Substituent Scrambling in the Thiophene Molecular Ion

M. E. Rennekamp, W. O. Perry, and R. G. Cooks*

Contribution from the Chemistry Department, Kansas State University, Manhattan, Kansas 66502, and the Chemistry Department, Purdue University, Lafayette, Indiana 47907. *Received November 27, 1971*

Abstract: Molecular ion isomerization reactions occurring in 3-phenylthiophene and two brominated derivatives have been followed in both slow and fast reactions using ^{13}C labeling. Substituent isomerization by way of group migration has been demonstrated and is suggested to occur only after ring opening. Ring atom scrambling does not compete effectively with the substituent migration mechanism and is apparently limited to cyclic molecular ions. An increase in the degree of scrambling with increasing ion lifetime was noted in many of the reactions studied, but scrambling was frequently incomplete even when metastable ions were examined. The bearing of the present results upon thiophene photochemistry is emphasized.

Molecular rearrangements have always intrigued chemists, perhaps because they sometimes seem to threaten one of our earliest and fondest impositions upon matter, molecular structure. Scrambling[1] processes, therefore, constitute a special heresy and have been accorded due attention.

The importance of scrambling reactions in ions lies in these factors: (i) they pose mechanistic problems of intrinsic interest, (ii) they bear upon those analytical applications of mass spectrometry involving determination of the site(s) and extent of stable isotope incorporation, (iii) their unique[2] energetic and rate characteristics are of potential importance in testing the theory of mass spectra.

Most investigations of ionic scrambling have dealt with hydrogen migrations as studied by partial deuteration.[3] Nevertheless, the following information, bearing on the scrambling of other groups, is available. First, in many disubstituted aromatic compounds, indirect methods (metastable ion abundances, substituent effect considerations, and energetic studies) have led to the conclusion that substituent isomerization occurs.[4] Similarly, metastable ion abundance data provide evidence for interring chlorine scrambling in chlorinated biphenyls.[5] It is usually accepted, however, that doubt exists in the above cases as to whether the observed effects are due to isomerization or to the similarities in properties of the nonisomerized molecular ions. More direct evidence for substituent scrambling has been found using the *p*-fluorophenyl group as a label for the phenyl group. Applying this technique to tetraphenylthiophene and tetraphenylfuran, Bursey and coworkers[6] concluded that phenyl scrambling occurs in the thiophene but not in the furan, thus paralleling the earlier hydrogen scrambling observations.[7]

Hydrogen scrambling occurs in the benzene molecular ion by two processes, carbon scrambling, the bond to each substituent remaining intact, and by a mechanism involving carbon–hydrogen bond cleavage with hydrogen migration.[8] Photochemical reactions corresponding to the carbon scrambling mechanism are known.[9] Carbon scrambling has also been demonstrated in benzothiophene[10] and in thiophene.[11] For thiophene, partial carbon scrambling has been demonstrated to occur in those molecular ions which fragment in the ion source to give CHS^+; at low electron energies the degree of scrambling increases (compare the deuterium labeling results[7]). Similar results were found for other reactions of the molecular ion. Furthermore, comparison of thiophene-*2*-^{13}C and thiophene-*2*-^{2}H suggests that the carbon–hydrogen bond cleavage and re-formation process also occurs to some extent.[11a]

Our object in this study was to seek direct evidence for the scrambling of substituents other than hydrogen in an aromatic molecular ion and to establish whether ring atom scrambling or the alternative mechanism of bond cleavage was operative. The choice of thiophene as the aromatic nucleus in this study was based on these facts: (i) the scrambling reactions occurring in the thiophene molecular ion have been reasonably well delineated; (ii) substituted thiophenes have been inten-

(1) Scrambling is here defined as the statistical distribution of n groups over n available positions ($n > 2$). When just two groups are involved the term group interchange is used. Irreversible isomerization reactions may also lead to transposition of two groups but the element of mutual interchange is lost.

(2) Available evidence suggests that extremely low activation energies and low frequency factors are typical; see I. Howe, "Mass Spectrometry," Vol. 1 (A Specialist Periodical Report), The Chemical Society, London, 1971, p 63.

(3) For leading references see (a) H. M. Grubb and S. Meyerson in "Mass Spectrometry of Organic Ions," F. W. McLafferty, Ed., Academic Press, New York, N. Y., 1963, Chapter 10; (b) R. W. Rylander and P. Meyerson, *J. Amer. Chem. Soc.*, **78**, 5799 (1956); (c) K. R. Jennings, *Z. Naturforsch. A*, **22**, 454 (1967); (d) D. H. Williams, S. W. Tam, and R. G. Cooks, *J. Amer. Chem. Soc.*, **90**, 2150 (1968); (e) W. Carpenter, A. M. Duffield, and C. Djerassi, *ibid.*, **90**, 160 (1968); (f) G. G. Meisels, J. Y. Park, and B. G. Giessner, *ibid.*, **91**, 1555 (1969); (g) R. G. Cooks, I. Howe, and D. H. Williams, *Org. Mass Spectrom.*, **2**, 137 (1969); (h) B. Davis, D. H. Williams, and A. N. H. Yeo, *J. Chem. Soc., B*, 81 (1970); (i) A. V. Robertson and C. Djerassi, *J. Amer. Chem. Soc.*, **90**, 6992 (1968).

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(10) R. G. Cooks and S. L. Bernasek, *J. Amer. Chem. Soc.*, **92**, 2129 (1970).

(11) (a) F. DeJong, and H. J. M. Sinnige, and M. J. Janssen, *Recl. Trav. Chem. Pays-Bas*, **89**, 225 (1970); (b) A. S. Siegel, *Tetrahedron Lett.*, 4113 (1970).

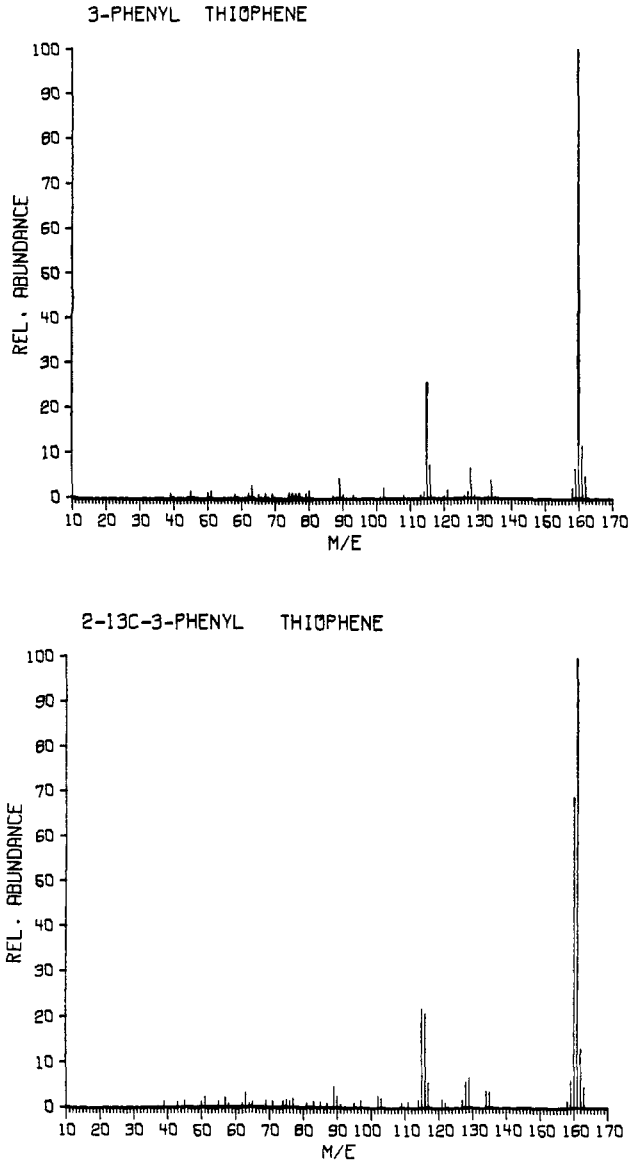

Figure 1. Mass spectra (70 eV) of 3-phenylthiophene and phenylthiophene-2-^{13}C.

sively studied for their photochemical rearrangements;[12] (iii) the necessary synthetic reactions are known and only one atom need be labeled in order to follow the relative positions of the ring atoms; (iv) the near identity of the mass spectra[13] of many isomeric mono- and disubstituted thiophenes points to the occurrence of substituent scrambling while the formation of $C_6H_5CS^+$ from 3-phenylthiophene[14] is most simply explained as the result of 1,2-phenyl migration. Our choice of thienyl substituents was governed both by the desire to include a phenyl group and by the fact that groups which form relatively stable free radicals were desired in order not to preclude carbon-substituent bond cleavage.

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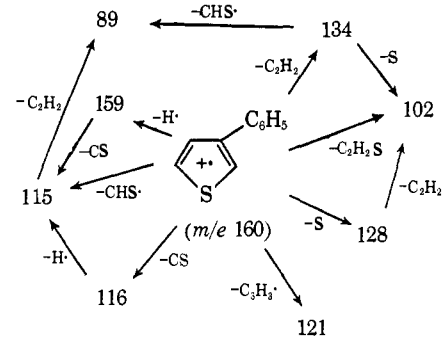
Results

3-Phenylthiophene. The normal 70-eV mass spectra of 3-phenylthiophene (**1**) and 3-phenylthiophene-2-^{13}C (**2**) are presented in Figure 1. The incorporation of ^{13}C in **2** was determined to be 59.7 ± 0.3% by low electron energy scans using both the MS-9 and the CEC 21-110B mass spectrometers. Hence the actual label at C-2, including natural abundance, is 60.8%. Major aspects of the fragmentation pattern of **1** are given in Scheme I,

Scheme I



all reactions having been substantiated by the observation of the corresponding metastable ion decompositions. The reactions of primary interest are those which can be used to follow scrambling in the molecular ion, *viz.*, the loss of C_2H_2, $C_3H_3\cdot$, or C_2H_2S. Daughter ion abundances for the labeled and unlabeled compounds covering these regions of the mass spectrum as well as the CHS^+ region are given in Table I. Exact mass measurements were employed to establish the assigned ionic compositions. Metastable ion fragmentations occurring in **2** are given in Table II, to-

Table I. Some Fragment Ions from the Phenylthiophenes (**1** and **2**)[a]

Reaction	Product ion			
$M\cdot^+ - C_2H_2$	*m/e* 133	134	135	136
1	17	100	1	1
2	24	100	83	1
$M\cdot^+ - C_3H_3\cdot$	*m/e* 120	121	122	123
1	5	100	6	0
2	10	100	61	2
$M\cdot^+ - C_2H_2S$	*m/e* 101	102	103	104
1	14	100	5	0
2	17	100	94	5
CHS^+	*m/e* 44	45	46	
1	3	100	3	
2	5	100	36	

[a] Corrected for natural ^{13}C and ^{34}S contributions and normalized in each region of interest.

Table II. Metastable Transitions in 3-Phenylthiophene-2-^{13}C (**2**)

Reaction		Peak area	Label loss,[a] %
$M\cdot^+ - C_2H_2$	161 → 134 160 → 134	51	21 ± 4
	161 → 135	49	
$M\cdot^+ - C_3H_3\cdot$	161 → 121 160 → 121	64	43 ± 5
	161 → 122	36	
$M\cdot^+ - C_2H_2S$	161 → 102 160 → 102	65	45 ± 7
	161 → 103	35	

[a] Calculated for 100% labeled compound, see text. Errors are estimates based on several scans; they vary widely because of differences in the abundances of the metastable ions.

Table III. Major Fragment Ions in the Mass Spectra of the Brominated Thiophenes (3–6)[a]

Compd	101	102	103	104	113	114	115	116	117	121	122	134	135	136	137	138	180	181	182	183	192	193	194	195	196	197
3	40	100	7	9	14	27	100	12	1	100	8						100	4	93	2	2	100	31	98	13	1
4	30	100	29	43	8	17	100	43	2	100	38						100	45	97	39	15	100	100	91	82	5
5	6	100	1	4	8	14	100	2	1	100	5	100	3	100	15	87					4	100	51	94	18	3
6	12	96	100	2	9	20	100	86	0	100	11	100	75	100	46	98					4	100	27	98	20	9

[a] Only ions $m/e > 100$ are included. Corrected for natural ^{13}C and ^{34}S contributions and normalized in each region of interest.

gether with the calculated percentage label loss in each reaction of **2**. The calculation of the label loss can be illustrated by the case of C_2H_2 elimination. The metastable peak obtained when transitions leading to *m/e* 134 are examined is an incompletely resolved doublet due to the reactions $161^+ \rightarrow 134^+$ and $160^+ \rightarrow 134^+$ while that obtained when the daughter ion is *m/e* 135 represents the single reaction $161^+ \rightarrow 135^+$. There is only one *m/e* 160 species ($C_{10}H_8S\cdot^+$) which can give *m/e* 134[15] but there are several *m/e* 161 ions which differ in the position of the ^{13}C label.

Now from the known label incorporation and natural ^{13}C abundance it follows that *m/e* 160 will be 38.1% of the combined *m/e* 160 + *m/e* 161 ion abundance and that 93.0% of all *m/e* 161 ions will be labeled in the 2 position, the remainder being randomly labeled. Hence 38.1 units must be subtracted from the normalized abundance of the unresolved *m/e* 161 → *m/e* 134 and *m/e* 160 → *m/e* 134 transitions to give the abundance (12.9 units) due to *m/e* 161 fragmentation. Hence *m/e* 161 gives *m/e* 134 (12.9 units) and 135 (49 units); of these *m/e* 161 ions 7% are randomly labeled in positions other than C-2 and fully two-thirds of these are labeled in the nonreactive[14] phenyl ring (six carbon atoms out of a total of nine) and cannot suffer label loss. The contribution of these phenyl-labeled *m/e* 161 ions must therefore be subtracted, hence $^2/_3 \times 7\%$ of the total 161 signal (12.9 + 49 units), *i.e.*, 2.9 units, must be subtracted from the $161^+ \rightarrow 135^+$ signal leaving 46.1 units due to thienyl-labeled molecular ions fragmenting with label retention. The remaining one-third of the randomly labeled *m/e* 161 ions, *viz.*, 2.3% of all *m/e* 161 ions, are randomly labeled in C-3, C-4, and C-5. These ions therefore have a two-thirds chance of losing labeled C_2H_2 and a one-third chance of losing unlabeled C_2H_2. This contribution to the total *m/e* 161 signal, 2.3% of 12.9 + 49 units = 1.4 units, must therefore be subtracted from the $161^+ \rightarrow 134^+$ and $161^+ \rightarrow 135^+$ signals in the ratio 2/3:1/3, *i.e.*, 1.0 to 0.4 unit. This leaves 11.9 units as the net signal due to formation of *m/e* 134 and 45.7 units as the net signal due to formation of *m/e* 135 from 100% labeled 3-phenylthiophene-*2*-^{13}C, *viz.*, 21% label loss occurs.

2-Bromo-3-phenylthiophene. The 70-eV mass spectra of 2-bromo-3-phenylthiophene (**3**) and the 2-^{13}C analog (**4**) appear, in part, in Table III. ^{13}C incorporation in **4** was equal to that in **2** (59.7%). Table IV gives the relative abundances of the ions due to those metastable fragmentations of **4** which can shed light on molecular ion isomerization. For each reaction the calculated fraction of the label lost from 100% 2-^{13}C labeled material is also presented. Values for the loss of CHS· have had to be corrected for the contribution of the minor CS loss process.

(15) The ^{13}C analog of the $M^+ - 1$ ion also has mass 160, but even unlabeled *m/e* 159 does not undergo detectable metastable loss of C_2H_2.

Table IV. Metastable Transitions in 2-Bromo-3-phenylthiophene-*2*-^{13}C (**4**)

Reaction		Peak area	Label loss,[a] %
$M\cdot^+ - CHS\cdot$[b]	238 → 193	41	16 ± 7
	239 → 193		
	239 → 194	59	
	238 → 194		
$M\cdot^+ - CBrS\cdot$	238 → 115	47	15 ± 4
	239 → 115		
	239 → 116	53	
$M\cdot^+ - C_2H_2S$	238 → 180	84	79 ± 10
	239 → 180		
	239 → 181	16	
$M\cdot^+ - C_3H_2Br\cdot$	238 → 121	80	68 ± 15
	239 → 121		
	239 → 122	20	

[a] See footnote *a*, Table II. Note that for this compound some peaks were scanned just once. [b] Contribution of $M\cdot^+ - CS$ (20% of $M\cdot^+ - CHS\cdot$) has been removed in deriving label loss.

2-Bromo-4-phenylthiophene. The 70-eV mass spectra of 2-bromo-4-phenylthiophene (**5**) and its 5-^{13}C analog (**6**) are given, in part, in Table III. Compound **6** (5-^{13}C incorporation equal to that in **2**) underwent some metastable reactions not observed in its isomer (**4**) and again those pertinent to the mechanistic question are detailed (Table V).

Table V. Metastable Transition in 2-Bromo-4-phenylthiophene-*5*-^{13}C (**6**)

Reaction		Peak area	Label loss,[a] %
$M\cdot^+ - CHS\cdot$[b]	238 → 193	73	60 ± 5
	239 → 193		
	239 → 194	27	
$M\cdot^+ - CBrS\cdot$	238 → 115	48	16 ± 3
	239 → 115		
	239 → 116	52	
$M\cdot^+ - C_2HC_6H_5$	238 → 136	62	39 ± 5
	239 → 136		
	239 → 137	38	
$M\cdot^+ - C_2HBr$	238 → 134	57	31 ± 4
	239 → 134		
	239 → 135	43	
$M\cdot^+ - C_3H_2Br$	238 → 121	55	27 ± 4
	239 → 121		
	239 → 122	45	
$M\cdot^+ - C_2HBrS$	238 → 102	70	53 ± 6
	239 → 102		
	239 → 103	30	

[a] See footnote *a*, Table IV. [b] Metastable reaction $M\cdot^+ - CS$ was not detected in **5**, hence no correction was necessary in this case.

Discussion

There are two important consequences of using metastable ion fragmentations to follow molecular ion reorganization reactions. Ambiguities of ion origin

can occur when normal daughter ions are examined but are removed by this procedure. Also the reaction time scale is changed so that rearrangement processes are preferred over simple cleavage and elimination reactions because of their generally low activation energies coupled with low frequency factors.[16]

It is therefore appropriate that the label loss accompanying reactions occurring in the ion source usually shows a simple correspondence to predicted cleavage modes of the molecular ion. Thus, in the unrearranged[17] molecular ion of 3-phenylthiophene, elimination of C_2H_2S is expected to involve C-4 and C-5 rather than C-2 and C-5 and the label retention in the normal daughter ions (*ca.* 77%[18]) is in agreement. Label retention in normal daughter ions can thus provide a means of identifying the fragmentation mode. In this regard interest focuses on the positions eliminated in a particular reaction rather than on the origin of the particular atoms which occur in these positions. Thus C_2H_2S loss involves C-4 and C-5 but the occupants of these positions might, after rearrangement, be the original C-2 and C-3 carbon atoms. It is in line with this mode of C_2H_2S loss that the process is barely detectable in **5** but is important in the 2-bromo compound **3** where, in ion source reactions, it is accompanied by less label loss and less scrambling than in metastable ion reactions.

Turning to C_2H_2 and $C_3H_3\cdot$ loss from 3-phenylthiophene one encounters the extra problem of whether these processes involve the thienyl or phenyl ring. Fortunately, Meyerson and Fields[14] have, by deuterium labeling, established that the thienyl ring is the predominant source of both fragments. The elimination of $C_3H_3\cdot$ from **1** necessarily involves rearrangement; thus processes occurring in the source cannot be used to indicate the basic fragmentation mode and it is reasonable that they should show a similar label loss (41 *vs.* 43%, respectively) to those occurring in the field-free region. The same is true of $C_3H_2Br\cdot$ loss from the brominated compound **4**, where agreement between source and field-free region reactions is good (62 and 68%). The corresponding results for **6**, 90 and 27%, point to a rearrangement reaction involving C-5–H cleavage in the slow but not the fast reaction. The faster rearrangement either occurs by ring atom scrambling or by phenyl–bromine isomerism.

The $M\cdot^+ - CHS\cdot$ reaction in **3** and **5** involves the unsubstituted α carbon in each case as witnessed by the fact that label retention in forming normal daughter ions is high (~70%) in **4** and low (~15%) in **6** (accurate determination using daughter ions is precluded by the presence of the $M\cdot^+ - CS$ ion). The process $M\cdot^+ - CBrS\cdot$ is completely analogous and therefore the label retention is reversed, 38% in **4** and 75% in **6**.

The remaining reactions of interest in the brominated thiophenes, $M\cdot^+ - C_2HC_6H_5$ and $M\cdot^+ - C_2HBrS$, are essentially restricted to one isomer (**5**) and are analogous to processes occurring in the phenylthiophene. Label losses in the source reactions (*ca.* 62 and 17%, respectively) are in line with the suggestion that the major fragmentation mode is simple C-2, C-3 loss.

We can now turn to a consideration of the mechanistic implications of the label loss results (Tables II, IV, and V) in the metastable ion fragmentations, dealing first with 3-phenylthiophene. Metastable $C_3H_3\cdot$ elimination from **1** proves the occurrence of a skeletal rearrangement whereby phenyl, with or without its attached carbon (C-3), becomes attached to sulfur. If this occurred by ring atom scrambling, loss of label in **2** should be 100%. The fact that it is only 43% proves that, at least in part, the process involves phenyl migration accompanied by C–phenyl bond cleavage, ^{13}C–hydrogen bond cleavage, and hydrogen migration back to the unit (if not the exact position) from which the phenyl migrated. Thus Ph–H substituent isomerization must occur; this may well be reversible although the results do not demand this. They do demand, however, that the isomerization, in addition to involving C-3 → C-2 rearrangement (which requires 100% label loss), includes some other mechanism, either carbon scrambling (0% label loss) or C-3 → C-5 rearrangement (0% label loss), or a more complex process involving both ring atom isomerism and phenyl migration.

The losses of C_2H_2S and C_2H_2 from 3-phenylthiophene should involve the same carbon positions (4 and 5), yet they occur with different amounts of label loss, 45 *vs.* 21%. For both reactions, zero scrambling implies 35% label loss, hence C_2H_2S loss occurs after more scrambling than C_2H_2 loss (C_2H_2 label loss is also depressed by an unknown but probably small factor due to the competing elimination from the phenyl ring). Carbon scrambling can explain the label loss in the C_2H_2S elimination or alternatively Ph–H substituent isomerization (C-3 → C-5) could be responsible. A complex mixture of both processes could also be occurring. The same mechanisms, occurring to a different extent prior to fragmentation, can account for the C_2H_2 elimination results.

The above results for 3-phenylthiophene, therefore, prove that phenyl and H attached to C-3 and C-2, respectively, can interchange positions in the fragmenting ions, and that the same isomerization between phenyl and the C-5 hydrogen may well occur too. These phenyl migration reactions may well involve ring opening at the C–S bonds (*vide infra*).

The most striking fact about the isomeric bromo compounds is that even in their metastable reactions they behave rather differently: whatever randomization reactions are at work are, therefore, incomplete even on this time scale. Three moderately abundant metastable transitions are common to the isomers, $M\cdot^+ - CHS\cdot$, $M\cdot^+ - CBrS\cdot$, and $M\cdot^+ - C_3H_2Br\cdot$. $CHS\cdot$ elimination from **4** occurs with some label loss; this requires that the C-2–Br bond break and that hydrogen rearrange to this portion of the molecule. In larger measure however, the label is retained and this is consistent with no rearrangement, or, more probably in view of the extensive rearrangement in other reactions of **4** and in the analogous reaction in **6**, ring atom scrambling among other more complex possibilities. In the isomer **6**, 60% label loss occurs; hence at least 40% of the reactions occur from rearranged ions. The simplest rearrangements consistent with this are (i) Br–H isomerization *via* C-2–Br and C-5–H bond cleavages and (ii) ring atom scrambling. Elimination of $CBrS\cdot$, unlike $CHS\cdot$ loss, involves equal label loss in

(16) R. G. Cooks, I. Howe, and D. H. Williams, *Org. Mass Spectrom.*, 2, 137 (1969).
(17) This should not be taken as excluding simple ring opening.
(18) Calculated from the data of Table I and including the two-step pathway to $M\cdot^+ - C_2H_2S$.

the two isomers (**4** and **6**). The low loss of label indicates very extensive scrambling, at least in **4**, where scrambling cannot be due to carbon rearrangement but must involve C–Br cleavage. Moreover, since bromine migration to either of the β positions is not relevant to this fragmentation, there must occur in **4**, by a direct or indirect route, bromine–C-2 cleavage and bromine–C-5 bond formation.

The third reaction common to the two isomers is formation of $C_6H_5CS^+$. Since the phenyl in both compounds is β to sulfur, nonrearranged ions cannot undergo this reaction. The fact that label is lost in both cases means that carbon scrambling cannot be the only mechanism operating; indeed, label loss from **4** necessitates C–phenyl cleavage, ^{13}C–Br cleavage, and phenyl migration to the labeled carbon unit. Thus we have a case of phenyl–bromine isomerization *via* the cleavage route. The sharp differences in the proportion of the label lost in each case, however, indicate that the carbon–phenyl cleavage and phenyl migration process occurs most readily to C-5 in both **3** and in **5**, *i.e.*, phenyl–H interchange is preferred over phenyl–bromine interchange. By contrast, the label loss is reversed in daughter ions (*vide supra*), a situation which points to a different type of rearrangement mechanism in these ions with ring atom scrambling the most likely possibility.

The loss of label accompanying C_2H_2S elimination from **4** offers further proof for the occurrence of carbon–bromine cleavage with hydrogen migration to substitute for the bromine. Both elimination from the unlabeled ion and ring atom scrambling require zero label loss, yet 79% label loss is seen. Complete scrambling of all four ring carbons requires 50% label loss, scrambling of C-2, C-4, and C-5 (*i.e.*, H–Br interchange) requires 67% label loss and the experimental data are in fair agreement. More complex possibilities such as a combination of bromine and phenyl migrations might also fit this data.

While C_2H_2S from **6** does not constitute a sufficiently intense metastable fragmentation for study, the corresponding loss of C_2HBrS does. Loss of half the label could be due to ring atom scrambling or complete substituent scrambling by the cleavage mechanism might be involved (requires 50% label loss, found 53 ± 6%).

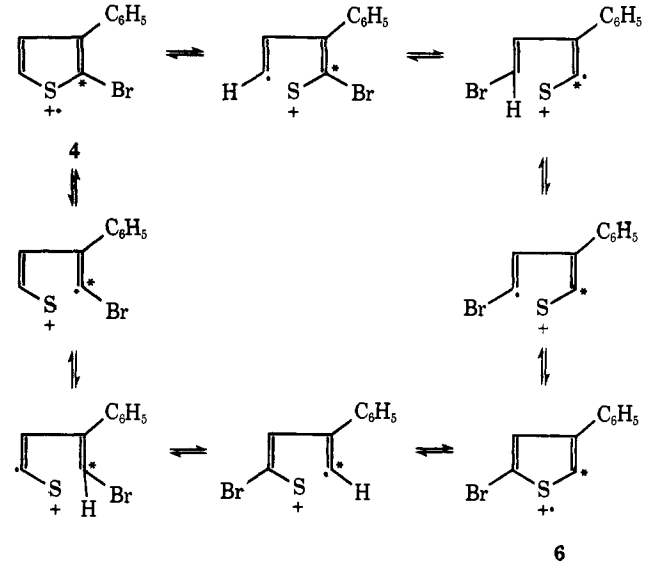
The remaining two reactions which could be studied in **6**, $C_2HC_6H_5$ and C_2HBr elimination, are analogous to C_2H_2 loss from 3-phenylthiophene. Approximately one-third of the label is lost in each of these reactions, yet the simple elimination process would involve total and zero loss, respectively. Substituent scrambling however requires 50% label loss and the results for the $C_2HC_6H_5$ elimination approximate this. C_2HBr elimination involves less label loss, but probably not because of incomplete randomization since the label loss found in the daughter ions (~26%) is equal to that found for metastable ions.

Conclusions

Carbon–hydrogen, carbon–bromine, and carbon–phenyl bond cleavages and substituent migration occur in the molecular ions of the thiophenes **1**, **3**, and **5**. The extent to which substituent isomerization is reversible is not clear but in several reactions of the brominated compounds scrambling by the bond cleavage process seems to be essentially complete. By contrast, no proof of the occurrence of ring atom scrambling (carbon scrambling) has been obtained and although the results do not preclude its operation in some reactions, it is definitely not a major process. This is in contrast to the situation in benzene and in thiophene itself where ions undergoing metastable fragmentation have usually undergone extensive ring atom scrambling. Steric factors may reduce ring atom scrambling, especially in the brominated compounds, or ring opening may preclude it. Our results strongly suggest that the scrambling Bursey[6] noted in tetraarylthiophenes was not due to ring carbon scrambling but due, at least in part, to aryl scrambling by the substituent cleavage mechanism.

The substituent interchange which we have uncovered involves C-3–C-2, C-5–C-2 and perhaps other processes. The importance of radical sites in initiating rearrangements in the mass spectrometer[19] suggests that C–S cleavage and ring opening may be a necessary prerequisite for these processes. At the very least this provides an eminently reasonable mechanistic basis for future work. The C-2–C-5 rearrangement which precedes $CBrS\cdot$ elimination from **4** (and probably **6**) is proposed to occur as illustrated in Scheme II.

Scheme II



While we have by no means completely elucidated the varied and complex reactions occurring in these systems the major point is clear: substituent isomerization is an important process and in some reactions complete substituent scrambling is indicated.

Our results prompt the suggestion that in the benzene and thiophene molecular ions, where substituent scrambling occurs both by ring atom scrambling and by the cleavage route, isomeric forms of the ion are responsible for each randomization mode. Specifically, it is suggested that only the cyclic form of the ion can undergo ring carbon scrambling and only the ring-opened form can undergo substituent migration.

Current discussion[12] as to whether photoisomerization of thiophenes involves the cyclopropenyl thioketone

(19) (a) F. W. McLafferty in "Topics in Organic Mass Spectrometry," A. L. Burlingame, Ed., Wiley–Interscience, New York, N. Y., 1970, p 223 *et seq.*; (b) R. G. Cooks, *Org. Mass Spectrom.*, 2, 481 (1969); (c) D. J. McAdoo, F. W. McLafferty, and J. S. Smith, *J. Amer. Chem. Soc.*, 92, 6343 (1970); (d) G. Eadon, C. Djerassi, J. H. Beynon, and R. M. Caprioli, *Org. Mass Spectrom.*, 5, 917 (1971).

(or aldehyde) or an intermediate in which sulfur 3d orbitals are utilized suggests that one or other mechanism may be responsible for the ring atom scrambling reaction occurring in the mass spectrometer. The limited amount of hydrogen–deuterium scrambling observed in furans[7] and oxazoles,[20] both cases in which photochemical analogies suggest that cyclopropenyl intermediates might be important, indicates, however, that reversible ring contraction is not important in the mass spectrometer. Ring opening as a prelude to isomerization has not yet been observed photochemically but our results suggest that it should perhaps be sought.

Experimental Section

3-Phenylthiophene-2-^{13}C (2). A mixture of diethyl malonate (43 g, 0.27 mol), benzaldehyde (32.7 g), piperidine (4 g), and benzene (86 ml) was refluxed for 20 hr, water being removed by a continuous extraction procedure. The resulting solution was allowed to cool, washed with water, 1 *N* hydrochloric acid, and saturated sodium bicarbonate solution, and then dried over sodium sulfate. After removal of benzene the residue was distilled to yield diethyl benzalmalonate (60 g, 90%), bp 140–141° (4 mm) (lit.[21] 140–142° (4 mm).

To diethyl benzalmalonate (3.58 g, 0.0145 mol) in absolute ethanol (36 ml) was added K^{13}CN (1 g, 0.0154 mol, nominal 61% labeled) dissolved in 2 ml of water. The solution was refluxed 18 hr and cooled and the precipitate was collected and washed with 95% ethanol (4 ml). The combined filtrate and washings were acidified with dilute HCl and concentrated under reduced pressure. The residue was extracted with an ether–water mixture (1:1); the extract was then dried over calcium chloride and concentrated under reduced pressure to yield the cyano addition product. This was hydrolyzed by addition of concentrated HCl and refluxed 18 hr. The mixture was cooled and the solid was collected on a glass filter, washed with cold water, recrystallized from water, and dried *in vacuo* to yield 2-phenylsuccinic-1-^{13}C acid (1.538 g, 54.6% yield), mp 165–166° (lit.[22] 165.5–166°).

Finally, the succinic acid (733 mg, 0.0038 mol) was intimately mixed with P_2S_5 (1.466 g) and the mixture was stirred for 8 hr at 110°. Sublimation yielded **2** (40%). Multiple sublimations gave the pure thiophene (170 mg, 28%), mp 91.5–92° (lit.[23] 91.4–92°).

2-Bromo-3-phenylthiophene-2-^{13}C (4) and 2-Bromo-4-phenylthiophene-5-^{13}C (6). 3-Phenylthiophene-2-^{13}C (**2**; 130 mg, 0.0008 mol) in 5 ml of a solution of HBr (6.7 g) in glacial acetic acid (100 ml) was treated slowly with a solution of bromine (130 mg, 0.0008 mol) in glacial acetic acid (5 ml). The mixture was refluxed 6 hr then poured onto ice, and the precipitate was collected, dissolved in ether, and subjected to gas chromatography. This was effected using a 12 ft × 1/8 in. column packed with Apiezon L on Chromosorb at 284° and employing a Wilkens Aerograph Autoprep (Model A-700) gas chromatograph. The products obtained[24] together with retention times and yields[25] were: **2** (5.4 min, 9%), 2-bromo-3-phenylthiophene-2-^{13}C (**4**, 8.7 min, 13%), 2-bromo-4-phenylthiophene-5-^{13}C (**6**, 11.5 min, 54%), and 2,5-dibromo-3-phenylthiophene-2-^{13}C (17.3 min, 24%).

The unlabeled analogs, **1**, **3**, and **5**, were in each case synthesized by the identical procedure and their physical and spectroscopic properties agreed with the assigned structures and the literature data.

Mass Spectra. Low resolution spectra were determined using a CEC-21-110B mass spectrometer operating at 70-eV electron energy, 100 μA trap current, 8 kV ion accelerating voltage, and a source temperature of approximately 150°. The low resolution data of Table I were obtained on an Hitachi RMU-6 instrument, operated at 70-eV electron energy, 40 μA trap current, 2.5 kV ion accelerating voltage, and a source temperature of approximately 150°. All low resolution data represent the average of several scans. Label incorporation in **2** was determined using both the above instruments and also an AEI MS-9 operating at 8 kV and a source temperature of *ca.* 150°: found 59.7% (nominal 9 eV, CEC 110), 59.7% (nominal 14 eV, MS-9), and 59.5% (70 eV, RMU-6). Label incorporation in compounds **4** and **6** was found to be identical, within experimental error, with that in **2**.

Exact mass measurements on all the major ions in **1** and **2** were obtained from photoplate data obtained on the CEC-110 instrument using perfluorokerosine as internal standard. The compositions of the $C_6H_5CS^+$ and $M\cdot^+ - CBrS$ ions in compound **3** were established by peak matching. All mass measurements were accurate to 4 mmu.

Metastable ion fragmentations were studied in the first field-free region of the Hitachi RMH-2 mass spectrometer using the accelerating voltage scan technique.[26] The instrument was operated at 75 eV, 1 mA electron current, *ca.* 160° source temperature, and with a narrow energy-resolving β slit. Typically, reactions of the labeled and unlabeled molecular ion to give the same daughter ion could not be resolved.

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(25) Yields are expressed as a percentage of the four compound mixture and were determined by weighing the areas under the curves.
(26) (a) M. Barber and R. M. Elliot presented at the 14th Annual Conference on Mass Spectrometry and Allied Topics, Montreal, June 1964. (b) K. R. Jennings in "Some Newer Physical Methods in Structural Chemistry," R. Bonnett and J. G. Davis, Ed., United Trade Press, London, 1967, p 15.