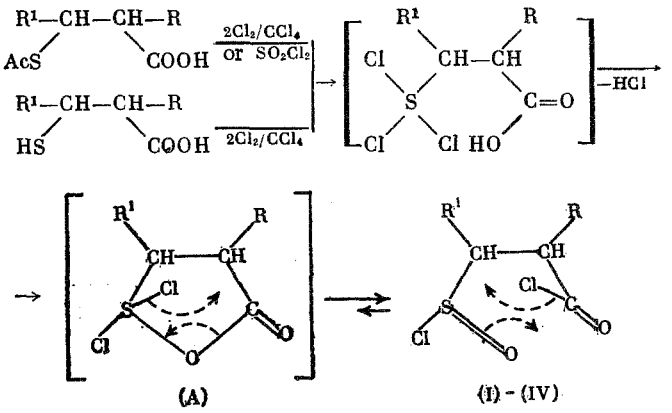
SYNTHESIS AND REACTIVITY OF ACID CHLORIDES OF ALIPHATIC β-(CHLOROSULFINYL)CARBOXYLIC ACIDS

T. P. Vasil'eva, M. G. Lin'kova,
O. V. Kil'disheva, and I. L. Knunyants

UDC 542.91:543.878:547.431.6

The formation of the bis(acid chlorides) of alkanesulfinocarboxylic acids was first mentioned when the γ-(mercapto)butyric and β-(mercapto)propionic acids were chlorinated [1], although the desired compounds were not isolated and characterized. In a similar manner the chlorination of dithiodiacetic acid gives the acid chloride of chlorosulfinylacetic acid, which also was not isolated [2].

We were the first to obtain in high yields the pure acid chlorides of aliphatic β-(chlorosulfinyl)carboxylic acids (I)-(IV) by the chlorination of the β-(acetylthio)- and β-(mercapto)carboxylic acids with either chlorine or sulfuryl chloride.



(A) (I)-(IV)

R^1=R=H (I); R^1=H, R=CH_3 (II); R^1=CH_3, R=H (III); R^1=H, R=Cl (IV).

The properties of (I)-(IV) are given in Table 1. The obtained compounds are pale yellow liquids, are stable in the absence of moisture, and can be vacuum-distilled without decomposition.

The compounds do not solidify at the temperature of liquid nitrogen, and consequently the use of the ^{35}Cl NQR and x-ray structure analysis methods is made difficult.

Since sulfoxides react vigorously with carboxylic acid chlorides even at ∿20°C [3], then intramolecular coordination of the Cl atom of the COCl group with the S atom, and of the O atom of the S(O)Cl group with the carbonyl C atom, is possible in acid chlorides (I)-(IV). The cyclic sulfuran structure (A) for (I)-(IV) can also be postulated on the basis of the NQR spectrum, taken at low temperatures, of the acid chloride of o-(chlorosulfinyl)benzoic acid (V) [1], which testifies to the equivalence of both Cl atoms.

Besides the expected molecular ions, the mass spectra of (I) and (II) contain the fragments with m/e 63, 65 (COCl) and 83, 85 (SOCl); for (I): 91, 93 (C_2H_4COCl) and 139, 141 (OSC_2H_4COCl); for (II): 105, 107 (C_3H_6COCl) and 153, 155 (OSC_3H_6COCl). Such fragmentation of the compounds in the mass spectrum corresponds more to the acid chloride structure.

The νSOCl value for the acid chlorides of arylsulfinic acids is 1150 cm^{-1} [4], whereas the absorption region of the SOCl group in the IR spectrum of compounds of the aliphatic series is unknown. To determine it we specially obtained CH_3SOCl [5] and methyl β-(chlorosulfinyl)propionate (VI).

A. N. Nesmeyanov Institute of Heteroorganic Compounds, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 1, pp. 159-165, January, 1981. Original article submitted January 3, 1980.

0568-5230/81/3001-0137$07.50

TABLE 1. Derivatives of Carboxylic Acids with Sulfinyl Group in β-Position

Compound	Yield, %	bp, °C (p, mm Hg) or mp, °C	n_D^{20} (d_4^{20})	Found/calculated, %				Empirical formula	Infrared spectrum, ν, cm⁻¹		PMR spectrum δ, ppm ($J_{CH_3-CH_2}$, Hz)
				C	H	S	Cl or N		SOCl	C=O	
(I)	83	56 (0,4)	1,5330 *m/e* 174	21,18 / 20,59	2,25 / 2,28	18,38 / 18,28	39,71 / 40,60	$C_3H_4Cl_2O_2S$	1152	1790	3,7 s (CH_2CH_2)
(II)	70	52–55 (0,3)	1,5180 (1,4350), *m/e* 187	25,40 / 25,39	3,23 / 3,17	16,86 / 16,93	35,30 / 37,55	$C_4H_6Cl_2O_2S$	1155	1790	1,65 d (CH_3, 6,6), 2,93–3,96 m (CH_2CH)
(III)	85	56 (0,4)	1,5220 (1,4340)	25,30 / 25,39	3,23 / 3,17	16,96 / 16,93	36,81 / 37,56	$C_4H_6Cl_2O_2S$	1152	1790	1,62 d (CH_3, 6,3), 2,97–4,2 m ($CHCH_2$)
(IV)	99	60 (0,4)	1,5430 (1,6280)	17,13 / 17,20	1,37 / 1,43	15,34 / 15,30	49,98 / 50,59	$C_3H_3Cl_3O_2S$	1158	1790	3,62–4,42 m (CH_2), 4,93–5,32 m (CH)
(VI)	86	56–58 (1)	1,4963	27,95 / 28,15	4,01 / 4,10	19,47 / 18,76	20,69 / 20,82	$C_4H_7ClO_3S$	1160	1730–1745	3,83 s (OCH_3). System AA′BB′: 3,14³ and 3,72 (CH_2CH_2, 6,7)
(VIII)	73	80–100	–	26,40 / 26,10	4,34 / 4,35	22,74 / 23,19	–	$C_3H_6O_4S$	1060, 1120 (S=O), 1715 (C=O), 2500–3200 (OH)		In CH_3CN: 2,54–3,07 (CH_2C), 3,31–3,76 q (CH_2S)
(XII)	100	Syrup	1,4869	31,67 / 31,57	5,02 / 5,26	21,14 / 21,05	–	$C_4H_8O_4S$	1055, 1130 (S=O), 1730–1740 (C=O) 2965 (OH)		In CH_2Cl: 2,69–3,05 m (CH_2C), 3,21–3,54 m (CH_2S), 3,72 s (OMe)
(XIII)	100	»	1,4753	36,10 / 36,14	5,98 / 6,02	19,20 / 19,27	–	$C_5H_{10}O_4S$	1055, 1130 (S=O), 1730–1740 (C=O), 2950–3000 (OH)		1,27 d.t (CH_3, 9), 2,5–3,2 m (CH_2CH_2), 4,1 m (OCH_2)
(XIV)	62	94–96 (3)	1,4550	40,49 / 40,05	6,63 / 6,66	17,55 / 17,77	–	$C_6H_{12}O_4S$	1030, 1128 (S=O), 1742 (C=O)		1,37 t (CH_3, 8), 2,56–3,14 m (CH_2CH_2), 3,79 s (OMe), 4,03 and 4,29 q (OCH_2, 8)
(X)	48	100–101	–	–	–	19,61 / 19,51	16,15 / 17,00	$C_5H_{12}N_2O_2S$	1025 (S=O), 720, 1270, 1570, 1650 (CON), 1420 (CH_3N), 3200–3300 (NH)		–

$$CH_3COSCH_2CH_2COOCH_3 \xrightarrow[Ac_2O]{2Cl_2} \underset{Cl}{\overset{O}{\diagdown\!\!\!\!\diagup}}SCH_2CH_2COOCH_3 + 3AcCl$$
(VI)

The νSOCl values for CH_3SOCl and ester (VI) are 1152 and 1160 cm^{-1}, a region where compounds (I)-(IV) also absorb, which confirms the acid chloride structure for the latter. In Table 1 are also given the PMR spectral data for (I)-(IV); a singlet of the methylene protons at 3.7 ppm is characteristic for the unsubstituted (I) compound.

The decomposition of acid chloride (I) using $NaHCO_3$ and subsequent treatment of the formed bis-Na salt (VII) with $SOCl_2$ leads to the starting (I), which also testifies to the noncyclic structure of (I)-(IV).

$$\underset{(I)}{\overset{CH_2-CH_2}{\underset{ClSO}{\diagup}\quad\diagdown\underset{COCl}{}}} \underset{\text{excess } SOCl_2}{\overset{4NaHCO_3/H_2O}{\underset{-2NaCl,\ -2SO_2}{\rightleftharpoons}}} \underset{(VII)}{\overset{CH_2-CH_2}{\underset{NaSO_2}{\diagup}\quad\diagdown\underset{COONa}{}}}$$
$$-2NaCl,\ -4CO_2$$

It is known [6] that, in contrast to the salts, the free alkanesulfinic acids are unstable and can disproportionate to thiosulfonates and sulfonic acids by the equation: $3RSO_2H \rightarrow RSSO_2R + RSO_3H + H_2O$.

The careful hydrolysis of (I) with the calculated amount of water in CCl_4 gives sulfinocarboxylic acid (VIII), whereas the hydrolysis of (I) with excess water proceeds vigorously to give di(2-carbethoxyethyl) thiosulfonate (IX), which is the disproportionation product. The treatment of (I) with excess methylamine gave bis(methylamide) (X).

$$(I) \xrightarrow[-2HCl]{4H_2O} \underset{SO_2H}{CH_2CH_2COOH} \quad (\rightarrow \underset{SCH_2CH_2COOH}{SO_2CH_2CH_2COOH})$$
(VIII) (IX)

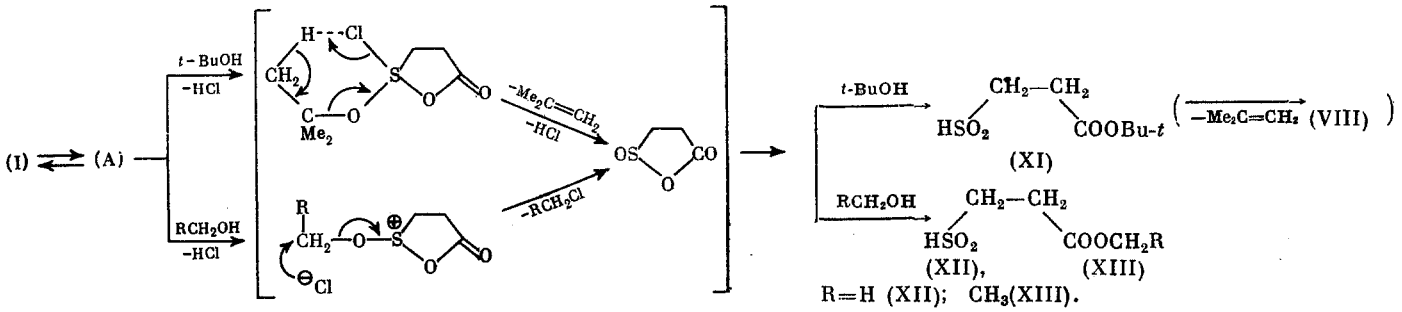
$$(I) \xrightarrow[2MeNH_2\cdot HCl]{4MeNH_2} \underset{O=S-NHMe}{CH_2CH_2CONHMe}$$
(X)

The sulfinoamides are mild agents for the oxidation of thiols to disulfides; for example, i-$PrSONH_2$ and $XOS-CH_2COX$ (where X = morpholide) act on the keratin of reduced hair the same as H_2O_2 [2].

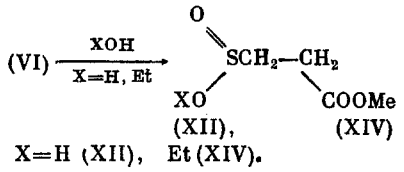
A further study of the properties of the obtained bis(acid chlorides) disclosed that in some cases (reaction with alcohols, PCl_5, and PCl_3), due to the presence of the intramolecular coordination $>S=O\ldots>C=O$, it is possible to have at the moment of reaction a tautomeric conversion of the stable acid chlorides (I)-(IV) to the exceedingly reactive labile dichlorosulfurans (A).

It is known that, in contrast to DMSO, which dehydrates secondary and tertiary alcohols to olefins only under drastic conditions (180°, 10 h), sulfurans are capable of similar reactions at low temperatures [7, 8]. Thus, $Ph_2S(OR_F)_2$ when treated with t-C_4H_9OH forms Ph_2SO and isobutylene, while it reacts with primary alcohols RCH_2OH to give ethers RCH_2OR_F [8]. In a similar manner acid chloride (I) when treated with t-C_4H_9OH liberates isobutylene under mild conditions, with the formation of the tert-butyl ester of β-(hydroxysulfinyl)propionic acid (XI), whereas reaction with methanol or ethanol results in the liberation of methyl or ethyl chloride and the formation of the corresponding esters of β-(hydroxysulfinyl)-propionic acid, (XII) and (XIII). tert-Butyl ester (XI), due to the presence of the acid SO_2H function, is unstable (characterized only by the IR and PMR spectra) and gradually is converted completely to bisacid (VIII).*

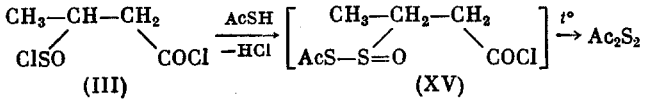
*Checked by the spectra and elemental analysis.



The structure of methyl ester (XII) was proved by the IR and PMR spectra and by hydrolysis of sulfinyl chloride (VI), which contains an uncoordinated SOCl group and, in contrast to bis(acid chloride) (I), reacts* with alcohol to give the ethyl ester of the sulfinic acid (XIV).

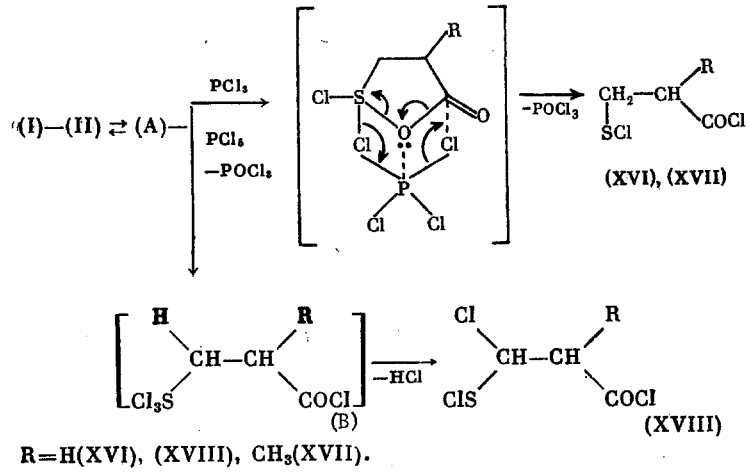


The reaction of acid chloride (III) with AcSH gives thiolsulfinate (XV), but the latter cannot be isolated pure due to the ease of symmetrization.



It is known that aliphatic thiolsulfinates are unstable and spontaneously disproportionate into a mixture of equimolar amounts of disulfide and thiolsulfonate [10]: $2RS(O)SR \rightarrow R_2S_2 + RSO_2SR$.

Information is lacking [6] on the reactions of sulfinic acid chlorides with electrophiles. It proved that either PCl_3 or PCl_5 converts acid chlorides (I) and (II) to the corresponding β-sulfenyl chlorides (XVI) and (XVII). The reaction of bis(acid chloride) (I) with PCl_5 quantitatively gives the chlorinated sulfenyl chloride (XVIII), apparently via the intermediate trichloride (B).



*The acid chlorides of alkanesulfinic acids react with alcohols to smoothly give the corresponding esters [9].

A study of the properties of the acid chlorides of β-(chlorosulfinyl)carboxylic acids is being continued.

EXPERIMENTAL

The IR spectra of the compounds [except (V)] were taken as KBr pellets for the solids and as a thin layer for the liquids. The PMR spectra were taken on a Perkin—Elmer R-12 spectrometer (60 MHz) using CCl_4 as the solvent and HMDS as the external standard. Absolute solvents and reagents were used in all of the experiments. The yields, constants, and IR and PMR spectral data are given in Table 1.

General Method for Preparation of Acid Chlorides of β-(Chlorosulfinyl)carboxylic Acids (I)-(IV). With stirring, 15 g (0.21 mole) of chlorine was passed at −30° into 150 ml of an 0.1 M solution of β-(acetylthio)carboxylic acid in CH_2Cl_2, after which the mixture was warmed up to ∿20°, the volatile products were removed in vacuo, and the residue was distilled.

For the example of β-(acetylthio)propionic acid it was shown that the acid chloride of β-(chlorosulfinyl)propionic acid (I) can be obtained by chlorination with excess SO_2Cl_2 (neat, 20°) in 88% yield. For the example of chlorinating β-(mercapto)propionic acid as described in [1] it was established that (I) is also formed smoothly here and, in contrast to [1], acid chloride (I) was isolated by vacuum distillation in ∿100% yield.

The consumption per mole of (I)-(IV) is 4 moles of NaOH (acidimetric titration) and 1 mole of $Na_2S_2O_3$ (iodometric titration in aqueous acetone).

Acid Chloride of o-(Chlorosulfinyl)benzoic Acid (V). The chlorination was run the same as described in [1] using 0.1 M of thiosalicylic acid. The unreacted starting acid was removed by filtration and the solution was evaporated. The yield of (V) was 22 g (98.5%), mp 55-57° (from [1], mp 62°). Infrared spectrum (CCl_4, ν, cm^{-1}): 1165 (S=O), 1742 (C=O). ^{35}Cl NQR spectrum (ν, MHz): 31.802 and 31.279.

Methylsulfinyl Chloride. Obtained by the chlorination of Me_2S_2 in the presence of acetic anhydride [5], bp 37-38° (12 mm), n_D^{22} 1.4930; found Cl 35.7% (Volhard), calculated 36.0%; 1152 cm^{-1} (νSO), δ ppm, 3.44 s (CH_3). The consumption of $Na_2S_2O_3$ was 0.13-0.22 mole per mole of MeSOCl (iodometric titration in aqueous acetone).

Methyl Ester of β-(Chlorosulfinyl)propionic Acid (VI). A mixture of 39.8 g (0.244 mole) of methyl β-(acetylthio)propionate and 24.9 g (0.244 mole) of Ac_2O in 150 ml of CCl_4 was saturated at −30° with 35 g (0.488 mole) of chlorine, after which the mixture was warmed up to ∿20°, the solvent was removed in vacuo, and the residue was distilled to give 35.7 g of ester (VI).

The consumption of $Na_2S_2O_3$ was 0.51 mole per mole of sulfinyl chloride (VI) (iodometric titration in aqueous acetone).

Counter Synthesis of Bis(acid chloride) (I). To 8.5 g (0.0485 mole) of (I) was added an excess (25.2 g, 0.3 mole) of $NaHCO_3$ in 50 ml of water and the solution tested alkaline. After distilling off the water in vacuo and drying the residue we obtained the di-Na salt (VII) (a mixture with NaCl and $NaHCO_3$) as a white powder. Infrared spectrum (ν, cm^{-1}): 1595, 1330 (COONa), 985-1050 (SO_2Na).

The ground (VII) salt was treated with 54 ml (0.75 mole) of $SOCl_2$ for 1 day at 20°, and then the mixture was refluxed for 1.5 h. The precipitate was filtered, the filtrate was evaporated, and the residue was distilled to give 4.75 g (56%) of (I).

β-(Hydroxysulfinyl)propionic Acid (VIII). With stirring, to a solution of 1.75 g (0.01 mole) of (I) in 10 ml of CCl_4 was added 0.36 g (0.02 mole) of water; heat was evolved and an oil deposited, which crystallized when rubbed. After 3 h the precipitate was filtered and dried over P_2O_5. The yield of (VIII) was 1 g, and the neutralization equivalent (NaOH) was 63, calcd. 69 (M/2). Acid (VIII) is insoluble in benzene or CCl_4, and its aqueous solution has pH ∿ 1. When it was attempted to purify (VIII) either by reprecipitation from aqueous $NaHCO_3$ solution or by long standing, the compound was converted almost completely to thiosulfonate (IX) with mp 135°.

Di(2-carboxyethyl) Thiosulfonate (IX). Acid chloride (I) was decomposed with excess water, and on cooling (IX) was deposited quantitatively as white crystals, which were purified by dissolving in aqueous $NaHCO_3$ solution, precipitated with 10% HCl solution, and dried

in the air; mp 148°. Infrared spectrum (KBr, ν, cm^{-1}): 1697 and 1712 (COOH), 1120 and 1320 (SO_2S): Found: C 29.10; H 4.26; S 26.40%; neutralization equivalent (NaOH) 119.5. $C_6H_{10}O_6S_2$. Calculated: C 29.70; H 4.14; S 26.42%; equivalent 121 (M/2).

Methylamide of β-(Methylamidosulfinyl)propionic Acid (X). With stirring, an excess (10 ml, 0.24 mole) of methylamine was passed at −60 to −70° through a solution of 7 g (0.04 mole) of (I) in 200 ml of ether. The next day the precipitate (10 g, mixture of $MeNH_2 \cdot HCl$ and product) was filtered and repeatedly extracted with a large amount of hot dioxane. White crystals, free of halogen, were obtained by removing the dioxane in vacuo; they were purified by reprecipitation from alcohol solution with ether and dried. Methylamide (X) is soluble in water, alcohol, acetone or $CHCl_3$, difficultly soluble in dioxane, and insoluble in ether or CCl_4.

General Method for Preparation of β-(Hydroxysulfinyl)propionic Acid Esters (XI)-(XIII). To a solution of 1.75 g (0.01 mole) of (I) in 10 ml of ether was added 0.02 mole of the appropriate alcohol; the reaction is exothermic. After 3 h the solvent and volatile products were distilled into a cooled trap at 35° (15 mm). The residue was a water-soluble colorless syrup; its aqueous solution has pH ∿ 1. Acidimetric titration revealed that 1 mole of NaOH is consumed per mole of acid (XII).

In the distillate from ethyl ester (XIII) was detected EtCl by GLC.

The reaction of (I) with t-BuOH was run with trapping of the gaseous products, among which was detected isobutylene (GC method). Traces of t-BuCl were also found in the distillate by GLC, which, after redistilling the ether distillate, remains in the still residue and has n_D^{20} 1.3800. The residual syrup (n_D^{20} 1.4705), together with ester (XI), contains bisacid (VIII). Infrared spectrum (ν, cm^{-1}): 1735 (COOBu-t (XI)), 1700-1715 (COOH (VIII)). The addition of CH_2Cl_2 to the mixture gives a precipitate of acid (VIII) with mp 70-72°, yield 25.4%. From the mother liquor after evaporating the CH_2Cl_2 we obtained ester (XI) as an oil. Infrared spectrum (ν, cm^{-1}): 1125 (S=O), 1735 (CO), 2950-2990 (OH). PMR spectrum (δ, CH_2Cl_2): 1.49 s (t-Bu), 2.65-3.47 m (CH_2CH_2).

Compound (XI) is unstable: according to the PMR spectrum and elemental analysis (C, H, S), after a day the sample contains 67% of (XI) and 33% of acid (VIII).

Counter Synthesis of Methyl β-(Hydroxysulfinyl)propionate (XII). To 2.3 g (0.0135 mole) of ester (VI) was added a mixture of 0.5 g of water and 10 ml of benzene, the mixture was stirred for 30 min, the excess water and solvent were removed in vacuo, and traces of water were distilled with benzene (3 × 10 ml) in vacuo. We obtained 1.52 g (74%) of (XII), n_D^{25} 1.4865. Methyl ester (XII) is soluble in water, difficultly soluble in CH_2Cl_2, and insoluble in CCl_4.

Methyl β-(Ethoxysulfinyl)propionate (XIV). To a solution of 13.85 g (0.1 mole) of (VI) in 50 ml of ether was added 5.06 g (0.1 M) of ethanol at −30°, and after 30 min (20°) the mixture was fractionally distilled; yield of (XIV) 11.27 g.

Reaction of Acid Chloride of β-(Chlorosulfinyl)butyric Acid (III) with Thiolacetic Acid. To a solution of 7.05 g (0.0373 mole) of (III) in 6 ml of CCl_4 at −10° was added 3.75 g (0.0494 mole) of AcSH; the reaction is exothermic. After 40 min (20°) the solvent was removed in vacuo, and the residue was thiolsulfinate (XV). Infrared spectrum (ν, cm^{-1}): 1115 (S=O), 1730-1740 (COS), 1800 (COCl). PMR spectrum (δ, ppm): 1.29-1.57 (CH_3, group of signals), 2.49 s and 2.55 s (CH_3CO), 2.67-3.6 m (CH_2CH).

After distilling (XV) we isolated 3.87 g (69%) of diacetyl disulfide, bp 75° (3 mm), n_D^{21} 1.5355, δ 2.54 s (CH_3) (cf. [11].

Acid Chloride of β-(Chlorosulfenyl)isobutyric Acid (XVII). A mixture of 5.92 g (0.031 mole) of (II) and excess PCl_3 (12.9 g, 0.094 mole) was refluxed for 3 h and then distilled to give 1.19 g (22%) of sulfenyl chloride (XVII), bp 75° (10 mm), n_D^{23} 1.5097, 1790 cm^{-1} (νCOCl). PMR spectrum (δ, ppm): 1.53 d (CH_3, $J_{CH_2-CH} = 7.3$ Hz), 2.91-3.81 m (CH_2CH). Found: C 27.75; H 3.26; S 18.53; Cl 40.07%. $C_4H_6Cl_2OS$. Calculated: C 27.76; H 3.49; S 18.53; Cl 40.97%.

In addition, we isolated 3.7 g (62.5%) of the starting (II) (according to the constants, elemental analysis, and IR and PMR spectral data).

In a similar manner, from (I) and PCl_3 we obtained the acid chloride of β-(chlorosulfenyl)propionic acid (XVI) in 23% yield, bp 55° (1 mm), n_D^{22} 1.5250, δ 3.46 s (CH_2CH_2) (cf. [12]), 1795 cm^{-1} (νCOCl).

Acid Chloride of β-Chloro-β-(chlorosulfenyl)propionic Acid (XVIII). A mixture of 3.5 g (0.02 mole) of (I) and 4.16 g (0.02 mole) of PCl_5 was heated for 1.5 h at 80° and then fractionally distilled. The yield of (XVIII) was 3.9 g (100%), bp 55-56° (3 mm), n_D^{19} 1.5405 (cf. [12]), 1795 cm^{-1} (νCO). PMR spectrum (δ, ppm): 3.5-3.9 d.d (CH_2), 5.61 t (CH), J_{CH_2-CH} = 6.6 Hz.

CONCLUSIONS

1. A convenient general method was developed for obtaining the acid chlorides of β-(chlorosulfinyl)carboxylic acids from β-(acetylthio)carboxylic acids.

2. The acid chlorides of β-(chlorosulfinyl)carboxylic acids react with water and amines as the acid chloride form, while with alcohols, PCl_3, and PCl_5 they apparently react via the tautomeric form of the cyclic dichlorosulfuran.

LITERATURE CITED

1. I. Douglass and B. Farah, J. Org. Chem., 26, 351 (1961).
2. Y. Chiang, J. Luloff, and E. Schipper, J. Org. Chem., 34, 2397 (1969).
3. A. Mancuso, S. Huang, and D. Swern, J. Org. Chem., 43, 2480 (1978); R. Michelot and M. Tchoubar, Bull. Soc. Chim. France, 1966, 3039.
4. S. Detoni and D. Hadzi, J. Chem. Soc., 1955, 3163.
5. I. Douglass and R. Norton, J. Org. Chem., 33, 2104 (1968).
6. C. Stirling, Int. J. Sulfur Chem., 6B, 277 (1971).
7. N. Hester, Int. J. Sulfur Chem., 8, 119 (1973).
8. R. Arhart and J. Martin, J. Am. Chem. Soc., 94, 5003 (1972).
9. I. Douglass, J. Org. Chem., 30, 633 (1965).
10. H. Backer and H. Kloosterziel, Rec. Trav. Chim., 73, 129 (1954).
11. A. Speziale and C. Tung, J. Org. Chem., 28, 1353 (1963).
12. T. P. Vasil'eva, M. G. Lin'kova, O. V. Kil'disheva, and I. L. Knunyants, Izv. Akad. Nauk SSSR, Ser. Khim., 1974, 700; 1973, 209.