The Photochemistry of Thiophenes. V. Investigation of Phenylthiophene Photorearrangements by Deuterium Labeling Techniques[1]

Richard M. Kellogg and Hans Wynberg

Contribution from the Department of Organic Chemistry, The University, Groningen, The Netherlands. *Received February 1, 1967*

Abstract: The photochemical rearrangement of 2-phenyl- to 3-phenylthiophene has been studied by a deuterium labeling nmr technique. 2-Pentadeuteriophenyl-5-deuteriothiophene was irradiated in ethyl ether solution until approximately equal amounts of the 2- and 3-substituted isomers were present. The recovered 3-pentadeuteriophenyl isomer was identified by its nmr spectrum as 85–90% 3-pentadeuteriophenyl-5-deuteriothiophene with smaller amounts of the other two positional isomers. The 2-substituted isomer had 75–80% of the deuterium remaining in the 5 position and approximately equal amounts of the other two deuterium positional isomers. 2-Deuterio-3-pentadeuteriophenylthiophene underwent no phenyl migration upon photolysis but the other two deuterium positional isomers were formed in a "no-reaction reaction." The synthesis of the pentadeuteriophenylthiophenes by a photochemical arylation reaction is described. The nmr parameters for 2- and 3-pentadeuteriophenylthiophenes have been obtained.

The photochemical rearrangement of 2-phenyl- to 3-phenylthiophene takes place with major reorganization of the thiophene ring.[2] Knowledge of the positions of the carbon atoms in the thiophene ring after rearrangement would greatly aid the mechanistic interpretation. Although a ^{14}C label had been successfully used to show that the phenyl group remains attached to the same carbon atom during rearrangement,[2b] the corresponding determination of the position of a ^{14}C label in the thiophene ring on nonphenyl-bonded carbons is difficult. Substituent labeling was chosen as an alternative method and in this particular publication the use of deuterium as a substituent is described.[3]

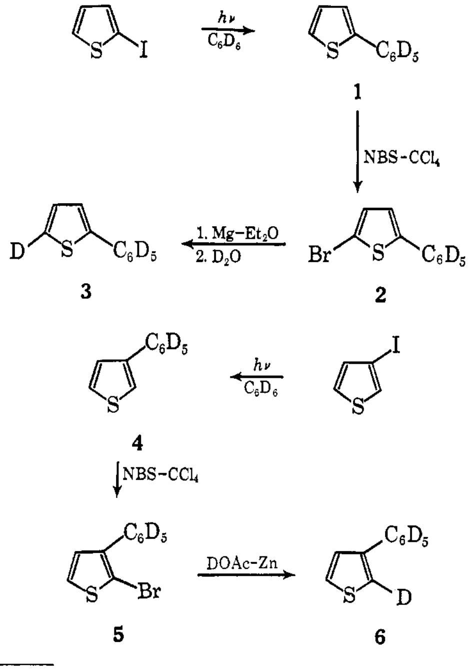
Deuterium would be expected to produce little substituent effect in this type of reaction and should distort the nature of the rearrangement under investigation to a minimal extent.[4] Location of the deuterium atom after rearrangement could be readily accomplished by nmr spectroscopy. The nmr spectra of disubstituted thiophenes have been extensively investigated by Gronowitz and Hoffman[5] who have shown that they give simple AB spectra with coupling constants characteristic of the mode of disubstitution.[6] Thus synthesis of only one specifically deuterated 2-phenylthiophene would be necessary and, for aid in nmr interpretation, one specifically deuterated 3-phenylthiophene.

Because of the severe overlap of the absorptions of the protons of the phenyl ring with those of the thienyl ring simple spectral analysis could not be carried out. Synthesis of pentadeuteriophenyl isomers was necessary to eliminate the phenyl proton absorptions.

Results

Syntheses of the 2- and 3-pentadeuteriophenylthiophenes were carried out by a modification of the photochemical arylation technique of Kharasch.[7] The overall syntheses of the two isomers are shown in Scheme I.

Scheme I



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[1] Presented in part at the 152nd National Meeting of the American Chemical Society, New York, N. Y., Sept 1966.

[2] (a) H. Wynberg and H. van Driel, *J. Am. Chem. Soc.*, **87**, 3998 (1965); (b) *Chem. Commun.*, 204 (1966); (c) H. Wynberg, R. M. Kellogg, H. van Driel, and G. E. Beekhuis, *J. Am. Chem. Soc.*, **88**, 5047 (1966); (d) H. Wynberg, H. van Driel, R. M. Kellogg, and J. Buter, *ibid.*, **89**, 3487 (1967).

[3] A similar experiment, using a methyl substituent, is described in the following paper.

[4] Extensive deuterium substitution in an aromatic molecule may produce the photophysical effect of slowing the $T_1 \rightarrow S_0$ *radiationless* transition and increasing phosphorescence quantum yield; see, for example: V. L. Ermolaev, *Soviet Phys.—Usp.*, **6**, 333 (1963), and J. G. Calvert and J. N. Pitts, Jr., "Photochemistry," John Wiley and Sons, Inc., New York, N. Y., 1966, pp 296–313. Striking photochemical effects on the relative rates of singlet *vs.* triplet reactions can occur; see, for example, D. R. Coulson and N. C. Yang, *J. Am. Chem. Soc.*, **88**, 4511 (1966). We obtain no differences in the type of reaction with perdeuteriophenylthiophenes; no attempt has been made to determine differences in fluorescence and phosphorescence quantum yields.

[5] S. Gronowitz, *Advan. Heterocyclic Chem.*, **1**, 8 (1963), and references cited therein.

[6] Values of J_{35} = 1.25–1.70 cps, J_{25} = 3.20–3.65 cps, J_{34} = 3.45–4.35 cps, and J_{45} = 4.90–5.80 cps are reported. An analysis of the AB spectra of the six isomeric phenylmethylthiophenes[3] gave average values of J_{35} = 1.4 cps, J_{25} = 3.0 cps, J_{34} = 3.5 cps, and J_{45} = 5.0 cps indicating no unexpected effect of the phenyl group on the coupling constants.

[7] These types of photoarylations have been investigated in this laboratory.[2a] A number of 2- and 3-arylthiophenes have been synthesized by this technique. Under the conditions used virtually no rear-

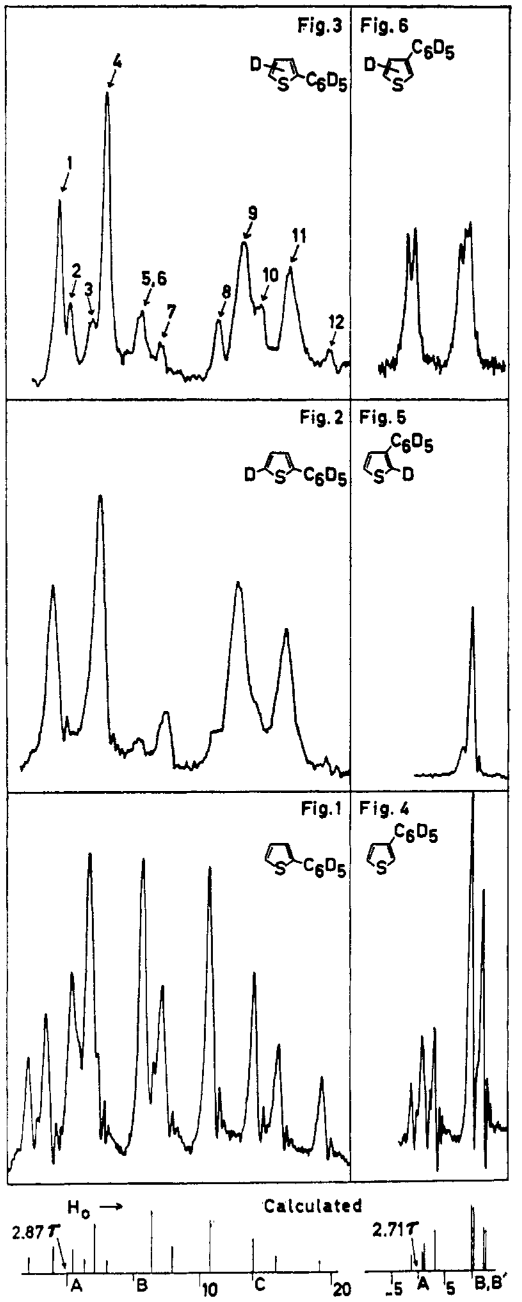
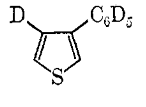


Figure 1–6. Spectra taken as 10% solutions in carbon tetrachloride for 2-pentadeuteriophenyl derivatives and in hexadeuterioacetone for 3-pentadeuterio derivatives.

Photolysis in hexadeuteriobenzene of 2- and 3-iodothiophenes gave, respectively, 2-pentadeuteriophenylthiophene (**1**) and 3-pentadeuteriophenylthiophene (**4**). Bromination of **1** with N-bromosuccinimide (NBS) gave 2-pentadeuteriophenyl-5-bromothiophene (**2**) and formation of the Grignard reagent from **2** followed by treatment with D_2O gave 2-pentadeuteriophenyl-5-deuteriothiophene (**3**). Similar bromination of **4** with NBS gave 2-bromo-3-pentadeuteriophenylthiophene (**5**).[8] Treatment of **5** with zinc and deuterioacetic acid under conditions described by Bak[9] gave 2-deuterio-3-pentadeuteriophenylthiophene (**6**). This procedure has been shown to occur with negligible H–D exchange;[9] all other syntheses were carried out in neutral or basic media to minimize the possibility of exchange.

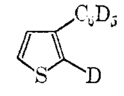
Irradiation of **3** was carried out for 6 hr in dilute (6×10^{-3} *M*) diethyl ether solution after which time about equal quantities of 2- and 3-substituted isomers were present. Under these conditions possible secondary photolysis of the 3-substituted isomer is minimized. The 2- and 3-substituted isomers were recovered and separated by preparative gas chromatography to give 2-pentadeuteriophenyl isomer **7** and 3-pentadeuteriophenyl isomer **8**. The nmr spectra of **7** (Figure 3) and **8** (Figure 6) as well as those of **1** (Figure 1), **3** (Figure 2), **4** (Figure 4), and **6** (Figure 5) are shown.

To interpret the nmr spectra for **7** and **8**, the relative chemical shifts and the coupling constants for 2- and 3-phenylthiophene must be determined. Parameters for 3-phenylthiophene are obtained from the spectrum of **4** (Figure 4). This is a spectrum of type ABB′ as designated by Richards and Schaefer[10] in which the chemical shifts of protons 4 and 5 (B and B′) are the same.[11] The spectrum may be readily solved for the difference in chemical shifts between A and BB′, $(\nu_B - \nu_A) = 10.1$ cps, and for $(J_{AB} + J_{AB'}) = 4.4$ cps, $J_{BB'}$ is not obtainable. The calculated line positions agree with those observed (Figure 4). Examination of Figure 6 shows two doublets for the 3-substituted product **8** $(\nu_B - \nu_A)$ the same as in Figure 4. A coupling constant of $J = 1.4$ cps is readily obtainable from the low-field doublet. This is obviously a J_{AB} coupling constant identifying the major product as 3-pentadeuteriophenyl-5-deuteriothiophene (**11**). A value of $J_{AB'} = 3.0$ cps is calculated by subtracting this value from the derived value of $(J_{AB} + J_{AB'})$. Thus a doublet, $J = 3.0$ cps, centered about the A and BB′ absorptions is expected for **9**. Within limits of detection (*ca.* 5%) this doublet is not seen. The singlet expected for the BB′ protons of **10** is observed in the high-field absorption of Figure 5. From the ratio of low-field to high-field protons, 0.83 to 1, and taking into account up to 5% of **9**, the composition of mixture **8** is 85–90% **11**, 5–10% **10**, and 0–5% **9**.



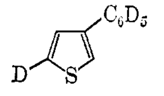
9

0–5%



10

5–10%



11

85–90%

The analysis of the spectrum of 2-substituted product **7** is more difficult. Nuclear parameters are difficult to directly obtain from the characteristic ABC spectrum of **1** (Figure 1).[12] However, examination of the nmr

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rangement of the arylthiophenes takes place. Similar arylations, namely with benzenoid derivatives, have been investigated: W. Wolf and N. Kharasch, *J. Org. Chem.*, **26**, 283 (1961); **30**, 2493 (1965).

[8] This reaction has been recently described: S. Gronowitz, N. Gjös, R. M. Kellogg, and H. Wynberg, *J. Org. Chem.*, **32**, 463 (1967).

[9] B. Bak, *ibid.*, **21**, 797 (1956).

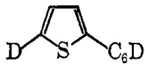
[10] R. E. Richards and T. Schaefer, *Mol. Phys.*, **1**, 331 (1958). These authors give expressions for the energies in the eight allowed and one combination transitions. The combination transition is not observed in the spectrum of 4.

[11] Spectra of 3-phenyl derivatives were always taken in acetone solution. In CCl_4 the chemical shifts of 3 become equal and the spectrum collapses to a singlet. Similar solvent effects have been noted with a number of other 3-substituted thiophenes; for instance 3,3′-dithienyl shows a singlet in CCl_4 but an ABB′ spectrum in acetone, whereas the thienyl protons of 3,3′-dithienylethylene are a singlet in acetone but give an ABB′ spectrum in CCl_4.

[12] J. D. Roberts, "Introduction to Spin-Spin Analysis," W. A. Benjamin, Inc., New York, N. Y., 1962; J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959.

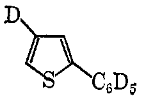
spectrum of **3** (Figure 2) allows assignment of the low-field doublet to the A proton and the high-field doublet to the C proton with $\nu_C - \nu_A = 14$ cps, $J_{AC} = 3.6$ cps. The deuterium broadening[13] of the high-field C proton identifies it as being in the 4 position adjacent to the deuterium atom in the 5 position. The location of the B proton may be guessed from the spectrum of product **7** (Figure 3) which shows what might be a doublet, $J = 1.5$ cps, centered 5 cps from the A proton. If this is due to the proton in the 5 position of 2-pentadeuteriophenyl-4-deuteriothiophene (**12**), this would locate the B proton. This assignment was checked by using values $(\nu_C - \nu_A) = 14$ cps, $(\nu_B - \nu_A) = 5$ cps, $J_{AC} = 3.6$ cps, $J_{AB} = 1.5$ cps, and an estimated value of $J_{BC} = 5.0$ cps to calculate the theoretical line positions of the ABC spectrum of **1**.[14] Reasonably good agreement is obtained as seen by inspection of Figure 1.

The spectrum of **7** (Figure 3) may be interpreted from these data. Peaks 1, 4 and 9, 11 are starting material **3** and account for 75–80% of product **7**. Peaks 2, 3 centered about the A absorption and 5, 7 centered about the B absorption, $J = 1.5$ cps, are from isomer **12**. Peaks 8, 10, and 12 are confusing because they are not centered about the B and C absorptions. An investigation of a sample of 2-phenyl-5-deuteriothiophene showed that absorptions in the region covered by peaks 8–12 are above the area of phenyl absorption eliminating the possibility of absorptions due to a partly protonated phenyl ring in **7**. The product **7** is gas chromatographically pure 2-pentadeuteriophenyl-substituted material and has good physical characteristics thus eliminating absorptions from extraneous impurities. The absorptions are most likely due to 2-pentadeuteriophenyl-3-deuteriothiophene (**13**). Peaks 10, 12, $J = 5.0$ cps, can be the high-field doublet of the C protons and peaks 8 and hidden peak 7 the doublet of the B proton. This requires an upfield shift of 1.5–2.0 cps for the B and C protons of **13**, a rather large shift for deuterium substitution,[13] but may rather be due to a concentration dependence of the chemical shift with this isomer. The composition of product **7** can be concluded to be 75–80% starting material **3** and roughly equal amounts of isomers **12** and **13**.



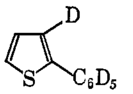
3

75–80%



12

ca. 10%



13

ca. 10%

Photolysis of 2-deuterio-3-pentadeuteriophenylthiophene (**6**) was carried out separately to check for the possibility of deuterium rearrangement. Under essentially similar conditions to the irradiation of **3**, gas chromatographically pure 3-substituted isomer was recovered uncontaminated by other products. Examination of the nmr spectra showed that approximately equal quantities of deuterium positional isomers **9**, **10**, and **11** had been formed. Coupling constants for all these isomers could be readily identified.

In all the reactions described in this publication, the spectra were carefully examined for evidence of hydrogen exchange reactions. The regions of phenyl proton absorption in 2- and 3-phenylthiophenes could be determined by comparison with the spectra of the pentadeuteriophenylthiophenes. Examination of photolysis products showed no unaccountable absorptions in the phenyl absorption regions. Such exchange reactions are in any case unlikely; photolysis of deuteriobenzene solutions and careful mass spectral examination of the products showed that no exchange occurred.[15] The photochemical hydrogen exchange reactions described by de Bie and Havinga[16] seem only to apply in highly acidic media.[17]

Discussion

The use of nmr spectroscopy–deuterium labeling in the solution this type of problem shows much promise. Large amounts of information may be derived from relatively simple experiments. Complete synthetic procedures for the synthesis of all isomers are not necessary so long as basic knowledge of the expected coupling constants is already in hand. This technique may be applied, with proper experimental design, to other systems.[18]

The results described in this paper are striking. The rearrangement of 2-pentadeuteriophenylthiophene to 3-pentadeuteriophenylthiophene occurs with a high degree of specificity. The rearrangement of 2-deuterio-3-pentadeuteriophenylthiophene represents a surprising "no-reaction reaction," the results of which suggest the necessity of extreme care in deciding that "no reaction" has occurred during an attempted photolysis.

The discussion of the mechanistic interpretations will be deferred to the last paper of this series.[19]

Experimental Section

Melting points are uncorrected; nmr spectra were taken on a Varian A-60 instrument with tetramethylsilane (TMS) as an internal reference; ultraviolet spectra were taken on a Zeiss PMQ II and wavelengths are given in millimicrons with the corresponding extinction coefficients (ϵ); analytical gas chromatography was done with an F & M 810 with hydrogen flame detectors, preparative gas chromatography with a Wilkens Aerograph A-700 Autoprep. Deuteriobenzene and deuterium oxide, both 99 atom % D, were purchased from Carl Roth (Karlsruhe). Merck activity 1 neutral aluminum oxide was used. N-Bromosuccinimide was commercial material carefully recrystallized from glacial acetic acid and thoroughly dried. 2- and 3-iodothiophenes were prepared by Mr. J. Buter.

2-Pentadeuteriophenylthiophene (1) was prepared by the photolysis of a mixture of hexadeuteriobenzene (100 g), 2-iodothiophene (1.5 g, 7.15 mmoles), and anhydrous sodium thiosulfate (3.0 g). Photolyses were carried out with a Hanau S-81 high-pressure mercury lamp equipped with a 15% sodium bromide in water filter-coolant which removed wavelengths below 245 mμ. The reaction was carried out under a nitrogen atmosphere at 65° for 5.75 hr. The hexadeuteriobenzene was distilled under aspirator vacuum

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(13) R. A. Hoffman and S. Gronowitz, *Arkiv Kemi*, **15**, 45 (1959). These authors have made detailed analyses of several deuterated thiophenes.

(14) Energy levels calculated by solution of third-order determinants as described in K. B. Wiberg and B. J. Nist, "Interpretation of NMR Spectra," W. A. Benjamin, Inc., New York, N. Y., 1962. The three combination transitions were not observed in the spectrum of **1**.

(15) J. P. Gragerov and M. Ya. Turkina, *J. Gen. Chem. USSR*, **33**, 1343 (1962).

(16) D. A. de Bie and E. Havinga, *Tetrahedron*, **21**, 2359 (1965); D. A. de Bie, Thesis, University of Leiden, Netherlands, 1966.

(17) The question of photoinduced intramolecular hydrogen (deuterium) shifts arises. Although the possibility cannot be unambiguously ruled out, such shifts accounting for an appreciable amount of rearrangement seem very unlikely in view of the fact that the more rearrangement prone phenyl group remains firmly attached to the same carbon atom during rearrangement.[2b]

(18) The elucidation of the dithienyl photolysis mechanism by a similar technique will be described: R. M. Kellogg, H. van Driel, J. Buter, and H. Wynberg, to be published.

(19) H. Wynberg, R. M. Kellogg, H. van Driel, and G. E. Beekhuis, *J. Am. Chem. Soc.*, **89**, 3501 (1967).

out of the reaction vessel into another reaction vessel held in a liquid nitrogen bath. Careful technique allowed the recovery of 96–97% of the hexadeuteriobenzene. The photolysis was repeated three times, each time with the same amount of 2-iodothiophene. The combined reaction residues were taken up in benzene, filtered, decolorized with Norit, and chromatographed on alumina (benzene eluent) to yield 2.35 g (14.6 mmoles, 68% yield) of crude **1**. Glpc (diethylene glycol succinate, 6 ft, 190°) showed the product **1** to contain less than 1% of the 3-phenyl derivative. Recrystallization (70% methanol–water) of a sample prepared in a separate reaction gave **1** as white platelets, mp 36–38°; ultraviolet spectrum in cyclohexane: λ_{max} 282 (13,700) and λ_{sh} 214 (8000).

2-Pentadeuteriophenyl-5-bromothiophene (2) was prepared by reaction of **1** (2.35 g, 14.6 mmoles) with NBS (2.64 g, 14.8 mmoles) and benzoyl peroxide (0.057 g, 0.24 mmole) in 24 ml of CCl_4.[20] Work-up followed by chromatography on alumina (benzene eluent) gave 2.89 g (1.2 mmoles, 81% yield) of crude **2**. Recrystallization from methanol gave white leaflets, mp 78° (lit.[20] for 2-phenyl-5-bromothiophene from methanol, 84–85°).

2-Pentadeuteriophenyl-5-deuteriothiophene (3) was prepared by treatment of **2** (1.44 g, 6 mmoles) with 280 mg of fresh magnesium in 7 ml of ethyl ether followed by reaction with deuterium oxide (1.0 ml). Filtration of the precipitate and chromatography of the product on alumina gave 0.83 g (5.1 mmoles, 85% yield) of **3**, mp 31–34°, after recrystallization from 70% methanol–water, 33.5–35°; ultraviolet spectrum in cyclohexane: λ_{max} 282 (14,500), and λ_{sh} 217 (7200).

3-Pentadeuteriophenylthiophene (4) was prepared by photolysis of 3-iodothiophene (3.0 g, 14.3 mmoles) in 1.5-g batches in hexadeuteriobenzene as described for **1**. Reaction temperature was maintained at 80°, and irradiation was carried out for 48–54 hr. Work-up as for **1** and recrystallization from 80% methanol–water gave 0.415 g (2.5 mmoles, 17% yield) of **4**, mp 89–90°; ultraviolet spectrum in cyclohexane: λ_{max} 258 (13,400) and λ_{max} 227 (14,800).

2-Bromo-3-pentadeuteriophenylthiophene (5) was prepared by treatment of **4** (0.317 g, 1.91 mmoles) with NBS (0.37 g, 2.08 mmoles) in 15 ml of refluxing CCl_4.[8] A small amount of benzoyl peroxide was added. When all the starting material had disappeared the reaction mixture was worked up as described for **2** to yield 0.3 g (1.22 mmoles, 64% yield) of the product **5**. The nmr spectrum in acetone showed two doublets, $J = 5.6$ cps, consistent with 4,5 coupling in the thiophene ring.[5,8]

2-Deuterio-3-pentadeuteriophenylthiophene (6) was prepared by refluxing **5** (0.30 g, 1.22 mmoles) with a mixture of acetic anhydride (1.3 ml) and deuterium oxide (1.3 ml) to which Zn (0.52 g, 8 mg-atom) had been added.[9] Reaction was carried out for 3 hr. The resulting mixture was diluted with water, filtered, and extracted three times with ether, and the ether extracts were washed with aqueous $NaHCO_3$ until neutral and once with water. The ether extracts were dried over $MgSO_4$. Removal of the ether left 2-deuterio-3-pentadeuteriophenylthiophene (**6**) (0.19 g, 97% yield), nmr (acetone) singlet.

Photolysis of 3 was carried out with 600 mg of **3** in 600 ml of analytical grade diethyl ether at 25° under a nitrogen atmosphere. A Hanau Q-700 industrial medium-pressure mercury lamp was used. After 5-hr irradiation, gas chromatography indicated that approximately equal amounts of 2- and 3-pentadeuteriophenylthiophenes remained. Filtration, concentration, and chromatography on alumina yielded 0.295 g of material of which an nmr (CCl_4) was taken. The mixture was separated by preparative gas chromatography (diethylene glycol succinate, 8 ft, 155°) and yielded 117 mg of 2-substituted material **8**, mp (after recrystallization from 70% methanol–water) 33–36.5° [ultraviolet spectrum in cyclohexane: λ_{max} 282 (14,100) and λ_{sh} 216 (7540)] and 135 mg of 3-substituted isomer **9**, mp (after recrystallization from 70% methanol–water) 89.5° [ultraviolet spectrum in cyclohexane: λ_{max} 258 (13,600) and λ_{max} 227 (15,300)]. The combined nmr spectra of **8** and **9** in CCl_4 were the same as that taken before gas chromatography; rearrangement during chromatography is thus precluded.

Photolysis of 2-deuterio-3-pentadeuteriophenylthiophene (6) (0.124 g, 0.75 mmole) was carried out with a Hanau S-81 medium-pressure mercury lamp in 125 ml of diethyl ether for 5.5 hr. Filtration and chromatography on alumina gave 65 mg (0.39 mmole) of material which by gas chromatography was shown to be only 3-pentadeuteriophenylthiophene. The nmr spectrum in acetone was that expected for a mixture of **9**, **10**, and **11** (see Figure 6).

Dark reactions of **3** or **6** were not observed when samples were allowed to stand in ether solution. No change in the nmr spectra occurred indicating no rearrangement in the absence of ultraviolet light.

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(20) A. Kosak, R. J. F. Palchak, W. A. Steele, and C. M. Selwitz, *J. Am. Chem. Soc.*, **76**, 4450 (1954).

The Photochemistry of Thiophenes. VI. Photorearrangement of Phenylmethylthiophenes

Hans Wynberg, G. E. Beekhuis, H. van Driel,[1] and Richard M. Kellogg

Contribution from the Department of Organic Chemistry, The University, Groningen, The Netherlands. *Received February 1, 1967*

Abstract: The six isomers of the phenylmethylthiophenes have been prepared and subjected to photolysis. The 2-phenyl-substituted isomers formed, as major rearrangement products, the 3-phenyl-substituted thiophene obtained by interchange of the 2,3-carbon atoms. Small amounts of the other possible isomers appear to be formed in the primary photochemical reaction. The 3-phenyl-substituted isomers formed one or two major products depending on the point of substitution of the methyl group. Small amounts of the other isomers were again formed in the primary photochemical process.

Arylthiophenes undergo deep-seated photoreorganization reactions involving changes in the order of carbon–carbon and carbon–sulfur bonding in the thiophene ring.[2,3] Interpretation of the mechanism can be furthered if the positions of all the carbon atoms in the thiophene ring after rearrangement are known. This may be accomplished by substituent labeling which involves preparation of each possible substituted isomer and determination of the rearrangement products. Analysis of the results from these types of experiments coupled with previous knowledge that the aryl group remains attached to the same carbon atom during rearrangement[2,4] and that no rearrangement occurs

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(1) Royal Dutch Shell Fellow, 1963–1966.

(2) H. Wynberg, H. van Driel, R. M. Kellogg, and J. Buter, *J. Am. Chem. Soc.*, **89**, 3487 (1967).

(3) R. M. Kellogg and H. Wynberg, *ibid.*, **89**, 3495 (1967).

(4) H. Wynberg and H. van Driel, *Chem. Commun.*, 204 (1966).