TRANSFORMATION OF ACETYLOXIRANES TO THIIRANE ANALOGS

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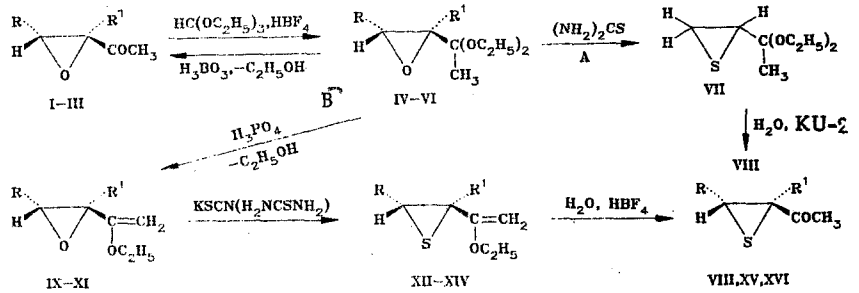
A method for the synthesis of acetylthiiranes was developed; this method includes the conversion of acetyloxiranes to diethylketals, dealkoxylation of the latter, replacement of the oxygen atom of the oxirane ring by sulfur, and acidic hydrolysis of the ethoxyvinylthiiranes to acetylthiiranes.

The synthetic possibilities of acetyloxiranes have been studied quite thoroughly. The significant degree of common character of the properties of oxiranes and thiiranes [1] makes it possible to expect that acetylthiiranes would also act as multipurpose synthones for the preparation of polyfunctional, sulfur-containing, acyclic, carbocyclic, and heterocyclic compounds.

Acetyl derivatives of thiirane in the pregnene steroid series [2], as well as 2,3-dibenzoylthiirane [3], are currently known. However, up until now, methods for the synthesis of the simplest acetylthiiranes have not been available. One of the most widely used methods for the preparation of thiiranes is replacement of the oxirane oxygen atom by sulfur via the method of Culvenor and co-workers [4], and it therefore seemed reasonable to use the readily accessible acetyloxiranes for the synthesis of acetylthiiranes.

We have established that the direct reaction of acetyloxiranes with thiourea or with thiocyanates does not lead to acetylthiiranes as a consequence of desulfuration of the latter under the reaction conditions to give unsaturated ketones; this is due to the presence of an electron-acceptor acetyl group. A similar phenomenon was previously observed for oxiranes with other electron-acceptor groups [1]. We therefore attempted to obtain acetylthiiranes by replacement of the oxirane ring oxygen atom of diethylketals of acetyloxiranes by sulfur via the Culvenor method (method A).

For this, acetyloxirane (I), 2-methyl-2-acetyloxirane (II), and trans-3-methyl-2-acetyloxirane (III) were converted to the corresponding ketals IV-VI (Table 1) by the action of ethyl orthoformate in the presence of alcohol and catalytic amounts of tetrafluoroboric acid. High yields (up to 90%) of the ketals are achieved in the case of catalysis by perchloric and tetrafluoroboric acids. p-Toluenesulfonic acid, sulfuric and hydrochloric acids, and ammonium chloride and nitrate were found to be ineffective catalysts for the synthesis of ketals IV-VI.



I, IV, VII, VIII, IX, XII R=R¹=H; II, V, X, XIII, XV R=H, R¹=CH₃; III, VI, XI, XIV, XVI, R=CH₃, R¹=H

A study of the reaction of ketals IV-VI with thiourea or potassium thiocyanate showed that only ketal IV reacts with thiourea to give acetyloxirane diethylketal (VII) in 36% yield, whereas ketals V and VI undergo polymerization under the reaction conditions.

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TABLE 1. Characteristics of IV-XVI

Compound	bp, °C (mm)	n_D^{20}	Found, %			Empirical formula	Calc., %			Yield, %
			C	H	S		C	H	S	
IV	62—63 (12)	1,4176	60,2	9,8	—	$C_8H_{16}O_3$	60,0	10,0	—	87,3
V	60—63 (10)	1,4189	61,9	10,5	—	$C_9H_{18}O_3$	62,1	10,3	—	85,0
VI	68—70 (13)	1,4162	62,0	10,4	—	$C_9H_{18}O_3$	62,1	10,3	—	90,0
VII	82—83 (12)	1,4582	54,3	8,7	17,8	$C_8H_{16}O_2S$	54,5	9,5	18,1	36,0
VIII	54—56 (15)	1,5070	47,3	6,0	31,7	C_4H_6OS	47,1	5,9	31,4	80,1*
IX	40—41 (12)	1,4385	63,0	9,0	—	$C_6H_{12}O_2$	63,2	8,8	—	79,7
X	37—38 (12)	1,4307	65,7	9,2	—	$C_7H_{14}O_2$	65,6	9,4	—	76,9
XI	45—46 (12)	1,4352	65,4	9,5	—	$C_7H_{14}O_2$	65,6	9,4	—	81,9
XII	65—66 (12)	1,5064	55,3	7,5	24,9	$C_6H_{10}OS$	55,4	7,7	24,6	69,3
XIII	60—61 (12)	1,4887	58,6	8,4	22,0	$C_7H_{14}OS$	58,3	8,3	22,2	69,7
XIV	70—71 (12)	1,4885	58,5	8,2	22,3	$C_7H_{14}OS$	58,3	8,3	22,2	69,5
XV	52—54 (11)	1,4950	51,8	6,7	27,5	C_5H_8OS	51,7	6,9	27,6	70,6
XVI	64—65 (18)	1,4947	51,9	6,8	27,4	C_5H_8OS	51,7	6,9	27,6	80,2

*The yield from thiirane XII was 78.8%.

Acetylthiirane (VIII) was obtained in 80% yield by hydrolysis of ketal VII at room temperature in the presence of KU-2 cation-exchange resin in the H^+ form.

Thus via method A we were able to synthesize only unsubstituted acetylthiirane (VIII), the yield of which was 28.8% based on oxirane I. The chief reason for the low reactivities of ketals V and VI with thiourea or potassium thiocyanate is the steric hindrance, created by the methyl groups and the diethylketal grouping, to nucleophilic processes involving the formation of the intermediate aminooxathiolane and its rearrangement to a thiirane [4]. The ease of replacement of the oxirane ring oxygen atom by sulfur in formyloxirane acetals [5, 6] may serve as an indirect confirmation of this.

To decrease the effect of steric hindrance on the formation of the thiirane ring ketals IV-VI were dealkoxylated by distillation in the presence of phosphoric acid to give the corresponding vinyl ethers IX-XI (in up to 82% yields, which were then transferred to acetylthiiranes via method B. The yields of vinyl ethers IX-XI are considerably lower in the case of catalysis of the reaction by p-toluenesulfonic acid, potassium and sodium bisulfates, anhydrous copper sulfate, and boron trifluoride etherate, as well as in the case of pyrolysis of ketals IV-VI at 300-330°C. However, heating 0.33 mole of boric acid with 1 mole of ketals IV-VI led to the starting oxiranes I-III in virtually quantitative yields.

By replacement of the oxirane oxygen atom by sulfur by means of potassium thiocyanate vinyl ethers IX-XI were converted to the corresponding thiiranes XII-XIV. The use of thiourea in the reaction under consideration leads to lower yields of thiiranes XII-XIV as a consequence of increased resinification during distillation.

Thiiranes XII-XIV are readily hydrolyzed by dilute tetrafluoroboric acid to acetylthiiranes VIII, XV, and XVI, the overall yields of which reach 41% based on the starting acetyloxiranes.

The proposed method for the synthesis of acetylthiiranes evidently has quite general character for the preparation of alkyl-substituted acetylthiiranes, and acetyloxirane ketals, ethoxyvinyloxiranes, and ethoxyvinylthiiranes may find independent application in fine organic synthesis and in the chemistry of high-molecular-weight compounds.

The structures of IV-XVI were confirmed by the results of elementary analysis and by spectral data. With regard to the chemical shifts, integral intensities, and character of the multiplicity of the signals, the PMR spectra of IV-XVI (Table 2) correspond to the structures of these compounds. The low values of the spin—spin coupling constants (SSCC) of the oxiranes and thiirane rings of III, VI, XI, XIV, and XVI and the mechanics of the replacement of the oxirane oxygen atom by sulfur [4] constitute evidence for retention of the spatial orientation of the substituents of the three-membered ring in the transformation of trans-oxirane III [7] to acetylthiirane XVI.

The IR spectra of ketals IV-VI and VII do not contain an absorption band of a carbonyl group, but a number of absorption bands over the 1040-1200 cm^{-1} range, which is characteristic for the COCOC fragments of ketals, are observed. Thiirane VII has an absorption band of a C—S bond at 690 cm^{-1}. The IR spectra of ethoxyvinyloxiranes IX-XI and ethoxyvinylthiiranes XII-XIV have similar structures and differ with respect to the absorption band of a C-S bond at

TABLE 2. PMR Spectra of Oxiranes and Thiiranes IV-XVI

Compound	X	Chemical shifts, δ, ppm (multiplicity, J, Hz)			
		H	R	R¹	R²
IV	O	2,53 (m, AB part of an ABX system, 6.0)	1H, 2,57 (m, AB part of an ABX system 6.5)	1H, 2,81 (m, X part)	3H, 1,18 (s); 4H, 3,45 (q, 7,0); 6H, 1,08 (t, 7,0)
V	O	2,19 (d, 6.0)	1H, 2,83 (d, 6.0)	3H, 1.18 (s)	3H, 1.18 (s); 2H, 3,43 (q, 7,0); 2H, 3,33 (q, 7,0); 6H, 1,03 (t, 7,0)
VI	O	2,88 (dq, 2.0, 5.5)	3H, 1,18 (d, 5,5)	1H, 2,53 (d, 2.0)	3H, 1,17 (s); 4H, 3,42 (q, 7,0); 6H, 1,07 (t, 7,0)
VII	S	2,26 (m, AB part of an ABX system, 0)	1H, 2,32 (d, AB part of an ABX system, 0)	1H, 2,90 (m, X part)	3H, 1,22 (s); 4H, 3,49 (q, 7,0); 6H, 1,10 (t, 7,0)
VIII	S	2,59 (m, AB part of an ABX system, 1.1)	1H, 2,64 (m, AB part of an ABX system, 1.1)	1H, 3,31 (m, X part)	3H, 2,02 (s)
IX	O	2,60 (AB part of an ABX system, 0)	1H, 2,66 (AB part of an ABX system, 0)	1H, 3,08 (m, X part)	2H, 3,66 (q, 7,0); 3H, 1,24 (t, 7,0); 1H, 4,10 (d, 2,0); 1H, 3,91 (d, 2,0)
X	O	2,53 (AB system, 6,0)	1H, 2,45 (AB system, 6.0)	3H, 1,35 (s)	2H, 3,65 (q, 7,0); 3H, 1,24 (t, 7,0); 1H, 4,10 (d, 2,0); 1H, 3,78 (d, 2,0)
XI	O	2,90 (m, AB part of an ABX system, 5,5)	3H, 1,21 (d, X_3 part of an ABX_3 system, 5.5)	1H, 2,8 (m, AB part of an ABX_3 system, 2.0)	2H, 3,64 (q, 7,0); 3H, 1,21 (t, 7,0); 1H, 4,03 (d, 2,0); 1H, 3,84 (d, 2,0)
XII	S	2,30 (d, AB part of an ABX system, 0)	1H, 2,43 (d, AB part of an ABX system, 0)	1H, 3,26 (m, X part of an ABX system)	2H, 3,62 (q, 7,0); 3H, 1,20 (t, 7,0); 1H, 4,15 (d, 2,5); 1H, 3,91 (d, 2,5)
XIII	S	2,71 (s, AX system, 0)	1H, 2,18 (s, AX system, 0)	3H, 1,74 (s)	2H, 3,65 (q, 7,0); 3H, 1,24 (t, 7,0); 1H, 4,63 (d, 2,5); 1H, 3,86 (d, 2,5)
XIV	S	2,86 (m, AB part of an ABX_3 system, 5,0)	3H, 1,43 (d, X_3 part of an ABX_3 system, 5.0)	1H, 2.95 (m, AB part of an ABX_3 system, 2.5)	2H, 3,64 (q, 7,0); 3H, 1,21 (t, 7,0); 1H, 4,12 (d, 2,2); 1H, 3,88 (d, 2,2)
XV	S	2,81 (d, 1,5)	1H, 2,48 (d, 1,5)	3H, 1,59 (s)	3H, 1,96 (s)
XVI	S	3,05 (m, AB part of an ABX_3 system, 5,4)	3H, 1,50 (d, X_3 part of an ABX_3 system, 5,4)	1H, 3,05 (m, AB part of an ABX_3 system, 2.0)	3H, 1,97 (s)

670 cm^{-1}. The two absorption bands of a double bond at 1645 and 1600 cm^{-1} for ethoxyvinyl ethers IX-XIV and the band of a carbonyl group at 1700-1715 cm^{-1} for acetylthiiranes VIII and XVI are due to the presence in solution of two conformers with different orientations of the ethoxyvinyl and acetyl groups with respect to the heteroring.

EXPERIMENTAL

The IR spectra of solutions of the compounds in CCl_4 were recorded with a Specord IR-75 spectrometer. The PMR spectra of solutions (10%) of the compounds in CCl_4 were obtained with a Tesla BS-467 spectrometer (60 MHz) with hexamethyldisiloxane (HMDS) as the internal standard.

The purity and individuality of the compounds were monitored by gas–liquid chromatography [LKhM-8M chromatograph with a catharometer, 2 m × 3 mm column, 5% Silicone XE-60 on Chromaton N-AW (0.20-0.25 mm), helium as the carrier gas (50 ml/min)] and thin-layer chromatography [Silufol UV-254 plates in a hexane–ether system (from 1:1 to 1:4), detection by iodine vapors or 4% $KMnO_4$ solution].

The characteristics of IV-XVI are presented in Table 1.

Acetyloxirane Diethylketals IV-VI. A 1-ml sample of 60% HBF_4 was added to a mixture of 220 g (1.25 mmole) of ethyl orthoformate with 70 ml of ethanol. After 30 min, 1 mole of acetylorirane I-III was added, and the mixture was maintained at 25-30°C for 2-3 h. It was then neutralized with calcined potassium carbonate and filtered. The ethanol and ethyl formate were removed by filtration, and the residue was distilled in vacuo with an efficient fractioning column to give IV-VI.

Acetylthiirane Diethylketal (VII). A mixture of 16 g (0.1 mole) of diethylketal IV, 7.6 g (0.1 mole) of thiourea, and 45 ml of absolute ethanol was heated in a sealed ampul on a boiling-water bath for 1.5 h, after which the alcohol was removed by distillation in vacuo, and the residue was treated with 100 ml of hexane–ether (1:1). The precipitate urea was removed by filtration, the solvent was removed, and the residue was distilled rapidly in vacuo to give VII.

Acetylthiirane (VIII). A mixture of 26.4 g (0.15 mole) of diethylketal VII, 25 ml of water, and 2 g of KU-2 cation-exchange resin in the H^+ form was stirred vigorously at room temperature for 1.5 h, after which it was extracted with ether (three 70-ml portions). The extract was dried with Na_2SO_4 and distilled in vacuo to give VIII.

2-(1-Ethoxyvinyl)oriranes IX-XI. A 1-mole sample of diethylketal IV-VI was placed in a 250-300 ml heat-resistant flask and heated on a metal bath to 160-170°C, after which 1-2 ml of 85% H_3PO_4 was added gradually dropwise, and the ethanol was distilled through a fractioning column of the rod and disk type at such a rate that the temperature of the vapors did not exceed 80-85°C. After 80-90% of the alcohol had been removed, the bath temperature was raised to 180-210°C, and the vinyl ether was removed by distillation and redistilled in vacuo to give IX-XI.

2-(1-Ethoxyvinyl)thiiranes XII-XIV. A 200-ml sample of ethanol and 1 mole of oxirane IX-XI were added to a solution of 126 g (1.3 moles) of potassium thiocyanate in 60 ml of water, and the mixture was refluxed for 30 min (IX), 1 h (X), or 2.5 h (XI). It was then filtered, and the precipitate was washed with 100 ml of hexane. The aqueous alcohol part was extracted with hexane (four 150-ml portions), and the combined extracts were dried with Na_2SO_4. The hexane was removed at reduced pressure, and the residue was distilled in vacuo to give thiiranes XII-XIV.

Acetylthiiranes VIII, XV, and XVI. A mixture of 300 ml of 0.3% HBF_4 and 1 mole of thiirane XII-XIV was stirred vigorously at 20-25°C for 40 min (XII), 1.5 h (XIII), or 3 h (XIV), after which the organic layer was separated, and the aqueous part was extracted with methylene chloride (three 150-ml portions). The extract was washed with water until the wash water was neutral with respect to a universal indicator, dried with Na_2SO_4, and distilled in vacuo to give VIII, XV, or XVI.

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