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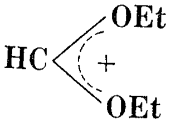
Activation of Weak Organic Bases. V.[1] The Alkylation of Thiono Esters by Diethoxycarbonium Hexachloroantimonate

 , $\overset{-}{S}bCl_6$

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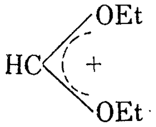
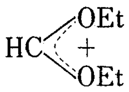
The alkylation of thiono esters by  , $\overset{-}{S}bCl_6$ was carried out at low temperature and the corresponding S-alkylated species were isolated. The thermal stability of these salts has been discussed and their reactions with several nucleophiles have also been described.

In the preceeding paper in this series, we reported the conversion of thiono esters (I) to thiol esters (II) by $Et_3\overset{+}{O}$, $\overset{-}{B}F_4$ catalysis.[1] The reaction is supposed to proceed *via* alkoxyethylthiocarbonium ion (III). However, an attempt to isolate III was not achieved because III, as soon as it was formed, was assumed to react with the remaining thiono esters at that temperature (51°) giving thiol esters. It is anticipated that if I are alkylated at much lower temperature using a still more effective reagent, the isolation of III could be possible. Thus, the alkyaltion of I was carried out using  , $\overset{-}{S}bCl_6$ (IV) which had been proved to be more reactive alkylating agent[3] than $Et_3\overset{+}{O}$, $\overset{-}{B}F_4$.

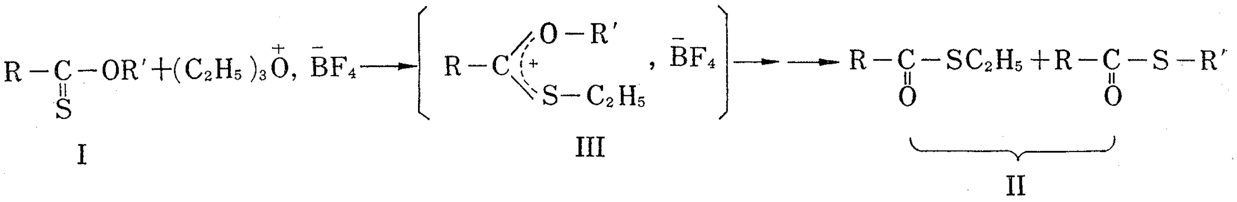


Chart 1

The reaction of ethyl thionbenzoate (V) with a molar equivalent of IV at room temperature was studied at first. The solution of IV and V in dichloroethane was allowed to come to room temperature and stand overnight at this temperature. The product isolated was found to be benzoyl chloride (74%). The mechanism will be discussed later.

Then, the alkylation was carried out at 0°. An equimolar mixture of IV and ethyl thionobenzoate (V) in dichloroethane was stirred at this temperature and the progress of the reaction was checked by thin layer chromatography. The spot due to V became almost undetectable within 3 hr. When n-hexane was added to this solution, a semi-solid precipitated out. From

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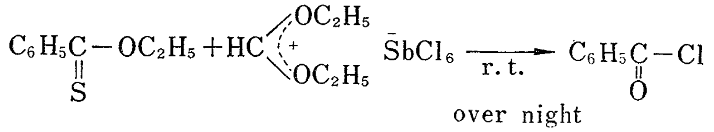
[1] Part IV: T. Oishi, M. Mori, and Y. Ban, *Tetrahedron Letters*, **1971**, 1777.

[2] Location: *Kita-12, Nishi-6, Sapporo.*

[3] S. Kabuss, *Angew. Chem. Intern. Ed. Engl.*, **5**, 675 (1966); T. Oishi, K. Kamata, and Y. Ban, *Chem. Commun.*, **1970**, 777.



$$C_6H_5\underset{\underset{S}{\|}}{C}-OC_2H_5 + HC\overset{+}{\diagup\!\!\diagdown}\begin{matrix}OC_2H_5\\OC_2H_5\end{matrix}\ \bar{S}bCl_6 \xrightarrow[\text{over night}]{\text{r.t.}} C_6H_5\underset{\underset{O}{\|}}{C}-Cl$$

V IV r.t. = room temperature

Chart 2

the n-hexane layer, there was obtained a mixture of esters, which weighed one fourth of the thiono ester (V) used. The structure of these esters and their relative ratios (ethyl thionobenzoate (V): ethyl benzoate (VI): ethyl thiobenzoate (VII)=1: 1: 0.5) were determined by the analysis of the nuclear magnetic resonance (NMR) spectra. The thiol ester (VII) must be formed by the same mechanism as described in the $(C_2H_5)_3\overset{+}{O}$, $\overset{-}{B}F_4$-catalysed conversion of thion esters to thiol esters,[1] and the ethyl benzoate (VI), by the hydrolysis of the S-alkylated species (VIII).[4] The semi-solid substance precipitated by the addition of *n*-hexane is suspected to contain the salt (VIII) as a main component along with a small amount of the unreacted reagent (IV). This fraction was dissolved in dichloroethane and stirred for 3 hr at 50° (bath temp.) to examine the thermal stability of VIII. After being cooled, the solvent was washed with water, dried and evaporated to give a black oil which again digested with *n*-hexane. An yellow oil was obtained from the *n*-hexane layer in good yield (calcd. from the thiono ester which was converted to the salt (VIII)). The component of this oil was found to be a 1: 1 mixture of benzoyl chloride and ethyl benzoate from physicochemical data but none of the thiol ester (VII) could be detected. Only a small amount of $(C_2H_5)_3\overset{+}{S}$, $\overset{-}{S}bCl_6$ (IX) was obtained from the *n*-hexane insoluble intractable tar. The significance of this finding will be disccussed in the subsequent paper[5] in connection with the character of VIII.

The fact that the salt which was precipitated by the addition of *n*-hexane and freed from any *n*-hexane soluble compounds generated ethyl benzoate on hydrolysis may be regarded as a strong evidence that the desired salt (VIII) was formed indeed. Moreover, it can be suggested that VIII is fairly stable in the absence of the substrate but gradually decompose into benzoyl chloride on heating. The liberated $SbCl_5$ is suspected to be playing an important role in this conversion. In fact, benzoyl cholride was obtained in good yield when ethyl thiobenzoate (VII) was treated with a molar equivalent of $SbCl_5$, which verified the above assumption. The mechanism of this conversion can be considered as shown in Chart 3. In an earlier part of this report, it was noted that benzoyl chloride was obtained when thiono ester (V) was allowed to stand overnight with the reagent (IV) at room temperature (Chart 2). This finding could be understood by considering the same mechanism noted here.

Then, the reactivity of the salt (VIII) toward ether was examined. The salt (VIII) obtained in the same way as described above was dissolved in a mixture of CH_2Cl_2 and ether, and the whole was refluxed for 3 hr. A white crystalline product separated out from the brownish-red solution. The solid was collected and purified by chromatography to give $(C_2H_5)_3\overset{+}{S}$, $\overset{-}{S}bCl_6$ (IX) in the yield of 24.5%. From the filtrate, a mixture of ethyl benzoate (VI) and ethyl thiobenzoate (VII) was obtained in a relative ratio of 2.7: 1 along with benzoyl chloride. The mechanism of this reaction may be considered as delineated in Chart 4. The evidence for this mechanism will be presented in the successive paper.[5] Anyway, in contrast with the above experiment, the sulfonium salt (IX) was obtained in a moderate yield when VIII was heated in the presence of ether. If $(C_2H_5)_2S$ is used as a substrate, the attack of $(C_2H_5)_2S$ on VIII may occur readily yielding the thiol ester (VII) and the sulfonium

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[4] *cf.* S.G. Smith and M. O'Leary, *J. Org. Chem.*, **28**, 2825 (1963); S.G. Smith and R.J. Feld, *J. Org. Chem*, **33**, 1022 (1968).

[5] Part VI: M. Mori, Y. Ban, and T. Oishi, *Chem. Pharm. Bull.* (Tokyo), in press.

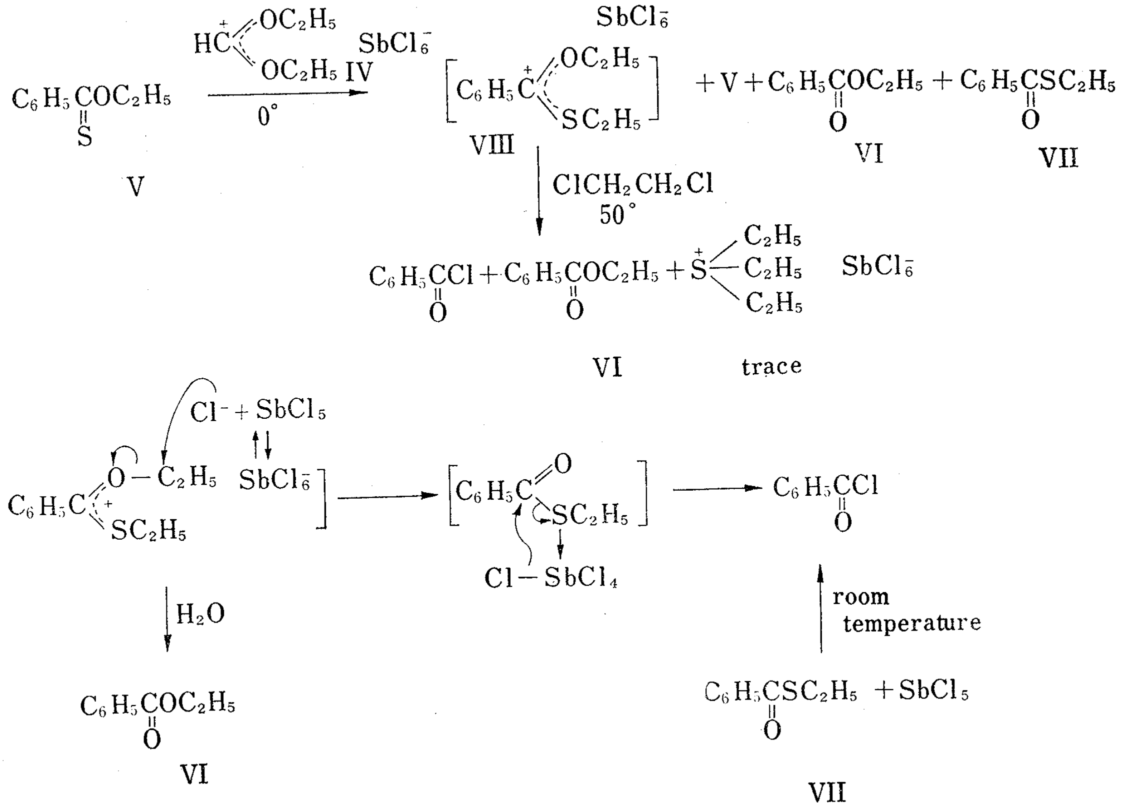

Chart 3

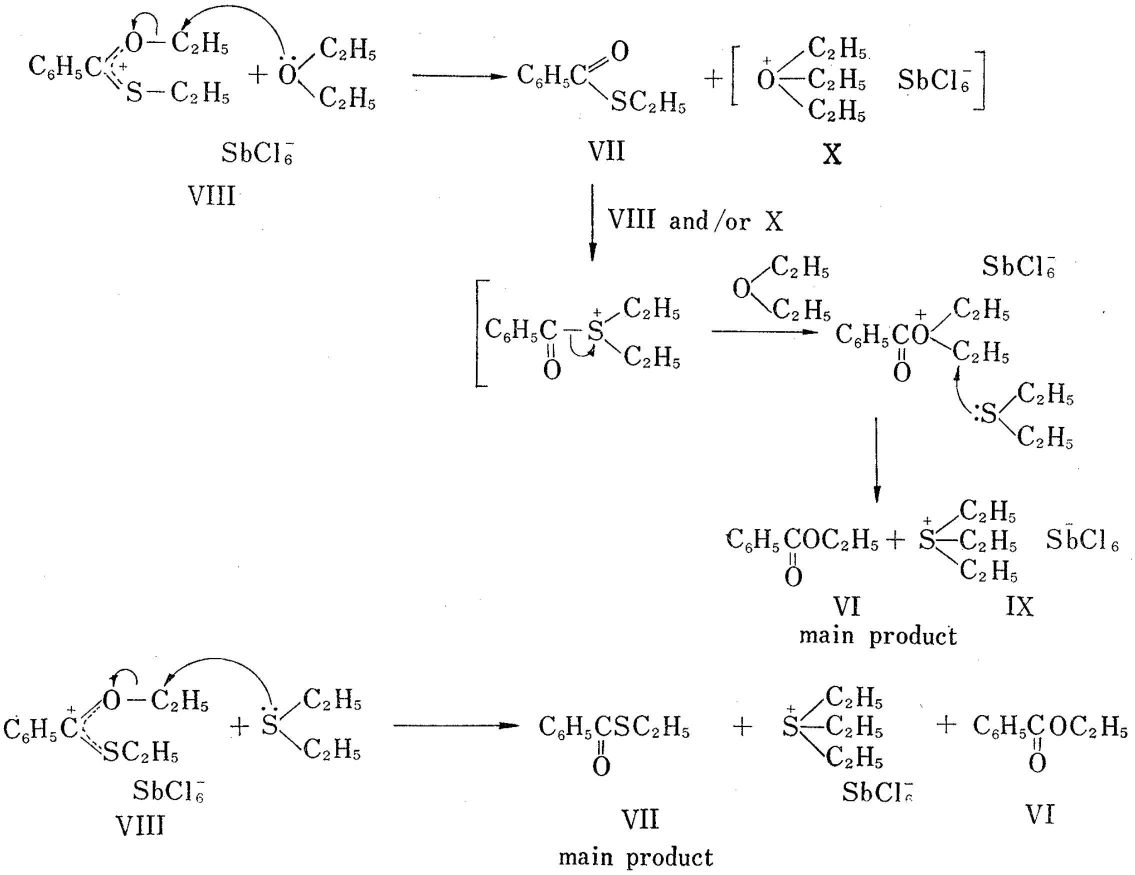

Chart 4

salt (IX) because the nucleophylicity of $(C_2H_5)_2S$ is much more stronger than that of ether. Actually, when VIII was treated with a large excess of $(C_2H_5)_2S$, ethyl thiobenzoate (VII) was obtained in good yield. However, appreciable amounts of ethyl benzoate (VI) was also obtained. The reason is not known at present but it could be assumed that water contained in $(C_2H_5)_2S$ reacted with VIII giving VI (see Chart 4).

Finally, the preparation of orthoester derivatives from the corresponding thiono esters was examined. As a model case, the ethoxyethylthiocarbonium ion (XII) prepared by the alkylation of ethyl β-phenylthionpropionate (XI) was treated with a large excess of sodium ethoxide in ethanol. If the structure of XII is correct, kinetically controlled addition of $\bar{O}C_2H_5$ anion on–$\overset{+}{C}\langle$ should take place in this case. The expected triethyl β-phenylpropionylorthoformate (XIII) was obtained in the yield of 29% after usual work-up, which firmly established that-XII was formed.

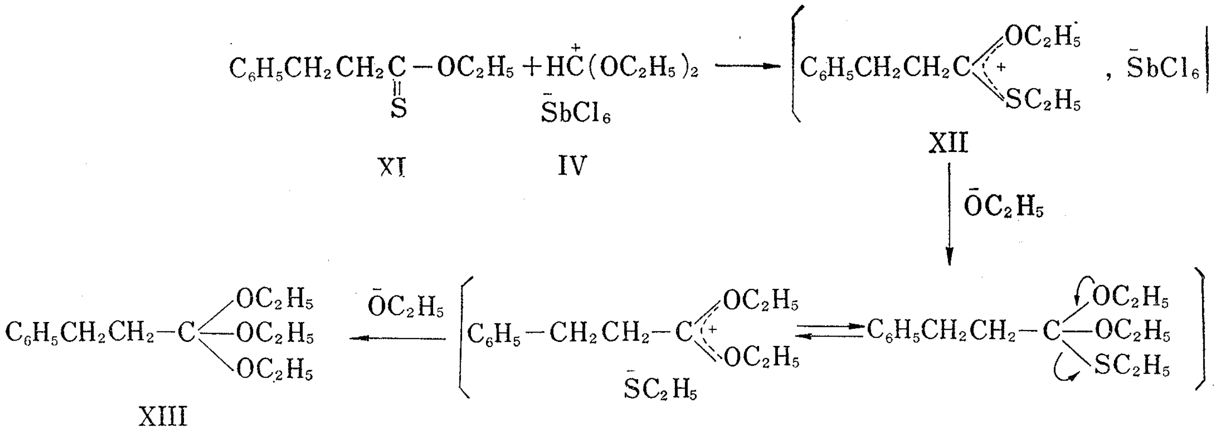

Chart 5

Experimental[6]

The Alkylation of Ethyl Thionobenzoate (V) with Diethoxycarbonium Hexachloroantimonate (IV)——To a solution of 1.67 g of IV in 2 ml of CH_2Cl_2 was added 580 mg of V at −10° and the solution was allowed to come to room temperature and stand overnight at this temperature. When CCl_4 was added, a semisolid precipitated out. The organic phase was separated and the solvent was evaporated off. The residue was dissolved in CH_2Cl_2 again and the organic phase was washed with 10% HCl, dried and evaporated to afford 396 mg of an oil, which was identified as benzoyl chloride in comparison with the authentic specimen.

The Alkylation of Ethyl Thionobenzoate (V) with IV at 0°——To a solution of 2.5 g of IV in 1.7 ml of dichloroethane was added 815 mg of V at 0° and the mixture was stirred for 3 hr at this temperature. When *n*-hexane was added to this solution, a semi-solid substance precipitated out. The *n*-hexane layer was separated by decantation and the solvent was evaporated affording 243 mg of a mixture of the esters. The analysis of NMR spectrum exhibited that they were V, VI, and VII (relative ratios; 1:1:0.5). The precipitated semi-solid substance was dissolved in 7 ml of dichloroethane and the solution was stirred for 3 hr at 50°. After the mixture had been cooled, more CH_2Cl_2 was added and the solvent was washed with water, dried and evaporated to give a black oil, which was digested with *n*-hexane. From the *n*-hexane layer, there was obtained 504 mg of an yellow oil, which was dissolved in ether. The solution was stirred with sat. $NaHCO_3$ solution for 6 hr giving 245 mg of ethyl benzoate (VI). On acidification of $NaHCO_3$ solution, there was obtained 250 mg of benzoic acid (crude). The *n*-hexane insoluble intractable tar was subjected to silica gel chromatography repeatedly. Elution with CH_2Cl_2 afforded 18 mg of a white solid, which was, after recrystallized from ethanol, identified as $(C_2H_5)_3\overset{+}{S}$, $\overset{-}{S}bCl_6$.

The Reaction of Ethyl Thiobenzoate (VII) with $SbCl_5$——To a solution of 482 mg of VII in 1 ml of dichloroethane was added 900 mg of $SbCl_5$ at −10°. After 30 min, the solution was allowed to come to

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[6] Melting points are uncorrected. All NMR spectra were measured with a Hitachi H-60 spectrometer. Chemical shifts are reported as values measured from tetramethylsilane as an internal standard.

room temperature and stand for 3 hr. To a yellow solution was added CCl_4. After the precipitated oil had been removed, the solvent was washed with 10% HCl solution and evaporated to give 384 mg of a mixture of benzoyl chloride and benzoic acid. The mixture was treated with sat. $NaHCO_3$ solution in ether. Evaporation of the organic solvent gave 211 mg of benzoyl chloride.

The Reaction of the Salt (VIII) with Ether——To a solution of 1.69 g of IV in 1 ml of dichloroethane was added 550 mg of V in 0.5 ml of dichloroethane at 0°. After being stirred for 3 hr, *n*-hexane was added and from the *n*-hexane layer, there was obtained 143 mg of a mixture of VI and VII. The precipitated semi-solid (VIII) was dissolved in a mixture of 10 ml of dichloroethane and 5 ml of ether and the whole was refluxed for 3 hr. A white crystalline solid was washed with ether to give 403 mg of crystalline material, which was subjected to silica gel chromatography. Elution with 2% C_2H_5OH–CH_2Cl_2 gave 290 mg of $(C_2H_5)_3\overset{+}{S}$, $\overset{-}{S}bCl_6$ (24.5%) of mp 214—215° (after recrystallization with C_2H_5OH). *Anal.* Calcd. for C_6H_{15}-$SSbCl_6$: C, 15.88; H, 3.33; S, 7.07; Cl, 46.89. Found: C, 15.91; H, 3.41; S, 7.10; Cl, 46.81. NMR (in $CDCl_3$) δ: 3.35 (2H, quartet, $-SC\underline{H}_2CH_3$), 1.5 (3H, triplet, $-SCH_2C\underline{H}_3$). From the ether solution, there was obtained 214 mg of a mixture of VI and VII in a relative ratio of 2.7:1.

The Reaction of the Salt (VIII) with $(CH_2CH_3)_2S$——A mixture of 170 mg of V and 511 mg of IV was treated as described above. The *n*-hexane soluble oil (57 mg) was discarded and the insoluble semi-solid was treated with 900 mg of $(CH_2CH_3)_2S$ and allowed to stand for 5 hr at room temperature. CCl_4 was added and after the precipitated semi-solid had been removed, the solvent was evaporated to give 132 mg of a mixture of VI and VII in a relative ratio of 2:1 (based on gas chromatographic analysis). The precipitated substance was dissolved in CH_2Cl_2. On addition of CCl_4, deposited 640 mg of crude $(CH_2CH_3)_3\overset{+}{S}$, $\overset{-}{S}bCl_6$, the structure of which was identified in comparison with the authentic specimen.

The Synthesis of Orthoester Derivative (XIII) from Ethyl β-Phenylthionopropionate (XI)——To a solution of 2.5 g of IV in 2 ml of CH_2Cl_2 was added 1.0 g of XI at −17°. The starting material (XI) was almost consumed within 1 hr at 0°. To this solution was added ethanolic CH_3CH_2ONa which had been prepared from 1.3 g of Na and 50 ml of ethanol. The turbid solution was allowed to stand for 3 hr at room temperature. The precipitates were removed centrifugally and the solvent was evaporated. The residue was treated with ether and the ether soluble portion was distilled under reduced pressure to give 380 mg of a colorless oil of XIII, bp 112° (12 mmHg). IR: No absorption was observed in carbonyl region. NMR (in $CDCl_3$) δ: 7.07 (5H, singlet, $C_6\underline{H}_5CH_2-$), 3.48 (6H, quartet, $-OC\underline{H}_2CH_3$), 1.7—2.8 (4H, multiplet, $C_6H_5C\underline{H}_2C\underline{H}_2-$), 1.14 (9H, triplet, $-OCH_2C\underline{H}_3$).