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Reaction of Trichloromethyl Anion with 9-Thiofluorenone *S*-Oxide (Fluorenylidenesulfine)

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The reactions of 9-thiofluorenone *S*-oxide (fluorenylidenesulfine, 1) under a variety of dichlorocarbene-generating conditions have been studied. In the case of the "neutral" generation conditions, *i.e.*, trichloroacetate or phenyl(bromodichloromethyl)mercury thermolyses, 9-dichloromethylenefluorene (2) is produced in high yield, whereas methods of carbene generation involving strong bases were found to be inapplicable because of the extreme rapidity of the reaction of 1 with nucleophiles. Attempted halogen-metal interchange between bromotrichloromethane and *n*-butyllithium was shown to yield very little trichloromethyl anion.

Addition of carbenes to the carbon-sulfur double bond of a sulfine is a possible method for the preparation of another class of noval organosulfur compounds, the episulfoxides.[2] Since sulfines are themselves photoactive,[4] and since they cycloadd to diazo compounds[5,6] in the dark, the common carbene-generating procedures involving the photolysis, thermolysis, or catalytic decomposition of diazo compounds cannot be used. Methods for the generation of dihalocarbenes are not photolytic processes, nor do they involve reagents which are likely to react directly with sulfines. Therefore, we set out to systematically study the reactions of 9-thiofluorenone *S*-oxide (1) with a variety of dichlorocarbene precursors.

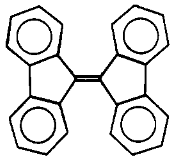
One possible complication arises from the fact that almost all of the standard methods for the generation of the dihalocarbenes proceed by first forming a trihalomethyl anion, which then decomposes to the desired carbene.[7] In view of the documented rapidity of nucleophilic attack at sulfinyl centers,[8] one must keep in mind that the C=S=O function of sulfines may react with trichloromethyl anion prior to its decomposition to dichlorocarbene.

Results

The results of experiments in which 1 was treated with trichloromethyl anion and/or dichlorocarbene, generated by a number of standard methods, are shown in Table I. In only two cases, the sodium trichloroacetate and phenyl(bromodichloromethyl)mercury thermolyses, were there extensive reactions with chlorine-containing intermediates, the major product being 9-dichloromethylenefluorene (2) in each case (reactions 1-3 in Table I). These two methods of carbene generation avoid the use of strong base.

Other standard methods employed for generating trichloromethyl anion and dichlorocarbene all require the use of strong bases. Reactions 4 and 5 (Table I) involve the use of alkoxide bases, which lead to difluorenylidene (3) formation. In these two cases the reaction of sulfine 1 with alkoxide is so rapid that formation of any halogen-containing products is virtually excluded.[9]

We felt that the reaction of 1 with alkoxide could be minimized by adding a solution of the alkoxide dropwise to a chloroform solution of 1 (reaction 6). Alkoxide should abstract hydrogen from the large molar excess of chloroform to form the trichloromethyl anion required for reaction. Surprisingly, alkoxides, even the sterically hindered *tert*-butoxide, react faster as nucleophiles with 0.05 *M* sulfine than they abstract hydrogen from solvent chloroform (12.5 *M*). Since the pK_a of chloroform is not a matter of complete agreement,[10] it is possible that these results could be explained by an unfavorable acid-base equilibrium lying to the side of the *tert*-butoxide anion. In order to be assured that deprotonation of the chloroform would be a kinetically controlled process, the procedure was repeated, this time dropping *n*-butyllithium in hexane into the chloroform solution of 1 (reaction 7). Here again, the basic reagent reacted faster with the sulfine than it did with solvent chloroform, in this case giving both 3 and 9-fluorenyl *n*-butyl sulfoxide (5). Schultz and Schlessinger[14] have shown that 1 reacts with lithium alkyls to give sulfoxides and 3.



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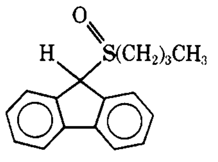

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Since bromine-metal interchange is known to be faster than proton abstraction in the reactions of bromomethanes with alkyllithiums,[15] we next attempted kinetic formation of trichloromethyl anion by halogen-metal interchange between *n*-butyllithium and $BrCCl_3$ (reaction 8). Although the large amount of unreacted 1 remaining at the end of reaction was puzzling, the comparable yields of 2 and 3 showed that the addition at sulfine sulfur and bromine-metal interchange were at least competitive. In attempts to improve the yield of 2, the $BrCCl_3$ concentration was increased from a twofold molar excess in reaction 8 to a tenfold excess in reaction 9. Finally, $BrCCl_3$ was used as solvent in reaction 10. As the initial concentration of $BrCCl_3$ increased, the amount of recovered 1 increased. With $BrCCl_3$ as solvent, all of the sulfine was recovered unchanged. In an attempt to ascertain if the $BrCCl_3$ were trapping the trichloromethyl anion formed, the reaction of 1 with sodium trichloroacetate in the presence of added $BrCCl_3$ was carried out (reaction 11). There was no effect of added $BrCCl_3$.

Discussion

One can postulate the following scheme to account for the 9-dichloromethylenefluorene (2) produced in the trichloroacetate thermolysis (Scheme I). Trichloromethyl anion adds to the sulfur atom of the sulfine in the same manner as do other nucleophilic reagents. The intermediate carbanion would be expected to be relatively stable, since it is derived from the acidic hydrocarbon fluorene and is, in addition, α to an acid-strengthening sulfinyl function. This carbanion undergoes a Ramberg-Bäcklund reaction, similar to that of trichloromethyl sulfones,[16] yielding an intermediate episulfoxide which loses sulfur monoxide to give the observed olefin product, 2.

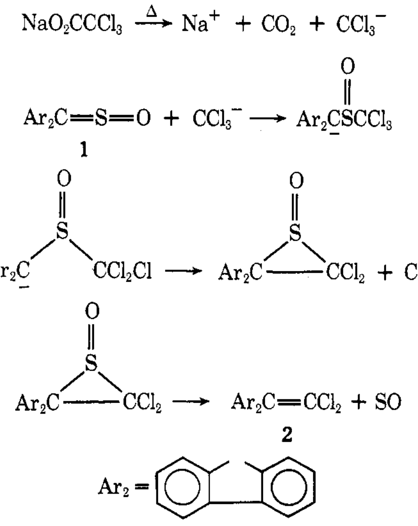
The postulation that sulfine reacts with trichloromethyl anion rather than dichlorocarbene is based on the following argument. Since 1 is a highly electron-deficient

Table I
Reactions of 1 with Carbenoid Reagents

Reaction no.	Reagent and conditions	Product yield, % 2	3	Fluorenone[a]	5	Recovered 1
1	CCl_3CO_2Na (5 equiv) in DME, reflux, 2 hr	80	0	0		0
2	$PhHgCCl_2Br$ (1 equiv) in PhH, reflux, 2 hr	63	1	0		28
3	$PhHgCCl_2Br$ (1 equiv) in PhH, 25°, 10 days	30	9	56		0
4	$CHCl_3$ (1 equiv), *t*-BuOH, Et_2O, KO-*t*-Bu, −15°	0	94	0		0
5	CCl_3CO_2Et (1 equiv), NaOMe, PhH,C_6H_{12}, −5°	6	35	24		0
6	$CHCl_3$ (solvent), *t*-BuOK, −15°	8	47	11		0
7	$CHCl_3$ (solvent), *n*-BuLi, −15°	1	18	30	20	0
8	$BrCCl_3$ (2 equiv), *n*-BuLi, Et_2O, −15°	13	17	0	0	67
9	$BrCCl_3$ (10 equiv), *n*-BuLi, Et_2O, −5°	0	0	0	0	90
10	$BrCCl_3$ (solvent), *n*-BuLi, Et_2O, −15°	0	0	0	0	100
11	CCl_3CO_2Na, $BrCCl_3$, DME, reflux, 2 hr	73	0	0		0

[a] The origin of fluorenone as a product in reactions 3, 5, 6, and 7 has not been determined. Decomposition of 1 over the long reaction time is probable in 3. In 5, 6, and 7, fluorenone likely arises from unreacted 1 on work-up. Having shown that those conditions were not conducive to achieving our goal, we did not further pursue the origin of the fluorenone.

Scheme I



sulfine, one would expect that it would be more susceptible to nucleophilic attack than would the more electron-rich di(*p*-anisyl)sulfine (4). In contrast, one would expect the more electron-rich sulfine, 4, to be more susceptible to electrophilic attack, owing to the electron-donating methoxyl groups. In fact, 4 has been found to be inert to the nucleophile *tert*-butoxide.[9] Thus, one can gain insight into the electronic nature of the chlorine-containing intermediate by a comparison of the relative rates of reaction of 1 and of 4. Since 4 does not react under conditions where 1 reacts (reaction 1), one concludes that the reactive intermediate here is the nucleophilic trichloromethyl anion rather than the electrophilic dichlorocarbene.

Phenyl(bromodichloromethyl)mercury has been shown by Seyferth to decompose directly to dichlorocarbene and phenylmercuric bromide.[17] Thus, reaction of 1 with $PhHgCCl_2Br$ should give a different result than did the trichloroacetate, since trichloromethyl anion would not be involved. Surprisingly, the two experiments led to virtually the same results. Recently, it has been suggested that both carbonyls[18] and thiocarbonyls[19] may in fact react directly with $PhHgCCl_2Br$, and that dichlorocarbene may not be involved in "carbenoid" reactions with those particular groups. We believe that this is the most likely interpretation of our data also.

Let us now turn our attention to the attempts to generate trichloromethyl anion kinetically. Reaction 7 shows that *n*-butyllithium reacts faster with 1 than it removes a proton from chloroform. This might at first seem surprising, but it should be recalled that even such acidic hydrocarbons as triphenylmethane[20] and fluorene[21] are deprotonated by *n*-butyllithium very slowly. Considering that the intramolecular competition of carbonyl addition and proton abstraction represented by the treatment of a simple ketone with a lithium reagent in most cases gives carbonyl addition, and considering that, in a recent review,[22] Kice suggests that, in general, sulfinyl surfur reacts with a given nucleophile about 10^4 times faster than does carbonyl carbon, it is not surprising that sulfine 1 is an efficient trap of *n*-butyllithium even in the presence of a solvent with an acidic hydrogen.

The high recovery of 1 from reactions 8–10 show that *n*-butyllithium reacts faster with $BrCCl_3$ than it does with 1. The low yield of 2 in reaction 8 and its absence in reactions 9 and 10 can be explained in two alternative ways. Either the trichloromethyl anion produced in the halogen-metal interchange reacts with solvent before it can react with 1, or no trichloromethyl anion is produced at all. In order to distinguish between these two possibilities, trichloromethyl anion was generated *via* trichloroacetate decomposition in the presence of $BrCCl_3$ (reaction 11). There was no reaction of the added $BrCCl_3$ with trichloromethyl anion. Therefore, the lack of 2 among the reaction products must be attributed to the fact that trichloromethyl anion constitutes only a small fraction of the initially formed intermediates from the reaction of $BrCCl_3$ with *n*-butyllithium. We believe that the reaction of *n*-butyllithium with $BrCCl_3$ takes place *via* the now generally accepted radical-pair mechanism that has been proposed for other alkyllithium-alkyl halide reactions.[23-26] Products expected of such a mechanism, in particular 1-butene, chloroform, and 1,1,1-trichloropentane, have been tentatively identified.[27]

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer 237 spectrophotometer. Nmr spectra were run on a Varian A-60A spectrometer using tetramethylsilane as an internal standard. Melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Combustion analysis were performed by M-H-W Laboratories, Garden City, Mich. Sodium trichloroacetate was purchased from City Chemical Corp. and dried at 90° in a vacuum oven for 24 hr before use. $BrCCl_3$ (Matheson Coleman and Bell) was used without purification. Commercial *n*-butyllithium (Foote Mineral Co.) was titrated by the method of Watson and Eastham[28] just prior to use. 9-Thiofluorenone *S*-oxide (1) was prepared by the method of Zwanenburg, Thijs, and Strating,[29] as was di(*p*-anisyl)sulfine (4). 9-Dichloromethylenefluorene (2), pale yellow crystals, mp 131–132° (lit.[30] mp 132–133°), and difluorenylidene (3), red needles, mp 187–188° (lit.[31] mp 186–187.5°), were identified by their melting points and colors. Their nmr and ir spectra were consistent with their structures.

Reaction of 1 with Sodium Trichloroacetate (Reaction 1). To a solution of 1 (1 g, 4.7 mmol) in 100 ml of dry dimethoxyethane was added dry sodium trichloroacetate (4.4 g, 23.8 mmol). The reaction mixture was refluxed for 2.5 hr and filtered, and the solvent was evaporated. Chromatography over silica gel afforded 0.93 g (80%) of **2**.

Reaction of 1 with Phenyl(bromodichloromethyl)mercury (Reaction 2). To 150 ml of dry benzene was added **1** (2.1 g, 10 mmol) and $PhHgCCl_2Br$[32] (4.4 g, 10 mmol) and the mixture was refluxed for 2 hr. The reaction mixture was cooled and 3.2 g (90%) of PhHgBr was removed by filtration. The filtrate was evaporated and the residue was chromatographed over silica gel, giving 1.51 g (63%) of **2**, 0.02 g (1%) of **3**, and 0.59 g (28%) of recovered **1**.

Reaction of 1 with Phenyl(bromodichloromethyl)mercury at 25° (Reaction 3). Reaction 2 was repeated except that the reaction mixture was allowed to stir under an inert atmosphere for 10 days. After filtration and evaporation of the solvent, chromatography over silica gel afforded 0.73 g (30%) of **2**, 0.14 g (9%) of **3**, and 1.0 g (56%) of fluorenone.

Reaction of 1 with Chloroform and Potassium *tert*-Butoxide (Reaction 4). To a freshly prepared solution of KO-*t*-Bu (10 mmol) in *t*-BuOH-Et_2O (50 ml, 1:1) under an inert atmosphere was added **1** (2.1 g, 10 mmol) in one portion, while maintaining a temperature of −15°. Dry $CHCl_3$ (1.2 g, 10 mmol) was then added dropwise. The reaction mixture was allowed to warm to room temperature, whereupon it was poured into water, extracted with $CHCl_3$, and dried over $MgSO_4$. Evaporation of the solvent afforded 1.53 g (93%) of red **3**.

Reaction of 1 with Ethyl Trichloroacetate and Sodium Methoxide (Reaction 5). To a solution of **1** (2.1 g, 10 mmol) in 100 ml of dry benzene-hexane (1:1) cooled to −5° was added under N_2 dry NaOMe (1.1 g, 20 mmol) quickly followed by CCl_3CO_2Et (3.8 g, 20 mmol). The reaction mixture was allowed to warm to room temperature and stirred overnight. It was then poured into water and extracted with benzene. Evaporation of the solvent and chromatography over alumina afforded 0.14 g (6%) of **2**, 0.58 g (35%) of **3**, and 0.43 g (24%) of fluorenone.

Reaction of 1 with Chloroform and Potassium *tert*-Butoxide. Inverse Addition (Reaction 6). To a solution of **1** (2.1 g, 10 mmol) in 200 ml of dry $CHCl_3$ cooled to −15° under N_2 was added dropwise a solution of KO-*t*-Bu (10 mmol) in 10 ml of *t*-BuOH. The reaction mixture was allowed to warm to room temperature, poured into water, and extracted with $CHCl_3$. After drying over $MgSO_4$, the solvent was evaporated and the residue was chromatographed over alumina, giving 0.12 g (8%) of **2**, 0.77 g (47%) of **3**, and 0.2 g (11%) of fluorenone.

Reaction of 1 with Chloroform and *n*-Butyllithium (Reaction 7). To a solution of **1** (2.4 g, 11.3 mmol) in 200 ml of dry $CHCl_3$ under N_2 cooled to −15° was added dropwise 7.9 ml of a 1.46 *M* solution of *n*-BuLi in hexane. The reaction mixture was allowed to warm to room temperature, poured into water, and extracted with $CHCl_3$. After drying over $MgSO_4$, the solvent was evaporated and the residue was chromatographed over alumina, giving 0.03 g (1%) of **2**, 0.33 g (18%) of **3**, 0.62 g (30%) of fluorenone, and 0.6 g (20%) of a viscous oil identified as 9-fluorenyl *n*-butyl sulfoxide (**5**) by comparison to a sample prepared by oxidation of the sulfide.

9-Fluorenyl *n*-Butyl Sulfoxide (5). **5** was prepared by a modification of the method of Leonard and Johnson.[33] Thus, to a solution of $NaIO_4$ (2.24 g, 10.5 mmol) in 30 ml of water, 30 ml of acetone, and 15 ml of methanol was added 9-fluorenyl *n*-butyl sulfide[34] (2.54 g, 10 mmol). The reaction mixture was allowed to stir at room temperature for 2 days, extracted with $CHCl_3$, and dried over $MgSO_4$, and the solvent was evaporated. Chromatography over alumina afforded, besides small amounts of starting sulfide and fluorenone, 2.51 g (93%) of the desired sulfoxide as an oil which crystallized after standing at −25° for several days. An analytical sample was obtained by recrystallization from hexane by cooling in increments to −78° to give white crystals: mp 48–49°; ir 1025 cm^{-1} (sulfoxide); nmr ($CDCl_3$) δ 0.5–2.0 (broad multiplet, 9 H), 5.3 (s, 1 H), 7.2–8.1 (broad multiplet, 8 H).

Anal. Calcd for $C_{17}H_{18}OS$: C, 75.52; H, 6.71; S, 11.86. Found: C, 75.31; H, 6.69; S, 11.70.

Reaction of 1 with Bromotrichloromethane (2 Equiv) and *n*-Butyllithium (Reaction 8). To a solution of **1** (2.1 g, 10 mmol) in 200 ml of dry Et_2O containing $BrCCl_3$ (3.96 g, 20 mmol) cooled under N_2 to −15° was added dropwise 16.4 ml of a 1.22 *M* solution of *n*-BuLi in hexane. The reaction mixture was allowed to warm to room temperature, poured into water, and extracted with Et_2O. After drying over $MgSO_4$, the solvent was evaporated and the residue was chromatographed over silica gel, giving 0.33 g (13%) of **2**, 0.28 g (17%) of **3**, and 1.41 g (67%) of recovered **1**.

Reaction of 1 with Bromotrichloromethane (10 Equiv) and *n*-Butyllithium (Reaction 9). To a solution of **1** (2.1 g, 10 mmol) in 200 ml of dry Et_2O containing $BrCCl_3$ (19.8 g, 100 mmol) cooled under N_2 to −15° was added dropwise 12.3 ml of a 1.22 *M* solution of *n*-BuLi in hexane. The reaction mixture was allowed to warm to room temperature, poured into water, and extracted with Et_2O. After drying over $MgSO_4$, the solvent was evaporated; the residue was chromatographed over silica gel, giving 1.91 g (90%) of recovered **1**.

Reaction of 1 with Bromotrichloromethane (Solvent) and *n*-Butyllithium (Reaction 10). To a solution of **1** (2.1 g, 10 mmol) in 60 g of $BrCCl_3$ cooled to −15° under N_2 was added dropwise 10.6 ml of a 1.41 *M* solution of *n*-BuLi in hexane. The reaction mixture was allowed to warm to room temperature, poured into water, and extracted with $CHCl_3$. After drying over $MgSO_4$, the solvent was evaporated and the residue was chromatographed over silica gel, giving quantitative recovery of **1**.

Reaction of 1 with Sodium Trichloroacetate in the Presence of Bromotrichloromethane (Reaction 11). Reaction 1 was repeated except that $BrCCl_3$ (4.73 g, 23.8 mmol) was added to the reaction mixture. After filtration and evaporation of the solvent, chromatography over silica gel afforded 0.85 g (73%) of **2**.

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Registry No. 1, 4440-32-8; **5**, 42579-21-5; sodium trichloroacetate, 650-51-1; phenyl(bromodichloromethyl)mercury, 3294-58-4; chloroform, 67-66-3; potassium *tert*-butoxide, 865-47-4; ethyl trichloroacetate, 515-84-4; sodium methoxide, 124-41-4; 9-fluorenyl *n*-butyl sulfide, 22010-50-0; bromotrichloromethane, 75-62-7.

References and Notes

(1) (a) Texas Christian University Research Foundation Fellow, 1969–1970; Robert A. Welch Foundation Predoctoral Fellow, 1970–1972. (b) Robert A. Welch Foundation Undergraduate Scholar, 1969.

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(9) For example, the conversion of **1** into **3** is complete in less than 1 min after mixing even at −15° in the presence of KO-*t*-Bu. A complete account of the reactions of aromatic sulfines with alkoxides will be published in the near future.

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Oxygenation of Thiophenes with Diisopropyl Peroxydicarbonate–Cupric Chloride[1]

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The reaction of thiophene and certain derivatives (2-methyl, 2-chloro, 2-bromo, 2-nitro, 2,5-dichloro, and 2,5-dibromo) with diisopropyl peroxydicarbonate in acetonitrile was investigated in the presence and absence of cupric chloride catalyst. In catalyzed reactions, thienyl isopropyl carbonates were formed in 41–74% yields in most cases, along with by-products. Without cupric chloride, different product distributions were generally observed. The mechanistic aspects are discussed. Dealkylation and decarboxylation of the esters gave hydroxythiophenes whose tautomeric nature was studied by nmr spectroscopy.

Oxygenated thiophenes[4,5] have been prepared by various methods which can be divided conveniently into two main categories: (1) ring closure of suitable open-chain compounds,[4] *e.g.*, synthesis of 5-methyl-2-hydroxythiophene from levulinic acid and phosphorus sulfides,[5b,6] and (2) replacement of a substituent on the thiophene nucleus.[7] The displacement reaction is illustrated by conversion of 2-iodothiophene to the corresponding methoxy derivative by treatment with sodium methoxide and cupric oxide.[8] Syntheses by way of organometallic compounds have proved useful,[9] as in the formation of 2-*tert*-butoxythiophene from 2-thienylmagnesium bromide and *tert*-butyl perbenzoate.[10] Another technique entails oxidation of thiopheneboronic acids.[11]

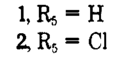
Direct oxygenation (replacement of nuclear hydrogen by an oxygen function) has been noted in a few systems.[12,13] The most pertinent prior literature describes peroxide decomposition in thiophene: 2-thenoyl peroxide gave 2-thienyl-2-thenoate (30%);[14a] 3-thenoyl peroxide produced 2-thienyl-3-thenoate (13%);[15] and benzoyl peroxide afforded 2-thienyl benzoate[14b] (15%).[14a]

The tautomeric nature of hydroxythiophenes is evidenced in part by their dual reactivity as phenols and active methylene compounds.[9a,16] Some authors made qualitative estimates of the position of equilibrium from ir data,[9d] but since about 1960 nmr has been used in a quantative approach.[9f-i,11,17]

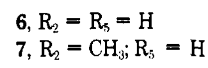
Recently it was shown that aromatic comounds can be oxygenated with diisopropyl peroxydicarbonate (IPP) and cupric chloride in acetonitrile.[18-20] The present work was undertaken to determine the applicability of this technique to compounds in the thiophene series. Principal attention was devoted to the mechanistic and synthetic features. Hydroxythiophenes were obtained from the ester products by dealkylation and decarboxylation.

Results and Discussion

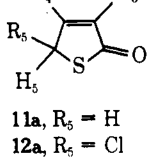
Oxygenation of Thiophenes. Thiophene. Catalytic oxygenation of thiophene with diisopropyl peroxydicarbonate (IPP) resulted in a 67% yield of 2-thienyl isopropyl carbonate (**1**) and 3% of the 3 isomer (**6**), along with small amounts of 5-chloro-2-thienyl isopropyl carbonate (**2**), 2,2′-bithienyl (**17**), 2,5-dihydroxythiophene bis(isopropyl carbonate) (**5**), and 2-isopropoxy-5-chlorothiophene (Table I). A thiophene:IPP:cupric chloride ratio of 10:1:0.3 in acetonitrile at 60° was found to give the best yield of major product (Table II). In general, similar results were observed when the temperature was reduced from 60° to 30°, but extended periods of time were required. A kinetic experiment revealed that reaction was substantially complete within the first 10 min at 60°, in agreement with the observation that essentially all gas evolution took place during that time. When the amount of solvent was halved, the yield of carbonate decreased to 55%, and to 50% when solvent was omitted. This is in sharp contrast to the behavior of toluene as the aromatic component, which gave only 7% of the corresponding ester in the neat system.[21] A possible explanation for the difference in behavior is that cupric chloride is 125 times more soluble in thiophene than in toluene at 60°. In view of the fact that benzene is cleanly oxygenated,[19] the number of by-products observed in the reaction with thiophene is noteworthy.



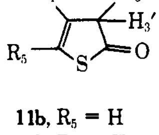
1, R_5 = H
2, R_5 = Cl
3, R_5 = Br
4, R_5 = CH_3
5, R_5 = $OCO_2CH(CH_3)_2$



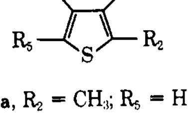
6, R_2 = R_5 = H
7, R_2 = CH_3; R_5 = H
8, R_2 = R_5 = Cl
9, R_2 = R_5 = Br
10, R_2 = Br; R_5 = Cl or R_2 = Cl; R_5 = Br



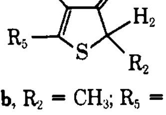
11a, R_5 = H
12a, R_5 = Cl
13a, R_5 = Br
14a, R_5 = CH_3



11b, R_5 = H
12b, R_5 = Cl
13b, R_5 = Br
14b, R_5 = CH_3



15a, R_2 = CH_3; R_5 = H
16a, R_2 = R_5 = Cl



15b, R_2 = CH_3; R_5 = H
16b, R_2 = R_5 = Cl