Syntheses of Substituted Phenyl-2-thienyliodonium Halides and Their Pyrolysis Reactions

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Various substituted phenyl-2-thienyliodonium halides were prepared by the reaction of thiophene with substituted phenyliodoso acetates in acetic anhydride–concentrated sulfuric acid. In the pyrolysis reaction of substituted phenyl-2-thienyliodonium chlorides it was found that the chloride ion selectively attacked the 1-carbon of the phenyl group. The product ratios in the pyrolysis reaction of substituted phenyl-2-thienyliodonium bromides can be explained on the basis of a bimolecular aromatic nucleophilic substitution except for *p*-chlorophenyl-2-thienyliodonium bromide. In the case of *p*-chloro substituted derivative an interesting effect of *p*-chloro group was observed. The pyrolysis reaction of substituted phenyl-2-thienyliodonium iodides gave substituted phenyl iodides and 2-iodothiophene. The solution reaction of phenyl-2-thienyliodonium halides in *N,N*-dimethylformamide gave halobenzene and 2-iodothiophene. These results suggest that the reaction proceeds *via* an interaction between the halide ion and the phenyl group in a trigonal-bipyramidal structure.

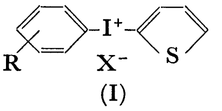
Many reactions of diaryliodonium salts with various nucleophiles have been studied.[1] However, scarcely any reactions of phenyl-2-thienyliodonium salts containing the thienyl group as a ligand of iodonium salts have been reported except for the electroreduction and the nucleophilic displacement with sulfite ion in water by Beringer and his co-workers.[2] They reported that the replacement of the phenyl group in diphenyliodonium cation by the 2-thienyl group increases the ease of electroreduction and the susceptibility to nucleophilic attack. When phenyl-2-thienyliodonium cation was cleaved by sulfite ion in water, the ratio of attack on the thiophene ring to that on the benzene ring was 2: 1.

$$\text{Ph-I}^+\text{-Th} + \text{SO}_3^{2-} \longrightarrow \left\{\begin{array}{l}\text{PhSO}_3^- + \text{ThI}\\ \text{ThSO}_3^- + \text{PhI}\end{array}\right. \qquad (1)$$

They attributed such a result to the predominant resonance interaction between the iodine and the phenyl ring or to the difference in electronegativity between the phenyl and 2-thienyl groups.

We have investigated the synthesis of polymeric iodonium salt (PSJ$^+$X$^-$) containing the polystyryl structure as one of the ligands and the possibility of their application to synthetic chemistry.[3]

Various substituted phenyl-2-thienyliodonium halides (I) were synthesized and allowed to react in the molten state for investigation of the difference in reactivity between the substituted phenyl and thienyl groups.



(I)

Results and Discussion

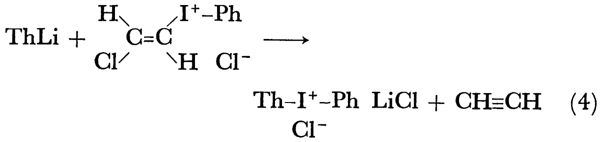
Syntheses of Substituted Phenyl-2-thienyliodonium Halides. Phenyl-2-thienyliodonium salts can be synthesized in three ways. The first method is the reaction of iodosobenzene with thiophene in acetic acid–acetic anhydride–sulfuric acid (Yield 49%).[2]

$$\text{PhIO} + \text{ThH} + \text{H}_2\text{SO}_4 + \text{Ac}_2\text{O} \longrightarrow \text{Ph-I}^+\text{-Th} + \text{HSO}_4^- + 2\text{AcOH} \qquad (2)$$

The second method is the reaction of iodosobenzene diacetate with thiophene in acetic acid–acetic anhydride–trifluoroacetic acid (Yield 92%).[2]

$$\text{PhI(OAc)}_2 + \text{ThH} + \text{CF}_3\text{COOH} \longrightarrow \text{Ph-I}^+\text{-Th} + \text{CF}_3\text{COO}^- + 2\text{AcOH} \qquad (3)$$

The third is the reaction of 2-thienyllithium with phenyl(*trans*-chlorovinyl)iodonium chloride in toluene giving phenyl-2-thienyliodonium salt in 38% yield.[4]



$$\text{ThLi} + \text{(H)(Cl)C=C(I}^+\text{-Ph)(H)}\ \text{Cl}^- \longrightarrow \underset{\text{Cl}^-}{\text{Th-I}^+\text{-Ph}}\ \text{LiCl} + \text{CH}\equiv\text{CH} \qquad (4)$$

We prepared the substituted phenyl-2-thienyliodonium salts by modifying the reaction (3), *viz.*, the substituted phenyliodoso diacetate was allowed to react in the presence of concentrated sulfuric acid in acetic anhydride.

$$\text{ArI(OAc)}_2 + \text{ThH} + \text{H}_2\text{SO}_4 \longrightarrow \underset{\text{HSO}_4^-}{\text{Ar-I}^+\text{-Th}} + 2\text{AcOH} \qquad (5)$$

The desired iodonium halides were precipitated by adding the aqueous solution of corresponding metal halides to the reaction mixture obtained. The results are summarized in Table 1. The structures were confirmed by elemental analysis and infrared spectrum. The solubility in polar solvents such as water, methanol, and *N,N*-dimethylformamide (DMF) decreases in the order, chloride>bromide>iodide.

Pyrolysis Reactions of Iodonium Halides in the Molten State. There are two paths as shown below in the nucleophilic displacement of substituted diphenyliodonium salt in the solution.

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[1] F. M. Beringer and R. A. Falk, *J. Chem. Soc.*, **1964**, 4442; O. A. Ptitsyana, G. G. Lyatiev, and O. A. Reutov, *Zh. Org. Khim.*, **6**, 1353 (1970); *Chem. Abstr.*, **73**, 87551j (1970).

[2] F. M. Beringer, H. E. Bachofner, R. A. Falk, and M. Leff, *J. Amer. Chem. Soc.*, **80**, 4279 (1958).

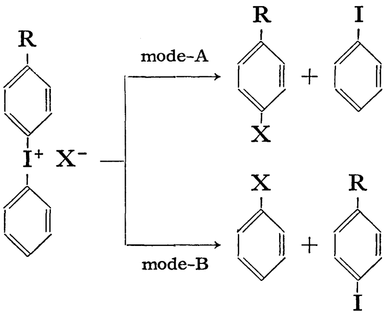
[3] Y. Yamada and M. Okawara, *Markomol. Chem.*, **152**, 153 (1972); *ibid.*, **152**, 163 (1972).

[4] F. M. Beringer and R. A. Nathan, *J. Org. Chem.*, **35**, 2095 (1970).

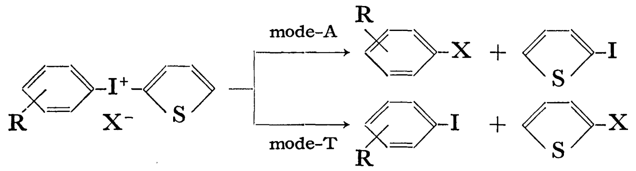
TABLE 1. PREPARATION OF SUBSTITUTED PHENYL-2-THIENYLIODONIUM HALIDES

Substituted group R–	Counter anion X^-	Mp (°C)	Yield (%)	Elemental analysis (%) Found C	H	Calcd C	H
p-MeO[d]	Br^-	180—185	38.4	33.11	2.46	33.27	2.54
	I^-	150—155	39.4	29.67	2.19	29.75	2.27
p-Me[d]	Br^-	180—185	58.3	34.50	2.78	34.67	2.65
	I^-	138—143	58.3	30.46	2.32	30.86	2.35
m-Me	Cl^-	210—213	71.5	38.85	3.14	39.25	2.99
	Br^-	215—217	98.0	34.44	2.64	34.67	2.65
	I^-	155—157	98.0	30.31	2.44	30.86	2.35
p-Cl	Cl^-	170—177	55.4	33.13	1.94	33.64	1.98
	Br^-	180—185	57.1	30.08	1.68	29.92	1.76
	I^-	145—148	58.5	26.76	1.45	26.78	1.57
m-Cl	Cl^-	195—210	20.6	33.53	2.13	33.63	1.98
	Br^-	185—187	28.5	29.59	1.69	29.92	1.76
	I^-	135—143	48.6	26.58	1.33	26.78	1.57
H	Cl^-	220—225[a]	—	35.73	2.62	37.23	2.49
	Br^-	200—205[b]	20.6	32.80	2.27	32.72	2.20
	I^-	142—144[c]	—	29.16	1.80	29.00	1.94
	ClO_4^-	157—162	64.0	31.21	1.97	31.07	2.09

a) Lit. gives 217—225°C.
b) Lit. gives 170—174°C.
c) Lit. gives 129—132°C: F. M. Beringer, R. A. Falk, and M. Leff, *J. Amer. Chem. Soc.*, **80**, 4279 (1958).
d) The corresponding iodonium chlorides were not isolated because of their poor crystallizability.



When the substituent of phenyl group is electron-releasing, the reaction of mode-B predominates and *vice versa*, and the rate of the reaction is always faster in the latter than in the former. Similarly, there are two paths conceivable for the reaction of substituted phenyl-2-thienyliodonium salts as follows.



The results of a number of pyrolysis reactions conducted for 5 min. at 235°C are summarized in Table 2. It is clear that the product ratios show a selective nucleophilic attack of the chloride ion on the phenyl ring regardless of the effect of substituent group. However, the product ratios in the case of the iodonium bromide can be explained on the basis of a bimolecular aromatic nucleophilic substitution except for the reaction of *p*-chlorophenyl-2-thienyliodonium bromide. In the case of phenyl-2-thienyliodonium iodide substituted phenyl iodide and 2-thienyliodide alone were obtained.

TABLE 2. CLEAVAGE TENDENCY OF SUBSTITUTED PHENYL-2-THIENYLIODONIUM HALIDES

Substituted group	Counter anion	Mode-A : (mol %)	Mode-T
H	Cl^-	100	0
m-Cl	Cl^-	100	0
p-Cl	Cl^-	100	0
m-Me	Cl^-	100	0
H	Br^-	100	0
m-Cl	Br^-	100	0
p-Cl	Br^-	76.1	23.9
m-Me	Br^-	100	0
p-Me	Br^-	70.7	29.3
p-MeO	Br^-	60.0	40.0

In every case biaryl, bithienyl, and 2-thienylarene which are considered to be produced in a free radical process were not found by glc analysis. It is of interest that the pyrolysis reaction of the iodonium chloride proceeds *via* the reaction of mode-A alone.

In general, the thiophene ring is more susceptible to the nucleophilic substitution than the benzene ring.[5] As an example, it was reported that the nucleophilic substitution on 2-bromo-5-nitrothiophene was more than one hundred times faster than that on *p*-bromonitrobenzene.[6] Therefore, some factors other than electronic effect should be taken into account for the predominant reactivity of benzene ring obtained in our experiment.

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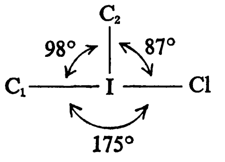
[5] L. Melander, *Arkiv Förmkem.*, **8**, 361 (1955).

[6] R. Motoyama, S. Nishimura, Y. Murakami, K. Hari, and E. Imoto, *Nippon Kagaku Zasshi*, **78**, 954 (1957).

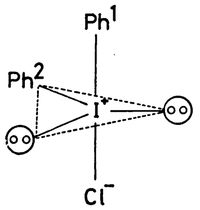
Khotsyanova has studied the crystal structure of diphenyliodonium chloride.[7] The molecular is T-shaped, containing a linear C_1 (1-carbon at one phenyl ring) –I–Cl group perpendicular to a C_2 (1-carbon at another phenyl ring) –I group as shown in II.



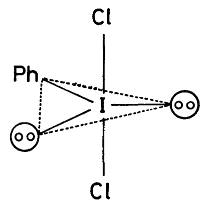
(II)

$C_1-I=C_2-I=2.08$ Å
$I-Cl=3.08$ Å

Taking into account the two lone pairs the molecule should have trigonal-bipyramidal structure (III), the one phenyl ring and two lone pairs on the equatorial position, another phenyl ring and the chloride ion at the apices.



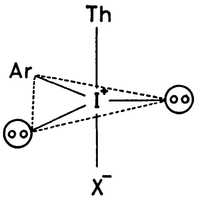
(III)



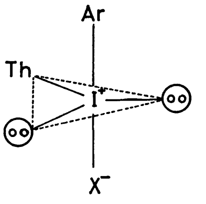
(IV)

Such a trigonal-bipyramidal structure has also been reported for the case of iodobenzene dichloride as shown in IV.[8]

In view of these facts the substituted phenyl-2-thienyliodonium halide should have a trigonal-bipyramidal structure (Va), the phenyl ring and two lone pairs on the equatorial position and the thienyl ring and halogen atom at the apices. On the basis of this assumption the reaction is considered to proceed *via* the overlap of π-orbital of the aryl group and the *p*-orbital of halide ion with concomitant cleavage of the bond between the 1-carbon of the aryl group and iodine atom. A similar type of reaction which proceeds through the orbital interaction of the halide ion and the aryl group has been reported for the pyrolysis reaction of triarylsulfonium halides.[9] If the aryl-2-thienyliodonium halide exists in a structure such as Vb, it is expected that the formation of 2-halothiophene predominates. However, hardly any 2-chlorothiophene was produced in the case of the iodonium chlorides. Furthermore, 2-bromothiophene was not produced except for *p*-chloro-, *p*-methyl-, and *p*-methoxy-substituted derivatives in the case of the iodonium bromides. It is reasonable to assume that the more electronegative thienyl ring compared to phenyl ring is located in the site opposite to the halide anion because of their electronic repulsion.[10] These results suggest a structure such as Va rather than Vb in the transition state.

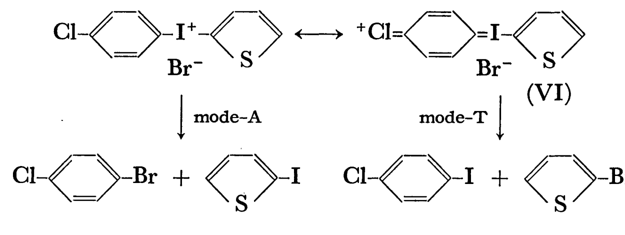


(Va)



(Vb)

The proton chemical shifts (δ-value) of substituted phenyl-2-thienyliodonium bromides are greater (0.01—0.27 ppm) than those of the corresponding chlorides.[11] Thus, the chloride ion is found to be situated in the position more closely to the iodine atom than the bromide ion (that is, the I–Cl bond occupies more covalent character in comparison with the I–Br bond,[12] and the positive charge on the iodine atom of the iodonium bromide is greater than that of the iodonium chloride. The preferred chloride-aryl coupling over bromide-aryl coupling arises since the bond between aromatic-1-carbon and iodine atom of the iodonium bromide acquires a double bond character through the resonance of the substituent as compared with that of the iodonium chloride. Thus, the reaction of mode-A is liable to occur in the case of the iodonium chlorides compared to that of mode-T by the effective orbital interaction between the aryl ring and the chloride ion. On the other hand, the bromide ion attacked not only the aryl ring (mode-A) but also the thienyl ring (mode-T) in the case of *p*-chloro-, *p*-methyl-, and *p*-methoxyphenyl-2-thienyliodonium bromides. *p*-Methyl and *p*-methoxy substituents prevent the reaction of mode-A owing to their electron-releasing effect. In the *p*-chloro substituent, however, the occurence of the reaction of mode-T could not be explained on the basis of the inductive effect of the *p*-chloro group. The resonance structure (VI) participating with the lone pair of the chlorine atom makes the reaction of mode-T possible. The bond linking the $-I^+$-2-thienyl group to the aromatic ring acquires a double bond character, making it more difficult to be broken. As shown in Table 3, the increase in λ_{max} in going from *m*-substituted or unsubstituted to *p*-chlorophenyl-



(VI)

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[7] T. L. Khotsyanova, *Kristallografiya*, **2**, 51 (1957); *Chem. Abstr.*, **52**, 1704b (1958).

[8] E. M. Archer and T. G. D. van Schalkwyk, *Acta Crystallogr.*, **6**, 88 (1953); D. F. Banks, *Chem. Rev.*, **66**, 260 (1966).

[9] G. H. Wiegand and W. E. McEwen, *J. Org. Chem.*, **33**, 2671 (1968).

[10] Imoto and his co-workers have reported the aryl value (σ_a) on various aromatic compounds. According to them, the aryl values of phenyl and 2-thienyl groups have been reported as 0.00 and 0.30, respectively. Y. Otsuji, K. Kubo, and E. Imoto, *Nippon Kagaku Zasshi*, **80**, 1300 (1959).

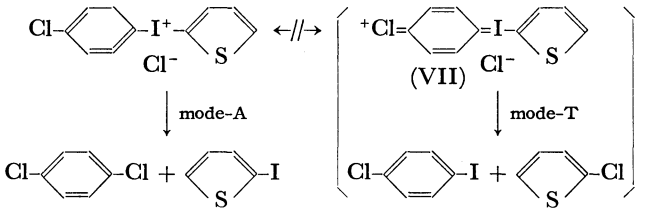
[11] Y. Yamada and M. Okawara, unpublished data.

[12] Petrosyan has reported from the NMR spectra of diphenyliodonium halides that the bond between chloride ion and iodine atom occupies more covalent character than that between bromide ion and iodine atom. V. S. Petrosyan, *Dokl. Acad. Nauk SSSR*, **175**, 613 (1967); *Chem. Abstr.*, **68**, 7940u (1968).

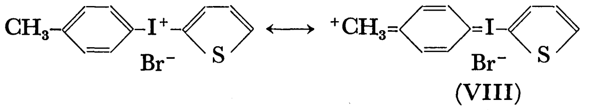
TABLE 3. UV SPECTRA OF SUBSTITUTED PHENYL-2-THIENYLIODONIUM HALIDES (in Methanol)

Substituted group	Counter anion	λ_{max} (nm)	log ε
H	Cl^-	241	4.03
m-Cl	Cl^-	240	3.98
p-Cl	Cl^-	241	4.20
m-Me	Cl^-	239	4.02
H	Br^-	238	3.88
m-Cl	Br^-	240	3.97
p-Cl	Br^-	244	4.13
m-Me	Br^-	239	4.17
p-Me	Br^-	242	4.11
p-MeO	Br^-	254	4.19

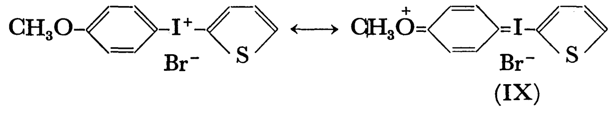
2-thienyliodonium bromide suggests the presence of such a conjugated system. If the resonance structure such as VI contributes to the reaction, the iodine atom and the bromide ion become far apart in contrast to the case of absence of such a resonance structure and orbital interaction will occur between not only the bromide ion and the aryl ring but also between the bromide ion and the thienyl ring. Thus, the reaction of not only mode-A but also of mode-T occurs. In the case of *m*-chloro substituted derivative the reaction of mode-T did not occur since the resonance structure due to the lone pair of the chlorine atom was not possible. It is also understandable from the small difference in λ_{max} between phenyl- and *m*-chlorophenyl-2-thienyliodonium bromide. In the case of the iodonium chloride, the contribution of the resonance structure such as VII is neglected from the ultraviolet spectra data. The λ_{max} in *p*-chlorophenyl-2-thienyliodonium chloride is much the same as that in *m*-chlorophenyl-2-thienyliodonium or phenyl-2-thienyliodonium chloride.



In view of the results of *p*-chlorophenyl-2-thienyliodonium bromide it is considered that the cleavage tendencies of *p*-methoxy- and *p*-methyl-phenyl-2-thienyliodonium bromide are ascribed not only to the inductive effect of the substituent group but also to the conjugated structure:



(VIII)



(IX)

The difference in λ_{max} between *m*- and *p*-methylphenyl-2-thienyliodonium bromide suggests the presence of the hyperconjugated system such as VIII. The absence of the reaction of mode-T in the case of *m*-methylphenyl-2-thienyliodonium bromide suggests a larger contribution of the resonance effect to the occurrence of the reaction than that of the inductive effect. The significant increase in λ_{max} in going from the unsubstituted phenyl-2-thienyliodonium bromide to *p*-methoxyphenyl-2-thienyliodonium bromide suggests the presence of the conjugated system such as IX. The large difference in λ_{max} between *p*-methyl- and *p*-methoxyphenyl-2-thienyliodonium bromide reflects on the mode of reaction *viz.*, the reaction of mode-T is liable to take place in the case of *p*-methoxy substituted derivative in comparison with *p*-methyl substituted derivative.

Beringer and his co-worker also reported on the possibility of the conjugation on *p*-methoxy and *p*-methyl groups in diphenyliodonium salt from the study of ultraviolet spectra.[13] Such a conjugated system has also been reported in the case of *p*-methyl- and *p*-methoxyphenyl diazonium salts.[14]

When the halide ions (Cl^-, Br^-) were allowed to react with phenyl-2-thienyliodonium ion in DMF, the results were similar to that of pyrolysis reaction, *viz.*, only the reaction of mode-A occurred. When the nitrite or thiocyanate ion was used as a nucleophile in DMF, only the reaction of mode-A occurred to give nitrobenzene or phenyl isothiocyanate and 2-iodothiophene, respectively. In the reaction of phenyl-2-thienyliodonium ion with sulfite ion, the ratio of mode-A to mode-T is 1 : 2.

It was found that the iodonium halides containing the thienyl group as a ligand exhibited high activity against a variety of microorganisms, especially against pseudomonas aeruginosa. It has been reported that 2,5-thiophenediyl-bis(phenyliodonium salts) are bioactive against various microorganisms.[15] While the question in toxicity remains unsettled, these distinctive bioactivities resulting from a combination of iodonium and thienyl structures are very interesting.

Experimental

All the melting points are uncorrected. The electronic spectra were obtained on a Hitachi EPS-3T Spectrometer at room temperature using a well-matched pair of 1 cm-cells. Gas chromatographic analysis was carried out with a Hitachi Gas Chromatograph 023-5051 at 100°C using chlorobenzene as an internal standard. Column used was placed with Silicon DC 703 (20%) on Celite 545 (stainless tube 1 m).

Materials. Thiophene of commercial grade was used without further purification. Substituted phenyl iodides were prepared by standard procedure from the corresponding aniline derivatives. 2-Iodothiophene was prepared from thiophene and iodine in the presence of mercuric oxide.[16] 2-Bromothiophene was prepared from thiophene and bro-

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[13] F. M. Beringer and I. Lillien, *J. Amer. Chem. Soc.*, **82**, 5135 (1960).

[14] Z. Jezic, presented at the 161st ACS National Meeting, Division of Medicine Chemistry, Los Angeles, March, 1971; Preprint, 34.

[16] W. Minnis, "Organic Syntheses", Coll. Voll. II, (1943) p. 357.

mine.[17] Substituted phenyl iodine diacetates were prepared by modification of the method of Leffler and Story.[18] The other substituted phenyl iodine diacetates were prepared by a procedure similar to that given for *m*-chlorophenyl iodine diacetate as follows. To a mixture of 51.6 g (0.22 mol) of *m*-chloroiodobenzene and 140 m*l* of purified acetic acid was added dropwise with stirring 110 g (0.43 mol) of 30%-peracetic acid. The flask was chilled with an ice–water bath during the course of slow addition (0.5 hr). The solution was stirred at 10°C for three additional hours and then allowed to stand overnight at room temperature. The solvent was evaporated *in vacuo*. The remaining white crystals were washed with petroleum ether and dried under reduced pressure to give 66.7 g (85.2%) of the product. Purity was estimated iodometrically to be better than 99.8%.

Syntheses of Substituted Phenyl-2-thienyliodonium Halides. Substituted phenyl-2-thienyliodonium halides were prepared by a procedure similar to that given for *p*-chlorophenyl-2-thienyliodonium halides. To a well-stirred mixture of 10.8 g (0.03 mol) of *p*-chlorophenyliodoso diacetate, 5 g (0.06 mol) of thiophene, and 100 m*l* of acetic anhydride kept below 5°C was added 4 m*l* of concentrated sulfuric acid over one hour. After having been stirred under 10°C for 2 hr, the reaction mixture was diluted with 200 m*l* of water, extracted with ether until color was no longer removed and treated with activated carbon. Addition of 10 g of potassium iodide in water gave a colorless precipitate, which was collected, washed with water and methanol and dried to yield 7.88 g of *p*-chlorophenyl-2-thienyliodonium iodide. From similar reaction mixtures *p*-chlorophenyl-2-thienyliodonium bromide and *p*-chlorophenyl-2-thienyliodonium chloride were also obtained. The bromide and the chloride were recrystallized from methanol but the iodide was not recrystallized because of its poor solubility. The results are shown in Table 1.

Pyrolysis Reactions of Substituted Phenyl-2-thienyliodonium Halides. Each iodonium halide in Table 1 was pyrolyzed in a 15 mm Pyrex tube about 15 cm long, sealed at one end at 245±5°C until the reaction was complete. About 10 cm of the sealed end of the tube was immersed into an oil bath, the remainder of the tube being used as an air condenser. In all cases the composition of the pyrolyzates were determined by means of gas chromatograph. Identification of the products was accompanied by means of retention time. In no case was any significant amount of unexpected product found. All the iodonium halides, when pyrolyzed, gave the products expected from their thermal decomposition. Resolution and appropriate shape of the halide peaks obtained in the chromatograms of the pyrolyzates were sufficient to permit determination of the relative ratios of the halides formed in each pyrolyzate. Approximate peak areas were obtained by multiplying the peak height by the peak width at half height. In the case of the bromide the reaction mode was determined from the amounts of 2-iodothiophene and 2-bromothiophene, and in the case of the chloride from the amounts of 2-iodothiophene and the corresponding substituted phenyl iodide, respectively.

Reaction of Phenyl-2-thienyliodonium Ion with Various Nucleophiles in DMF. The mixture of 0.97 g (0.0025 mol) of phenyl-2-thienyliodonium perchlorate and 0.65 g (0.005 mol) of sodium sulfite dissolved in 50 m*l* of DMF and 30 m*l* of water was held at 100°C for 5 hr. At the end of the reaction the reaction mixture was poured into cold water, extracted with ether two times and the extract was dried over anhydrous sodium sulfate. On removing the solvent by distillation, the residual mixture was redissolved in a small quantity of ether and then the amounts of iodobenzene and 2-iodothiophene were determined by glc analysis. When chloride or bromide ion was used as a nucleophile, 0.97 g (0.0025 mol) of the iodonium perchlorate and 0.29 g (0.005 mol) of sodium chloride or 0.52 g (0.005 mol) of sodium bromide dissolved in 50 m*l* of DMF was held at 100°C for 5 hr. When nitrite or thiocyanate ion was used as a nucleophile, 0.97 g (0.0025 mol) of the iodonium perchlorate and 0.35 g (0.005 mol) of sodium nitrite or 0.49 g (0.005 mol) of potassium thiocyanate dissolved in 40 m*l* of DMF and 10 m*l* of water was held at 100°C for 5 hr. In each case the subsequent experiment was carried out in the same way as mentioned above.

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[17] D. A. Shirley, "Preparation of Organic Intermediates", John Wiley & Sons Inc., London (1951), p. 60.

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