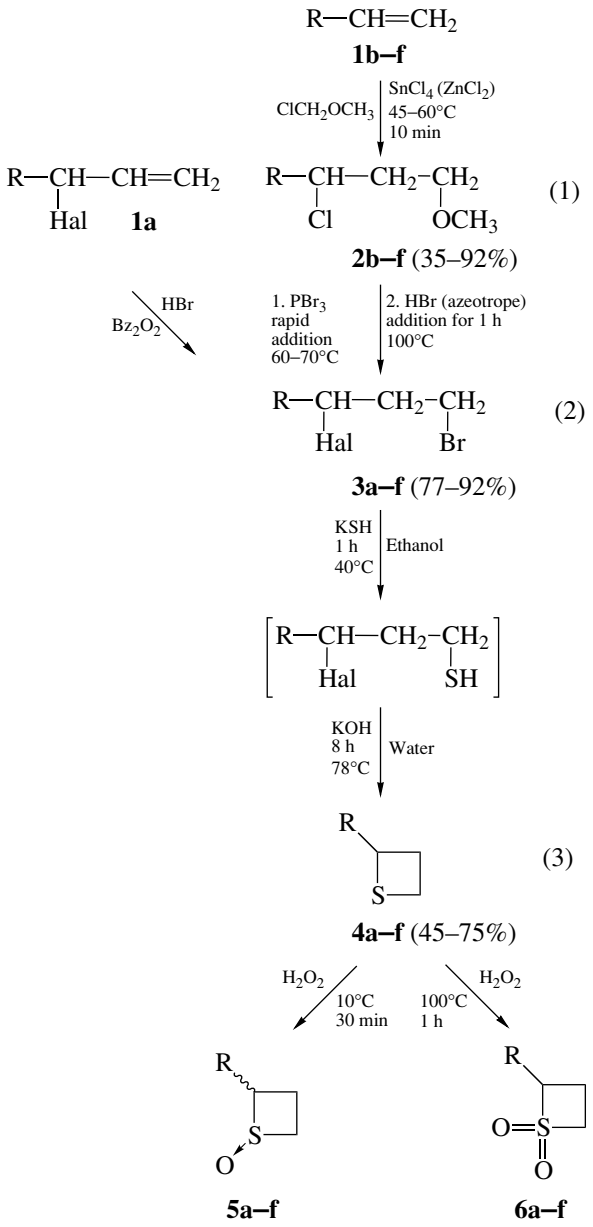
Intermediate and final products were determined by gas chromatography coupled with mass spectrometry (GC–MS) on a Finnigan MAT 95 XL high-resolution GC–MS spectrometer using an Agilent 6890+ gas chromatograph, helium as a carrier gas, a Supelco SPB-5 capillary column (95% polydimethylsiloxane, 5% polydiphenylsiloxane), and sample injection with a split ratio of 1 : 30. The temperature regime was as follows: the injector temperature was 250°C, and the column temperature was programmed from the initial temperature of 30°C by heating to 150°C at a rate of 5°C/min and, next, to 290°C at a rate of 10°C/min. The mass spectrometer had an ionization energy of 70 eV, an ion source temperature of 200°C, a scanning range of 20–800 amu, and a resolution of ~1000. GLC analysis was carried out on an LKhM-8 MD instrument modified for operation with capillary columns (25 m × 0.32 mm) with a film thickness of d_f = 1.1 micron, helium as a carrier gas, the SE-54 stationary phase, and a flame-ionization detector. Proton NMR spectra were obtained on a Bruker MSL-300 spectrometer in a $CDCl_3$ solution at 24°C (the frequency was 300.13 MHz, scan number was 12 with a sweep of 11 905 Hz (39.7 ppm), 90° pulse was 3 μs); chemical shifts were calculated from the signal of residual protons of chloroform (7.24 ppm) using the PAPS.PC pulse program with the subsequent Fourier transformation. The sulfur and halogen contents were determined with the use of the double combustion method with an average measurement error of ±0.3% on a semiautomated instrument designed by N.P. Volynskii [9, 10]. An analysis for C and H was carried out on a Carlo Erba Instruments system with a CHNS-O EA1108 analyzer.

The general scheme of synthesis of thietane and 2-alkyl(aryl)thietanes, as well as the procedures of synthesis at individual steps are given below.

† Deceased.

[1] This work was carried out at in a laboratory, whose equipment and ventilating system had been described earlier [1].

General synthesis scheme[2]



a = R = H, Hal = Cl;
b = R = CH_3, Hal = Cl;
c = R = C_4H_9, Hal = Cl;
d = R = C_5H_{11}, Hal = Cl;
e = R = C_6H_{13}, Hal = Cl;
f = R = C_6H_5, Hal = Br.

*Synthesis of Thietane (**4a**)*

1-Bromo-3-chloropropane (3a). Freshly distilled allyl chloride (700 g, 9.2 mol), benzene (600 ml), and a dry solution of benzoyl peroxide (100 ml) were placed in a 2.5-l flask equipped with a stirrer, a reflux condenser, a thermometer, and a gas supply tube (to the bottom of the flask). (The solution of benzoyl peroxide in benzene was prepared in a special manner: wet benzoyl peroxide (14 g) was dissolved in 200 ml of benzene, isolated from 4 g of water, was separated, and dried over sodium sulfate; 100 g of this benzoyl peroxide solution was added to allyl chloride before passing HBr, and the rest was added 3 h after the beginning of the reaction.) Dry HBr was passed through the reaction mixture with stirring at 20°C for 6 h (HBr was obtained from NaBr heating with concentrated H_2SO_4; the gas was purified from bromine admixtures in a Tishchenko gas-washing bottle via bubbling through a red phosphorus suspension in concentrated HBr). Then, the reaction mixture was heated to 100°C for degassing, cooled to room temperature, and distilled from the flask with a high-performance fractionating column. 1-Bromo-3-chloropropane **3a** was obtained with a yield of 1174 g (Table 1).

Thietane (4a). An alcoholic solution of KSH (43 g, 0.6 mol), which was prepared by the saturation of a solution of KOH (33 g, 0.6 mol) in ethanol (300 ml) with hydrogen sulfide at 4°C, was placed in a 1-l flask equipped with a stirrer, a dropping funnel, a reflux condenser, and a thermometer. Then, 1-bromo-3-chloropropane (80 g, 0.5 mol) was added for 1 min with vigorous stirring and held at 40°C for 1 h. The mixture was heated to boiling, and a solution of KOH (33 g, 0.6 mol) in water (300 ml) was added dropwise within 3 h. After the completion of addition of the aqueous alkali solution, refluxing and stirring were continued for 5 h. Then, the solution was cooled to 10°C, ice-cold water was added, the organic layer was separated, and the aqueous layer was extracted with tridecane (10 × 25 ml). Thietane **4a** was obtained in the amount of 23.3 g (Table 2) by vacuum distillation in a closed system followed by column rectification (8 theoretical plates).

*Synthesis of 2-Alkyl(aryl)thietanes (**4b–f**)*

The synthesis of 2-alkyl(aryl)thietanes is described in detail for 2-butylthietane **4c** as an example.

3-Chloro-1-methoxyheptane (2c). Freshly distilled hex-1-ene (84 g, 1.0 mol) was placed in a 0.5-l flask equipped with a glass stirrer, a dropping funnel, a thermometer, and a reflux condenser with a water trap at the outlet for absorbing HCl. Then, $SnCl_4$ (1.5 ml) was rapidly added with stirring and cooling on an ice bath, and methyl chloromethyl ether[3] (58.3 g, 0.72 mol) was added in portions within 6 min at the temperature of the reaction mixture (2°C). Upon completion of the addition, cooling was stopped and stirring was continued for 20 min with monitoring for a spontaneous increase in the temperature of the reaction mixture up to the boiling point. Then, the reaction mixture was cooled again with an ice bath to 4°C, ice-cold water (150 ml) was added, and the upper organic layer was

[2] Compound **2a** is absent from the scheme, since the synthesis of thietane (**4a**) does not include the step of methyl chloromethyl ether addition (1).

[3] Methyl chloromethyl ether was synthesized according to [11].

Table 1. Yields and physicochemical properties of 1,3-dihaloalkanes (**3a–f**)

Compound	Yield, %	Empirical formula	Content, % found/calcd.		Bp, °C/mm Hg	n_D^{20}	d_4^{20}	MR_D, found/calcd.
			Cl	Br				
1-Bromo-3-chloropropane (**3a**)*	92	C_3H_6BrCl	–	–	75(82)	1.4855	1.5953**	28.32/28.53
1-Bromo-3-chlorobutane (**3b**)	77	C_4H_8BrCl	–	–	84(80)	1.4710	1.4115	34.18/33.96
1-Bromo-3-chloroheptane (**3c**)	92	$C_7H_{14}BrCl$	16.54/16.60	37.28/37.42	67(3)	1.4740	1.2675	47.34/47.10
1-Bromo-3-chlorooctane (**3d**)	78	$C_8H_{16}BrCl$	15.20/15.58	35.29/35.11	92(5)	1.4725	1.2181	52.37/51.68
1-Bromo-3-chlorononane (**3e**)	81	$C_9H_{18}BrCl$	14.23/14.67	32.76/33.08	88(2)	1.4737	1.2024	56.44/56.41
1,3-Dibromo-1-phenylpropane (**3f**)	85	$C_9H_{10}Br_2$	–	56.83/57.48	113(2)	1.5900	1.6595	56.35/55.76

Notes: * The values of constants d_4^{20} = 1.3140 and n_D^{20} = 1.4251 given in the handbook "Properties of Organic Compounds" (Ed. by A.A. Potekhin, 1984, p. 303) are wrong.

** Beilstein, Vol. 1, p. 109: bp = 140–142°C, d^8 = 1.63.

Table 2. Yields and physicochemical properties of 2-alkyl(aryl)thietanes (**4a–f**)

Compound	Yield, %	Empirical formula	Content, % found/calcd.			Bp, °C/mm Hg	n_D^{20}	d_4^{20}	MR_D, found/calcd.
			C	H	S				
Thietane (**4a**)	63	C_3H_6S	48.50/48.60	7.80/8.16	43.50/43.52	93–94(760)	1.5100	1.0167	21.81/21.84
2-Methylthietane (**4b**)	63	C_4H_8S	54.24/54.49	8.48/9.14	36.35/36.37	106–107(760)	1.4832	0.9516	26.59/26.52
2-Butylthietane (**4c**)	62	$C_7H_{14}S$	64.15/64.55	11.00/10.83	24.22/24.62	90(40)	1.4787	0.9197	40.14/40.02
2-Pentylthietane (**4d**)	74	$C_8H_{16}S$	66.70/66.59	10.80/11.18	22.14/22.23	93(20), 101(30)	1.4760	0.9077	44.82/44.67
2-Hexylthietane (**4e**)	75	$C_9H_{18}S$	68.45/68.29	11.00/11.46	20.02/20.25	94(10), 110(20)	1.4756	0.9055	49.27/49.32
2-Phenylthietane (**4f**)	54	$C_9H_{10}S$	71.65/71.95	6.90/6.71	21.70/21.34	86(3)	1.5883	1.0912	46.35/46.19

separated and distilled on a fractionating column (15 theoretical plates) after single washing of the organic layer with a 10% sodium bicarbonate solution and drying with anhydrous sodium sulfate. 3-Chloro-1-methoxyheptane **2c** was obtained in a yield of 31.7 g (Table 3).

1-Bromo-3-chloroheptane (3c). 3-Chloro-1-methoxyheptane (61 g, 0.37 mol) was placed in a 0.25-l flask equipped with a stirrer, a thermometer, a dropping funnel, and a reflux condenser with a water trap at the outlet. The dropping funnel was loaded with PBr_3(120 g, 0.44 mol). Then, the contents of the flask were heated on a glycerol bath to 60°C, and the whole amount of PBr_3 was added in portions for 3 min with stirring. The heating temperature was increased to 100°C, and HBr (20 ml) was added dropwise for 1 h with monitoring for he progress of the reaction by following the absorption of hydrogen bromide and the evolution of methyl bro-

Table 3. Yields and physicochemical properties of 3-chloro-1-methoxyalkanes (**2b–f**)

Compound	Yield, %	Empirical formula	Content of Cl, % found/calcd.	Bp, °C/mmHg	n_D^{20}	d_4^{20}	MR_D, found/calcd.
3-Chloro-1-methoxybutane (**2b**)	47	$C_5H_{11}ClO$	28.90/28.92	124(760)	1.4141	0.9587	31.96/31.82
3-Chloro-1-methoxyheptane (**2c**)	35	$C_8H_{16}ClO$	20.25/21.58	79(15)	1.4334	0.9379	45.67/45.75
3-Chloro-1-methoxyoctane (**2d**)	42	$C_9H_{19}ClO$	16.90/19.90	94(15)	1.4365	0.9257	50.52/50.42
3-Chloro-1-methoxynonane (**2e**)	42	$C_{10}H_{21}ClO$	16.30/18.40	102(10)	1.4385	0.9189	55.10/55.03
3-Chloro-1-methoxy-3-phenylpropane (**2f**)	92	$C_{10}H_{13}ClO$	18.90/19.20	95(4)	1.5165	1.0756	51.89/51.53

mide in the trap. After the end of addition, the reaction mixture was cooled to room temperature, ice-cold water was added, the bottom organic layer was separated, and the aqueous layer was extracted with chloroform (3 × 50 ml). The extract was added to the main layer, dried with sodium sulfate, and distilled on a fractionating column (8 theoretical plates). 1-Bromo-3-chloroheptane **3c** was obtained in a yield of 58 g (Table 1).

2-Butylthietane (4c). A solution of KSH, which was prepared by the saturation of a solution of KOH (14 g, 0.25 mol) in ethanol (150 ml) with hydrogen sulfide at 0–6°C, was placed in a 0.5-l flask equipped with a glass stirrer, a reflux condenser, a thermometer, and a dropping funnel. Then, 1-bromo-3-chloroheptane (50.5 g, 0.24 mol) was added for 1 min with stirring and cooling (during the addition, potassium bromide precipitated and the temperature in the flask spontaneously increased to 15°C). The reaction mixture was stirred at 40°C for 45 min and then heated to boiling for 3 h, and a solution of KOH (14 g, 0.25 mol) in water (150 ml) was added dropwise. Refluxing and stirring were continued for 5 h, the mixture was cooled to room temperature, and ice-cold water (150 ml) was added. Sulfide was extracted with hexane (3 × 50 ml). Hexane was distilled off, and the residue was distilled on a rectification column (8 theoretical plates). 2-Butylthietane was washed with concentrated H_3PO_4, water, and a sodium bicarbonate solution. 2-Butylthietane **4c** was obtained by distillation on a fractionating column (8 theoretical plates) in a yield of 18.8 g (Table 2).

^{1}HNMR, δ, ppm: α + α': 3.07 (m) + 3.53 (tt, J_1 = 7.5, J_2 = 7.3 Hz, 1H); β: 2.45 (m, 1H) + 2.66 (m, 1H); γ: 2.74 (q, J = 9.4 Hz, 1H) + 3.03 (q, J = 8.7 Hz, 1H); **1**: 1.69 (m, 1H) + 1.90 (m, 1H); **2–3**: 0.9–1.65 (m, 4H); **4**: 0.71 (t, J_1 = 7.3 Hz) + 0.74 (t, J_1 = 6.5 Hz, 3H). Mass spectrum, *m*/*z* (I_{rel}, %): $[M]^+$ 130(41), 115(5), 101(40), 96(5), 87(100), 81(17), 73(20), 60(24), 55(5), 41(32).

2-Pentylthietane (4d). ^{1}H NMR, δ, ppm: α + α': 3.25 (m) + 3.65 (tt, J_1 = 7.3 Hz, J_2 = 9.0 Hz, 1H); β: 2.53 (m, 1H) + 2.79 (m, 1H); γ: 2.85 (m, 1H) + 3.15 (m, J_1 = 9.4 Hz, J_2 = 8.0 Hz, 1H); **1**: 1.7 (m, 1H) + 2.06 (m, 1 H); **2–4**: 1.00 –1.80 (m, 6H); **5**: 0.85 (m, 3H). Mass spectrum, *m*/*z* (I_{rel}, %): $[M]^+$ 144(45), 115(100), 101(40), 87(88), 81(25), 73(42), 60(37), 55(56), 41(28).

2-Hexylthietane (4e). ^{1}H NMR, δ, ppm: α + α': 3.26 (m) + 3.66 (quintet, J_2 = 7.5 Hz, 1H); β: 2.57 (m, 1H) + 2.81 (m, 1H); γ: 2.88 (m, 1H) + 3.15 (m, 1H); **1**: 1.84 (m, 1H) + 2.04 (m, 1H); **2–5**: 1.00–1.80 (m, 8H); **6**: 0.85 (m, 3H). Mass spectrum, *m*/*z* (I_{rel}, %): $[M]^+$ 158(18), 129(12), 115(12), 101(8), 87(100), 81(4), 67(8), 60(37), 55(4), 41(5).

2-Phenylthietane (4f). ^{1}H NMR, δ, ppm: α: 4.94 (t, 7.5 Hz, 1H); β: 3.02 (m, 1H) + 3.14 (m, 1H); γ: 3.14 (m, 1H) + 3.38 (m, 1H); Ph: 7.10–7.60 (m, 5H). Mass spectrum, *m*/*z* (I_{rel}, %): $[M]^+$ 150(100), 135(12), 122(62), 117(19), 104(88), 91(12), 78(20), 63(5), 51(8), 39(8).

2-Butylthietane 1-oxide (5c). 2-Butylthietane (2.0 g, 0.015 mol) and glacial acetic acid (4 ml) were placed into a 30-ml Erlenmeyer flask. Then, 1 ml of a 25% solution of an equimolar amount of hydrogen peroxide in 1 ml of acetic acid was added dropwise with stirring for 30 min at 10°C. The reaction mixture was alkalized with a 15% NaOH aqueous solution, extracted with chloroform (3 × 10 ml), and dried with sodium sulfate. After the removal of chloroform by distillation, the residue was dissolved again in a minimum amount of chloroform, the resulting solution was filtered from mechanical admixtures, chloroform was distilled off, and the residue was stored in vacuum for 1 h.

Table 4. Yields and physicochemical properties of sulfoxides and sulfones (**5a**–**f** and **6a**–**f**)

Compound	Yield, %	Empirical formula	Content			Bp, °C/mmHg, mp, °C	n_D^{20}	d_4^{20}	MR_D, found/ calcd.
			C, %	H, %	S, %				
			found/ calcd.	found/ calcd.	found/ calcd.				
Thietane 1-oxide (**5a**)	83	C_3H_6SO	37.40 / 39.97	6.00 / 6.71	35.49 / 35.57	81(8)	1.5120	1.1965	22.61 / 22.88
Thietane 1,1-dioxide (**6a**)	85	$C_3H_6SO_2$	34.00 / 33.95	5.46 / 5.70	30.01 / 30.19	73–75			
2-Methylthietane 1-oxide (**5b**)	96	C_4H_8SO	45.20 / 46.12	7.90 / 7.74	30.88 / 30.79	75(6)	1.4985	1.1143	27.43 / 27.59
2-Methylthietane 1,1-dioxide (**6b**)	78	$C_4H_8SO_2$	40.00 / 39.98	6.25 / 6.71	26.65 / 26.69		1.4690	1.2199	27.43 / 27.13
2-Butylthietane 1-oxide (**5c**)	99	$C_7H_{14}SO$	57.65 / 57.40	9.40 / 9.65	21.82 / 21.93	115(6)	1.4875	1.0282	40.95 / 40.78
2-Butylthietane 1,1-dioxide (**6c**)	92	$C_7H_{14}SO_2$	51.97 / 51.82	9.09 / 8.70	19.56 / 19.77	–	1.4715	1.0972	41.37 / 41.06
2-Pentylthietane 1-oxide (**5d**)	93	$C_8H_{16}SO$	59.55 / 59.95	10.60 / 10.06	19.72 / 20.01	–	1.4850	0.9971	46.07 / 46.24
2-Pentylthietane 1,1-dioxide (**6d**)	94	$C_8H_{16}SO_2$	53.70 / 54.51	10.00 / 9.15	17.96 / 18.19	–	1.4690	1.0722	45.79 / 46.04
2-Hexylthietane 1-oxide (**5e**)	95	$C_9H_{18}SO$	62.30 / 62.02	10.90 / 10.41	18.04 / 18.39	–	1.4790	1.9815	50.35 / 50.89
2-Hexylthietane 1,1-dioxide (**6e**)	83	$C_9H_{18}SO_2$	56.90 / 56.80	10.40 / 9.53	16.63 / 16.88	–	1.4670	1.0403	50.75 / 50.69
2-Phenylthietane 1-oxide (**5f**)	70	$C_9H_{10}SO$	65.75 / 65.06	6.40 / 6.02	19.06 / 19.28	61–63	–	–	–
2-Phenylthietane 1,1-dioxide (**6f**)	75	$C_9H_{10}SO_2$	59.70 / 59.32	5.85 / 5.53	17.60 / 17.58	84–85	–	–	–

2-Butylthietane 1-oxide **5c** was obtained in a yield of 2.08 g (Table 4).

2-Butylthietane 1,1-dioxide (6c). A solution of 2-butylthietane (3.0 g, 0.023 mol) in glacial acetic acid (5 ml) was placed into a 30-ml round-bottom flask. A solution (10 ml) of 25% hydrogen peroxide in acetic acid (5 ml) was added with cooling and stirring. Then, the reaction mixture was heated to 100°C for 1 h with a reflux condenser, cooled to room temperature, alkalized with a 15% NaOH aqueous solution, and extracted with chloroform (3 × 10 ml). Chloroform was distilled off, the residue was dissolved again in a minimum amount of chloroform, and mechanical impurities were filtered off. Chloroform was distilled off again, and the residue was held in vacuum for 1 h. 2-Butylthietane 1,1-dioxide was obtained in a yield of 3.2 g (Table 4).

^{1}H NMR, δ, ppm: α: 4.16 (m, 1H); β: 2.00 (m, 2H); γ: 3.60–3.90 (m, 2H); **1**: 2.1–2.4 (m, 2H); **2–3**: 1.00–1.80 (m, 4H); **4**: 0.74 (m, 3H). Mass spectrum, *m/z* (I_{rel}, %): $[M]^+$ 162(4), 145(16), 120(6), 97(40), 81(4), 70(42), 69(32), 55(100), 41(32), 39(12).

2-Pentylthietane 1,1-dioxide (6d). ^{1}H NMR, δ, ppm: α: 4.27 (m, 1H); β: 1.8–2.1 (m, 2H); γ: 3.70–4.05 (m, 2H); **1**: 2.24(m, 2H); **2–4**: 1.1–2.4 (m, 6H); **5**: 0.84 (m, 3H). Mass spectrum, *m/z* (I_{rel}, %): $[M]^+$ 176(0), 159(6), 141(2), 110(6), 83(25), 69(100), 55(92), 41(48), 29(20).

2-Hexylthietane 1,1-dioxide (6e). ^{1}H NMR, δ, ppm: α: 4.26 (tt, J_1 = 8.0, J_2 = 8.7 Hz, 1H); β: 1.69 (m,

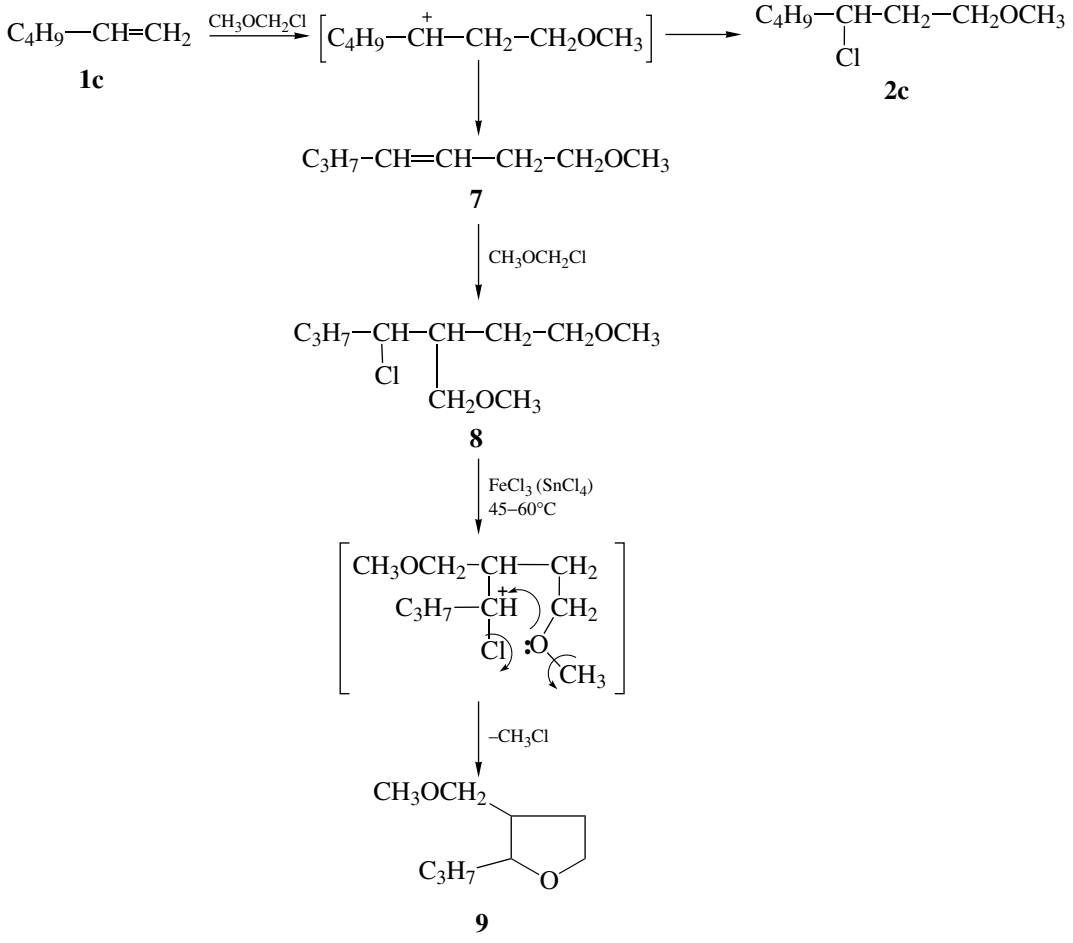
1H) + 2.02 (m, 1H); γ: 3.77–4.05 (m, 2H); **1**: 2.12 (m, 1H) + 2.23 (m, 1H); **2–5**: 1.10–2.10 (m, 8H); **6**: 0.86 (m, 3H). Mass spectrum, *m/z* (I_{rel}, %): $[M]^+$ 190(4), 173(26), 155(4), 134(6), 120(7), 97(14), 69(100), 55(80), 41(52), 28(22).

2-Phenylthietane 1,1-dioxide (6f). ^{1}H NMR, δ, ppm: α: 5.47 (t, J_1 = 10 Hz, 1H); β: 2.41 (m, 1H) + 2.55 (m, 1H); γ: 4.01 (m, 1H) + 4.14 (m, 1H); Ph: 7.40 (s, 5H). Mass spectrum, *m/z* (I_{rel}, %): $[M]^+$ 182(0), 118(80), 117(100), 115(19), 103(10), 91(21), 78(8), 65(6), 51(8), 39(6).

RESULTS AND DISCUSSION

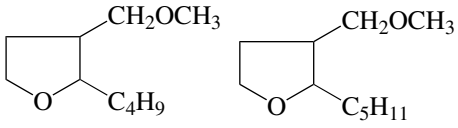
As can be seen, the scheme proposed for the synthesis of thietanes makes it possible to obtain 2-alkyl(aryl)-substituted derivatives only in three steps.

The first step (1) is the addition of methyl chloromethyl ether to the double bond of α-alkenes (**1b–f**) to form the corresponding γ-chloroethers (**2b–f**) (Table 3). We studied this step in detail[4] during the preparation of 3-chloro-1-methoxyheptane (**2c**). According to the elemental analysis data, 3-chloro-1-methoxyheptane (**2c**) contains only 20.25% Cl (calcd. 21.58), although the substance boils at a boiling point (79°C, 15 mmHg), rather than in a boiling range. We failed to isolate the individual product by distillation on a fractionating column (15 theoretical plates). According to GLC data, the substance contains three compounds: 3-chloro-1-methoxyheptane (~80%) and two unknown compounds. According to the GC–MS data, one of the mass spectra of the product displays a characteristic peak of the molecular ion at *m/z* 158. We assumed that a possible compound was the chlorine-free oxygen heterocycle 3-methoxymethyl-2-propyltetrahydrofuran (**9**) with the molecular mass 158 formed via the repeated addition of methyl chloromethyl ether and the subsequent cyclization:



[4] T.V. Rasskazchikova and I.Yu. Isa took part in the synthesis of 3-chloro-1-methoxyalkyl ethers.

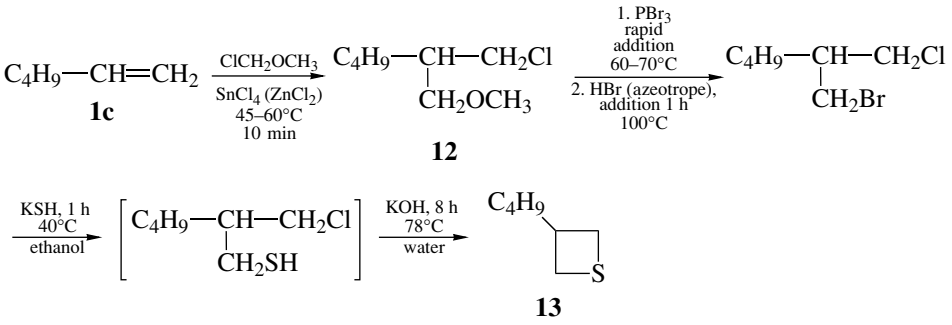
Indeed, the GLC data confirmed that one of the unknown by-products of the synthesis of 3-chloro-1-methoxyheptane (**2c**) was 3-methoxymethyl-2-propyltetrahydrofuran (**9**). This compound with bp 85°C (15 mmHg), n_D^{20} = 1.4385, d_4^{20} = 0.9220, and MR_D = 45.04 (calcd. 45.19) was prepared via unambiguous synthesis: the addition of methyl chloromethyl ether to methoxyhept-3-ene (**7**) on heating in the presence of Lewis acids [12]. Methoxyhept-3-ene (**7**) with bp 50°C (15 mmHg), n_D^{20} = 1.4200, d_4^{20} = 0.7967, and MR_D = 40.74 (calcd. 40.48) was isolated by the distillation of target 3-chloro-1-methoxyheptane (**2c**). It is noteworthy that the GC–MS data for 3-chloro-1-methoxyoctane (**2d**) and 3-chloro-1-methoxynonane (**2e**) are similar for those for 3-chloro-1-methoxyheptane (**2c**) and confirm the formation of the corresponding by-product 2,3-substituted tetrahydrofurans. The mass spectra contain characteristic peaks of molecular ions at *m/z* 172 for 2-butyl-3-methoxymethyltetrahydrofuran (**10**) and *m/z* 186 for 3-methoxymethyl-2-pentyltetrahydrofuran (**11**):



10 **11**

The synthesis of simple γ-haloethers was discussed long ago by Mamedov [13], who described 3-chloro-1-methoxynonane (**2e**), but nothing was said about the formation of side 3-methoxymethyl-2-pentyltetrahydrofuran (**11**). In the work cited, it was also found that halogen adds to the less hydrogenated carbon atom in the reaction of α-haloethers with α-alkenes.

On the basis of GLC and GC–MS data for the reactant 3-chloro-1-methoxyheptane (**2c**) and the product 2-butylthietane (**4c**), which contained a considerable amount of imparity, we assumed that the second unknown compound is isomeric 2-butyl-3-chloro-1-methoxypropane (**12**) formed via the halogen addition to the more hydrogenated carbon atom. The formation of 2-butyl-3-chloro-1-methoxypropane (**12**) as a by-product can result, in turn, in the appearance of an admixture of isomeric 3-butylthietane (**13**):

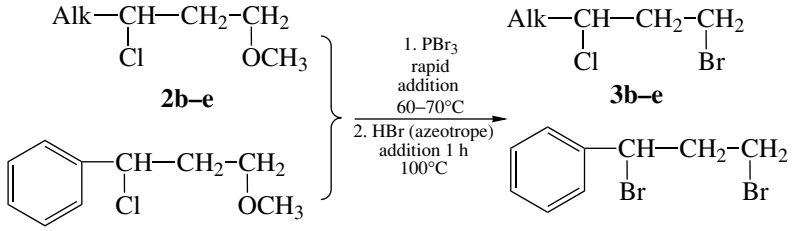


To confirm or disprove the presence of a possible 3-butylthietane (**13**) admixture in 2-butylthietane (**4c**), we synthesized **13** for this purpose[5] and established, on the basis of GLC data, that this isomer is absent from the desired product 2-butylthietane. This finding also confirms that the addition of methyl chloromethyl ether is extraordinary regioselective: chlorine adds to the less hydrogenated carbon atom.

As regards the admixture present in the desired 2-butylthietane, its structure remains unclear.

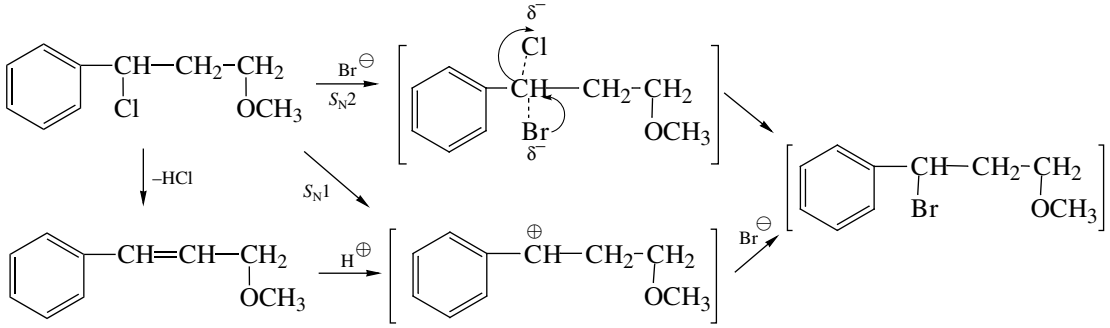
The step of replacement of the methoxy group by bromine (2) is important in the synthesis of target sulfides. In the case of the synthesis of 2-alkylthietane (**4c–e**), the expected chlorobromides (**3c–e**) were formed, whereas 1,3-dibromo-1-phenylpropane (**3f**) was isolated in a 85% yield of the theoretical value (Table 1) in the synthesis of 2-phenylthietane (**4f**).

[5] The synthesis of 3-alkyl(aryl)thietane will be reported in the forthcoming paper.

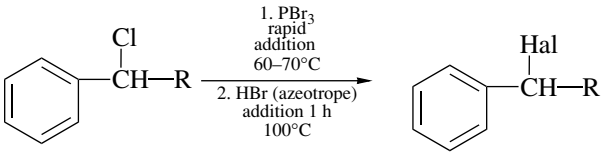


Alk = CH_3 (**b**), C_4H_9 (**c**), C_5H_{11} (**d**), C_6H_{13} (**e**)

The product had bp 113°C (2 mm Hg) and a high density (d_4^{20} = 1.6595). This result was confirmed by mass spectra. The direction of fragmentation of the compound corresponds to the structure of 1,3-dibromo-1-phenylpropane (**3f**). The substitution of bromine for the methoxy group by the PBr_3/HBr (azeotrope) system was considered in detail in [14]. Three routes are possible for bromine substitution for benzylic chlorine : S_N1, S_N2, or HCl elimination on heating followed by HBr addition to the double bond:



To reveal the mechanism of bromine substitution for benzylic chlorine, we used a series of chlorides (**14a–c**) for their further bromination and study of the reaction products:



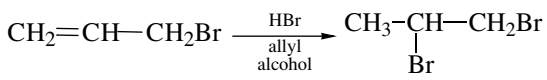
14a–c **15a–c**

a = R = H Hal = Cl;
b = R = *n*-C_3H_7, Hal = Br;
c = R = *tert*-C_4H_9, Hal = Br.

According to [15], benzyl chloride reacts via the S_N2 mechanism in a strong alkaline medium, whereas the S_N1 mechanism occurs in an acidic medium. We found that benzyl chloride (**14a**) is not transformed into benzyl bromide altogether under the conditions adopted for the substitution of bromine for the methoxy group. The recovery of benzyl chloride with bp 67°C (11 mm Hg) was 90%. However, for the bromination of 1-chloro-1-phenylbutane (**14b**), in which hydrogen chloride can be eliminated, and 1-chloro-2,2-dimethyl-1-phenylpropane (**14c**) without this possibility, the $S_N1$mechanism is feasible as for secondary chlorides. 1-Bromo-1-phenylbutane (**15b**) with bp 106°C (10 mm Hg) (Br, found: 37.76%, calcd.: 37.46%) and 1-bromo-2,2-dimethyl-1-phenylpropane (**15c**) with bp 104°C (10 mm Hg) (Br, found: 35.69%, calcd.: 35.18%) were obtained in 80 and 50% yields (of theoretical value), respectively. Thus, dibromide (**3f**) is formed as a result of the bromination of 3-chloro-1-methoxy-3-phenylpropane (**2f**) via the S_N1 substitution of bromine for chlorine.

The key step in the synthesis of thietane is the cyclization of the corresponding 1,3-dihaloalkanes (3). The yields of the target sulfides in the ring closure step are 45–75% (Table 2). It should be mentioned that the initial member of the series (thietane **4a**) was obtained in 63% yield (theor.). Thietane was prepared for the first time in 1916 by E. Grishkevich-Trokhimovskii [16] from 1,3-dibromopropane in a 4% yield (theor.). The low yield can be explained by the almost complete

absence of 1,3-dibromopropane in the obtained dibromide, because it was synthesized by the addition of hydrogen bromide to allyl bromide in the presence of allyl alcohol taken in the amount of 10% of the mass of allyl bromide:



It was difficult even to expect the formation of 1,3-dibromopropane under these conditions. The Kharash reaction (anti-Markovnikov addition) had not been discovered by that time.

CONCLUSIONS

The three-step procedure for the large-scale preparation of 2-alkyl(aryl)-substituted thietanes was developed. A series of new 2-substituted thietanes and their sulfoxides and sulfones were obtained. 2-Alkyl-3-methoxymethyltetrahydrofurans were found as by-products in the synthesis of 3-chloro-1-methoxyalkanes. 1,3-Dibromo-3-phenylpropane instead of 1-bromo-3-chloro-3-phenylpropane was shown to form via to the bromination of 3-chloro-1-methoxy-3-phenylpropane.

REFERENCES

1. N. P. Volynskii, Pozharovzryvobezopasnost, No. 5, 56 (2005).
2. E. P. Miknis and J. P. Biscar, J. Phys. Chem. **75,** 725 (1971).
3. S. Searles, H. Hays, and E. Lutz, J. Org. Chem. **27,** 2828 (1962).
4. M. Lancaster and J. H. Smith, Synlett Commun., No. 7, 582 (1982).
5. K. Nagasawa and A. Yoneta, Chem. Pharm. Bull. **33,** 5048 (1985).
6. C. Schaal, Bull. Soc. Chim. Fr., No. 8, 3064 (1971).
7. M. Sander, Chem. Rev. **66,** 341 (1966).
8. D. C. Dittmer and T. C. Sedergran, in *Small Ring Heterocycles*, Ed. by A. Hassner (Wiley, New York, 1985), Part III, p. 431.
9. N. P. Volynskii, Neftekhimiya **43**, 380 (2003) [Pet. Chem. *43*, 344 (2003)].
10. N. P. Volynskii and S. E. Shevchenko, Zavod. Lab. **70** (10), 20 (2004).
11. F. M. Litterscheid, Liebigs Ann. Chem. *330*, 112 (1904).
12. A. Kirrmann and N. Hamaide, Mem. Prez. Soc. Chim., No. 5, 789 (1957).
13. Sh. Mamedov, Zh. Org. Khim. **27**, 1499 (1957).
14. N. P. Volynskii and L. I. Perepelitchenko, Izv. Akad. Nauk SSSR, Ser. Khim., No. 4, 858 (1986).
15. O. A. Reutov, *Theoretical Principles of Organic Chemistry* (Mosk. Gos. Univ., Moscow, 1964) [in Russian].
16. E. O. Grishkevich-Trokhimovskii, *On Cyclic Sulfides* (Kiev, 1916) [in Russian].