$$k^\circ_{\text{obsd}} = [H^+](k_{\text{intra}}/K_a + k_{H^+}{}^{S}) = [H^+](k_{\text{intra}}/K_a + 2k_{H^+}{}^{SH^+}) \quad (10)$$

The values in Table I inserted in eq 6 give the results shown in Table III.

Hydrolysis of **3** and **4** occurs to 95% through the intramolecular pathway. Only 87% of **5** is hydrolyzed through the intramolecular route. If the mechanism for hydrolysis of prostacyclin was electrostatic catalysis, i.e., mechanism 1 in Scheme I, then the extent of intramolecular catalysis for the pyridine compounds in the present investigation would be zero or at least very small. The difference in reactivity between the base form and the acid form of the substrates should be small and only an electrostatic effect similar to the one observed in the investigation of **9**[13] should be obtained. The rate acceleration shown in Table I should thus amount to a factor of approximately 2. This would of course be reflected in the rate profile as a very small change in the intermediate pH region instead of the large change observed (Figure 1). The interpretation of the results obtained in the present investigation clearly supports the existing evidence[2-4] for the mechanism with intramolecular protonation of the vinyl ether double bond, i.e., mechanism 2 in Scheme I.

The rate acceleration obtained for **3** and **4** is only half of that observed for prostacyclin, which might be due to different steric requirements in the intramolecular proton-transfer step from the acid function to the vinyl ether double bond. The extent of intramolecular catalysis will diminish if the proton transfer becomes more difficult and thus the observed rate acceleration will decrease.

The isomer **5** shows a much smaller rate acceleration than those obtained for **3** and **4** (Table I). The reason behind this is probably that, in the case of **5**, the cyclic transition state (including the proton that is transferred) is a nine-membered ring, whereas it is only a seven-membered ring for **3** and **4**. A similar observation has been made by Kresge who obtained a rate acceleration of 8 for hydrolysis of homoprostacyclin where an eight-membered ring is formed in the transition state.[15]

Acknowledgment. We are grateful to the Swedish Natural Science Research Council for financial support.

Supplementary Material Available: Rate data for the hydrolyses of (*Z*)- and (*E*)-2-methoxy-6-(2-pyridyl)hex-2-ene (**3** and **4**) and 2-methoxy-6-(2-pyridyl)hex-1-ene (**5**) in various solutions and equilibrium data from the pK_a measurements (Tables S1–S7) (23 pages). Ordering information is given on any current masthead page.

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[15] Chiang, Y.; Kresge, A. J. *J. Chem. Soc., Perkin Trans. 2* **1988**, 1083.

Thiophenes as Traps for Benzyne. 2. Cycloaddition and Ene Reactions[1]

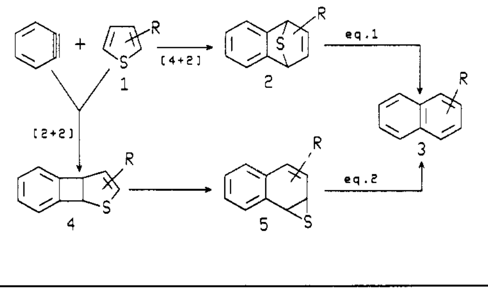
Manfred G. Reinecke* and Dario Del Mazza

Department of Chemistry, Texas Christian University, Fort Worth, Texas 76129

Received October 18, 1988

The reactions of 11 mono- and disubstituted thiophenes (**1b–1l**) with benzyne generated from diphenyliodonium 2-carboxylate (**7**) were studied under a standard set of conditions. The major products were naphthalenes (**3**) whose substitution patterns indicated that both [4 + 2] and [2 + 2] cycloaddition occurred, with the former predominating. A significant proportion of [2 + 2] cycloaddition was found only with the 3-halothiophenes **1i** and **1k**, suggesting enamine-like enhancement of the 2π-character of the thiophene. Benzo[*b*]thiophenes (**8**) were found in low yields in several of the reactions, and their substitution patterns suggested a [3 + 2] cycloaddition mechanism involving an intermediate betaine **11**. Ene (**17**) and especially double ene (**18**) products were observed with the alkylthiophenes **1b–d** and **1g**. The halothiophenes **1h–l** underwent substantial carbon–halogen bond cleavage leading to halogenated phenylthiophenes.

Recently we demonstrated that with the proper choice of precursor and reaction conditions benzyne could be induced to react with thiophene (**1**) to give primarily naphthalene (**3**), the product of apparent [4 + 2] cycloaddition to **2** followed by loss of sulfur (eq 1).[2] The present paper describes a more detailed investigation of this reaction as well as several others which lead to additional benzyne + thiophene-derived products.



Of particular interest is the extent to which naphthalene formation involves a stepwise [2 + 2] cycloaddition to **4** followed by rearrangement to **5** and loss of sulfur (eq 2) rather than a concerted [4 + 2] pathway (eq 1). The latter mechanism generally is much preferred in the reactions of benzyne with a wide variety of dienes,[3,4] including the related five-membered heterocycles furan[5] and pyrrole.[6] On the other hand, electron-rich thiophenes can react thermally with electron-deficient alkynes in a predominantly [2 + 2] manner.[7] Furthermore, the five-membered hetaryne, 2,3-didehydrothiophene (**6**), also reacts with appropriately labelled thiophenes to give products that

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[1] Taken in part from the Dissertation of D.D.M. submitted in partial fulfillment of the Ph.D. degree at Texas Christian University.

[2] Del Mazza, D.; Reinecke, M. G. *J. Org. Chem.* **1988**, *53*, 5799.

[3] Hoffman, R. W. *Dehydrobenzene and Cycloalkynes*; Academic Press: New York, 1967; Chapter 3.

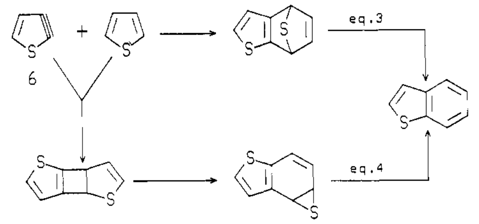
[4] Gilchrist, T. L. In *Supplement C, The Chemistry of Triple Bonded Functional Groups*; Patai, S.; Rappoport, Z., Eds.; John Wiley & Sons: New York, 1983; Part 1, Chapter 11.

[5] Newman, M. S.; Kannan, R. *J. Org. Chem.* **1976**, *41*, 3356.

[6] Gribble, G. W.; Allen, R. W.; Anderson, P. S.; Christy, M. E.; Colton, C. D. *Tetrahedron Lett.* **1976**, 3673.

[7] Benders, P. H.; Reinhoudt, D. N.; Trompenaars, W. P. In *Thiophene and its Derivatives*; Gronowitz, S., Ed.; John Wiley and Sons: New York, 1985; Part 1, Chapter X.

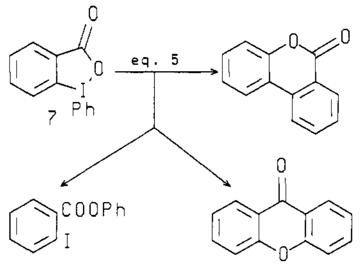
indicate that, instead of the [4 + 2] path (eq 3), [2 + 2] cycloaddition (eq 4) is the major reaction path.[8]

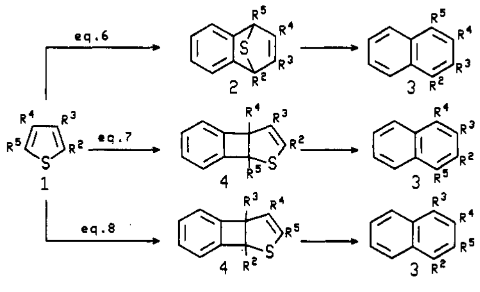


Knowledge of which mode of cycloaddition predominates in the benzyne + thiophene system therefore would contribute to an understanding of the chemistry of five-membered hetarynes[9,10] by indicating whether the preponderance of [2 + 2] cycloaddition in eq 4 is a characteristic property of the aryne **6** or of the thiophene **1**.

Results and Discussion

Accordingly, a series of 11 mono- and disubstituted thiophenes (**1**) were treated with benzyne in order to probe the regiochemistry as well as the effect of substituents on the course of the cycloaddition reaction. Benzyne was generated from that precursor, diphenyliodonium 2-carboxylate (**7**), and under those standard conditions (220 °C, 15 min, 0.05 M **7**) that had been determined for thiophene itself to maximize naphthalene (**3**) formation and minimize side reactions and analytical difficulties.[2,11] All of the benzyne + thiophene-derived products are summarized in the tables and discussed below except for some diaryl sulfides, which will be considered in a future publication.[12] In addition, side products arising from known[13] reactions (eq 5) of the precursor (**7**) alone, as well as alkylthiophene dimers analogous to that found in the decomposition of benzenediazonium 2-carboxylate in 2,5-dimethylthiophene (**1d**),[2] were sometimes observed in low yields but will not be discussed.





Naphthalenes, formed by [4 + 2] and [2 + 2] cycloaddition, are the major products observed for all thiophenes examined except **1j** (Table I). These two paths can be unambiguously distinguished with 3,4- (**1k**) or 2,5-disubstituted thiophenes (**1d,f,g,j,l**) since the former reaction gives 2,3- (**3k**) or 1,4-disubstituted naphthalenes (**3d,f,g,j,l**), respectively, according to eq 6 while the latter reaction gives 1,2-disubstituted naphthalenes (**3m,o–r**) with either type of thiophene according to either eq 7 or 8, which are redundant with these particular thiophenes. With the monosubstituted thiophenes, however, [2 + 2] cycloaddition can take place on two nonequivalent sides of the thiophene ring, only one of which will be detectable as arising via this path. Thus, for the 2-substituted thiophenes (**1b,e,h**) [2 + 2] attack on the substituted side (eq 8) will give the same product as [4 + 2] cycloaddition (eq 6) while 3-substituted thiophenes (**1c,i**) will do the same for [2 + 2] attack on the unsubstituted side (eq 7). With these thiophenes, therefore, the yields reported in Table I represent a minimum of reaction via the [2 + 2] route. It is unlikely, however, that a substantial portion of the so-called [4 + 2] product in Table I arises by a [2 + 2] reaction since, with two exceptions (**1i,k**) to be discussed below, this pathway, when unambiguously detectable, never accounts for more than a 3% yield of the particular naphthalene.

Table I. Naphthalenes (3) from Thiophenes (1) and Benzyne

substituents (thiophenes)	substituents (naphthalenes) (% yield)[a]	
	[4 + 2] products	[2 + 2] products
H (**1a**)	H (**3a**) (29)	
2-Me (**1b**)	1-Me (**3b**) (24)	2-Me (**3c**) (2)
3-Me (**1c**)	2-Me (**3c**) (25)	1-Me (**3b**) (1)
2,5-Me$_2$ (**1d**)	1,4-Me$_2$ (**3d**) (19)	1,2-Me$_2$ (**3m**) (2.5)
2-OMe (**1e**)	1-OMe (**3e**) (30)	2-OMe (**3n**) (1)
2,5-(OMe)$_2$ (**1f**)	1,4-(OMe)$_2$ (**3f**) (52)	1,2-(OMe)$_2$ (**3o**) (1.7)
2-OMe-5-Me (**1g**)	1-OMe-4-Me (**3g**) (54)	1-OMe-2-Me (**3p**) (1.9)[b]
2-Br (**1h**)	1-Br (**3h**) (18)	2-Br (**3i**) (0.4)
3-Br (**1i**)	2-Br (**3i**) (26)	1-Br (**3h**) (11.5)
2,5-Br$_2$ (**1j**)	1,4-Br$_2$ (**3j**) (<2)	1,2-Br$_2$ (**3q**) (<2)
3,4-Br$_2$ (**1k**)	2,3-Br$_2$ (**3k**) (12)[c]	1,2-Br$_2$ (**3q**) (9)
2,5-Cl$_2$ (**1l**)	1,4-Cl$_2$ (**3l**) (8)	1,2-Cl$_2$ (**3r**) (2.7)[d]

[a] Identification by GC/MS comparisons with authentic samples and quantitation by GC(FID) unless otherwise noted. [b] No other GC/MS peaks with $M^+ = 172$ were detected, and the mass spectra of **3g** and **3p** agree with literature values, which are significantly different from those of the other possible product, 2-methoxy-1-methylnaphthalene (**3s**) [Pelah, Z.; Wilson, J. M.; Ohashi, M.; Budzikiewicz, H.; Djerassi, C. *Tetrahedron* **1963**, *19*, 2233]. [c] Deduced from the identity of the mass spectra but the difference of the GC retention times compared to **3j** and **3q**. [d] Deduced by the identity of the mass spectra and the difference in the GC retention times compared to **3l**.

The consistently large perference for [4 + 2] over [2 + 2] cycloaddition products is clearly the most obvious result in Table I and indicates that this reaction is potentially competitive with the use of thiophene 1,1-dioxides for the synthesis of naphthalenes.[14] The absence of any other naphthalene isomers as well as the fact that isomeric thiophenes give isomeric naphthalenes indicates that relative rates of cycloaddition rather than relative product stabilities are being measured.

It can therefore be concluded that thiophenes preferentially react with benzyne as typical cisoid dienes[3–6] (eq 2), and the origin of the preferential [2 + 2] reactivity observed[8] with the hetaryne **6** (eq 4) is not due to the thiophene. While some pyrroles do give a minor proportion of [2 + 2] cycloadducts with tetrahalobenzynes,[15] the

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(8) Reinecke, M. G.; Newsom, J. G.; Almqvist, K. A. *Tetrahedron* **1981**, *37*, 4151.

(9) Reinecke, M. G. In *Reactive Intermediates*; Vol. 2, Abramovitch, R. A., Ed.; Plenum Press: New York, 1982; Chapter 5.

(10) Reinecke, M. G. *Tetrahedron* **1982**, *38*, 427.

(11) Del Mazza, D.; Reinecke, M. G. *Heterocycles* **1980**, *14*, 647.

(12) Reinecke, M. G.; Del Mazza, D.; Obeng, M., manuscript in preparation.

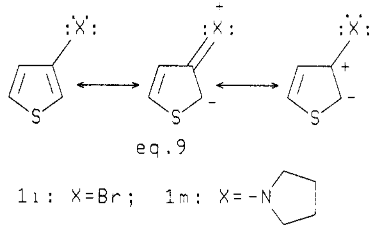
(13) Beringer, F. M.; Huang, S. J. *J. Org. Chem.* **1964**, *29*, 445.

(14) Nakayama, J.; Kuroda, M.; Hoshino, M. *Heterocycles* **1986**, *24*, 1233.

(15) (a) Ahmed, M.; Vernon, J. M. *J. Chem. Soc. Chem. Commun.* **1976**, 462. (b) Vernon, J. M.; Ahmed, M.; Kricka, L. J. *J. Chem. Soc., Perkin Trans. 1* **1978**, 837.

only cyclic, conjugated, cisoid dienes that preferentially react with six-membered arynes in this way are those that are nonplanar[16] or are constrained in rigid bicyclic systems.[17] The only reported exception to this generalization, the reaction of 3,4-didehydropyridine with cyclopentadiene,[18] recently has been shown in fact to yield the corresponding [4 + 2] product.[19]

The two examples in Table I that show the largest absolute and relative yields of [2 + 2] product are the 3-bromothiophenes **1i** and **1k**. It is further noteworthy that with 3-bromothiophene (**1i**) the more hindered, substituted side of the thiophene ring is substantially attacked. These not unrelated observations suggest the involvement of a resonance interaction (eq 9) similar to that proposed for



3-(1-pyrrolidinyl)thiophenes (**1m**) to explain their preferred [2 + 2] cycloaddition with electron-deficient alkynes *on the substituted side of the thiophene ring*.[20] The depicted bond polarization (eq 9) therefore could account for both the regiochemistry and the higher yields of the [2 + 2] products **3h** and **3q**. A similar polarization effect also may be responsible for the fact that the only detectable [2 + 2] product from 2-methoxy-5-methylthiophene (**1g**) was 1-methoxy-2-methylnaphthalene (**3p**) formed by attack on the methoxy side of the thiophene ring (eq 8) and not 2-methoxy-1-methylnaphthalene (**3s**), which would arise by attack on the methyl side (eq 7).

The variation in yield of cycloaddition products with the nature and position of thiophene substitution is probably the result of a complex interplay of steric and electronic effects as well as the availability of alternative reaction modes. Nevertheless, a few observations are possible. The highest yields were obtained with 2,5-dimethoxythiophene (**1f**) and 2-methoxy-5-methylthiophene (**1g**). Although the high diene reactivity of the former is well-known,[21] the high naphthalene yield in this case cannot be due entirely to the electron-donating effect of the methoxy substituents since replacing one with a methyl group does not lower the yield of naphthalenes. Another important factor is likely to be the blocking in **1f** and **1g** of both of the thiophene α-positions, which are especially susceptible to attack by electrophilic precursors of benzyne as demonstrated with thiophene itself.[2] This hypothesis is consistent with 2-methoxythiophene (**1e**) not giving significantly higher yields of naphthalenes than thiophene (**1a**) itself, since similar enhancement of both naphthalene formation and electrophilic side reactions at the open α-position would tend to balance out. Further support for this hypothesis comes from the observation that with the nucleophilic benzyne precursor (*o*-fluorophenyl)magnesium bromide, where electrophilic side reactions would not occur, naphthalene yields do increase markedly upon introduction of an α-methoxy group into the thiophene ring.[2] Finally, with the weaker electron-donating alkyl or halo substituents, where side reactions with electrophiles might be expected to be reduced, other side reactions such as the ene and double ene reaction or carbon–halogen bond cleavage (Table III) keep the naphthalene yields below 30%. The sole exception is 3-bromothiophene (**1i**) where the higher total yield of naphthalenes (37.5%) is due primarily to the increase in [2 + 2] product **3h** for reasons discussed previously.

Table II. Benzo[*b*]thiophenes (8) from Thiophenes (1) and Benzyne

substituents (thiophenes)	substituents (benzo[*b*]thiophenes) (% yield)[a]
H (**1a**)	H (**8a**) (0.5)
2-Me (**1b**)	H (**8a**) (0.5), 2-Me (**8b**) ca. (0.5)[b]
3-Me (**1c**)	H (**8a**) (0.5)
2,5-Me_2 (**1d**)	2-Me (**8b**) (3)
2-OMe (**1e**)	H (**8a**) (1)
2-Br (**1h**)	H (**8a**) (1.5)
3,4-Br_2 (**1k**)	3-Br (**8c**) (3.8)

[a] Identification based on GC/MS comparisons with authentic samples; yields determined by GC(FID) except for **1a** where GC/MS was used. [b] Approximate because of incomplete resolution from other reaction components.

Table III. Phenylthiophenes from Thiophenes (1) and Benzyne

substituents (thiophenes)	substituents (phenylthiophenes) (% yield)[a]
H (**1a**)	2-Ph (tr)[b]
2-Me (**1b**)	2-Me-3-Ph (**17a**) (1)[c,d] 2-CH_2Ph-3-Ph (**18a**) (3)
3-Me (**1c**)	3-Me-2-Ph (6),[d] 3-CH_2Ph-2-Ph (8)
2,5-Me_2 (**1d**)	2,5-Me_2-3-Ph (**17b**) (7)[d] 2-CH_2Ph-5-Me-3-Ph (**18b**) (13)
2-OMe-5-Me (**1g**)	5-OMe-2-Me-3-Ph (**18c**) (3)
2-Br (**1h**)	[e]ThPhBr_2 (4), ThPhBr (<2),[f] Th_2Ph (<2), $ThPh_2$Br (<2), Th_2PhBr (<2), **12b** (4), 13 (tr), 14 (9)
2,5-Br_2 (**1j**)	[e]ThPhBr_2, Th_2PhBr_2 (2 isomers),[g] Th_2PhBr_3,[g,h] **12b** (16)
2,5-Cl_2 (**1l**)[d]	ThPhCl_2 (3.8), **12a** (4.6), 15 (0.9)

[a] Unless otherwise noted the yields and structure assignments are based on GC/MS analyses and mechanistic rationales discussed in the text; Th = thienyl. [b] Identified by GC/MS comparison with an authentic sample. [c] Shown *not* to be 2-benzylthiophene by GC/MS comparison with an authentic sample (Table IV). [d] Yield by GC(FID). [e] Partial structural formula assigned from MS; i.e. M^+ and heteroatom content (isotope abundances). [f] Two isomers present, one of which was identified as 2-(*o*-bromophenyl)thiophene by GC/MS comparison with an authentic sample. [g] These three compounds are part of a preparative TLC fraction separated in 17–20% yield from the reaction mixture. [h] Only detected by solid inlet MS.

Benzo[*b*]thiophenes (**8**), although present in only low yields, are the second most prevalent products found in these reactions (Table II).[22] The parent compound **8a** has been reported previously from the reaction of thiophene with benzyne generated in the gas phase from the thermolysis of phthalic anhydride.[23] A mechanistic rationale

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[16] (a) Gassman, P. G.; Benecke, H. P.; Murphy, T. J. *Tetrahedron Lett.* **1969**, 1649. (b) Crews, P.; Beard, J. *J. Org. Chem.* **1973**, *38*, 522. (c) Lombardo, L.; Wege, D. *Tetrahedron* **1974**, *30*, 3945.

[17] (a) Yin, T. K.; Lee, J. G.; Borden, W. T. *J. Org. Chem.* **1985**, *50*, 531. (b) Anthony, I. J.; Byrne, L. T.; McCulloch, R. K.; Wege, D. *J. Org. Chem.* **1988**, *53*, 4123.

[18] (a) Kauffmann, T.; Hansen, J.; Udluft, K.; Wirthwein, R. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 650. (b) Kauffmann, T. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 543.

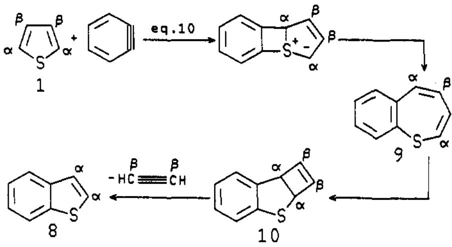
[19] Reinecke, M. G.; Brown, E. S.; Capehart, B. P.; Minter, D. E.; Freeman, R. K. *Tetrahedron*, **1988**, *44*, 5675.

[20] (a) Reinhoudt, D. N.; Okay, G.; Trompenaars, W. P.; Harkema, S.; van den Ham, D. M. W.; van Hummel, G. J. *Tetrahedron Lett.* **1979**, 1529. (b) Reinhoudt, D. N.; Geevers, J.; Trompenaars, W. P.; Harkema, S.; van Hummel, G. J. *J. Org. Chem.* **1981**, *46*, 424.

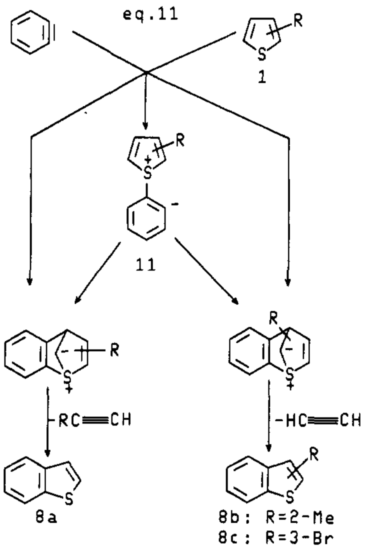
[21] Barker, J. H.; Huddleston, P. R.; Shutler, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 2483.

[22] A preliminary communication of these results has appeared in Del Mazza, D.; Reinecke, M. G. *J. Chem. Soc., Chem. Commun.* **1981**, 124.

was proposed that involved insertion of benzyne into the C–S bond of thiophene followed by rearrangement and elimination of a molecule of acetylene composed of the two original β-carbons of the thiophene ring (eq 10). Subsequent studies on some of the proposed intermediates in this scheme have found that benzothiepins (**9**) ring contract to cyclobutenes (**10**) under photochemical, not thermal, conditions,[24,25] which instead lead to sulfur extrusion and naphthalene formation.[25,26] The results in Table II are also incompatible with the mechanism in eq 10, since the substitution pattern of the products **8** reveals that it is not the two β-carbons but rather an α- and a β-carbon atom from the same side of the thiophene ring that are lost. The structural relation between the sulfur and the retained α- and β-carbon atoms in the product benzo[*b*]thiophene **8** is therefore the same as in the original thiophene **1**.



A mechanism consistent with this pattern involves a [3 + 2] cycloaddition of benzyne to the sulfur and β-carbon of the thiophene ring followed by elimination as an alkyne of the α- and β-carbon atoms of the other side of the thiophene ring (eq 11). With 2-methylthiophene (**1b**) both sides of the thiophene ring are attacked while in the other cases the only benzo[*b*]thiophenes observed are those from attack on the less hindered side.



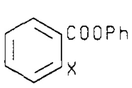
Benzyne is well-known to undergo [3 + 2] cycloadditions with a variety of classical 1,3-dipoles[27] as well as with several sulfur and selenium heterocycles of low aromaticity[28,29] or high dipolar character.[30,31] In the latter examples the overall reaction parallels eq 11 in that alkynes[28] or nitriles[29,30] are eliminated. The lower yields with thiophenes are probably due to the higher aromatic stabilization and lower dipolar character of this heterocycle.[32] Although it is not possible to determine the concertedness of this reaction from the present results, the intermediacy of the betaine **11** finds analogy in the above-cited reactions[28–30] and in the well-known reactions of benzyne with sulfides in general.[33] Furthermore, the nature and origin of several naphthyl sulfides and other previously observed products[2] support the intervention of intermediates similar to **11**.[12]

Table IV. Mass Spectra of Ene, Double Ene, and Related Products

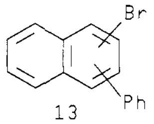
compounds[a]	mass spectra, *m/e* (rel intensity) M$^+$	M – H	M – Ph
2-Me-3-Ph (**17a**)	174 (94)	173 (100)	97 (25)
2-CH$_2$Ph	174 (98)	173 (100)	97 (52)
2-CH$_2$Ph-3-Ph (**18a**)	250 (100)	249 (38)	173 (91)
3-Me-2-Ph	174 (98)	173 (100)	97 (32)
3-CH$_2$Ph-2-Ph	250 (100)	249 (35)	173 (63)
2,5-Me$_2$-3-Ph (17b)	188 (100)	187 (77)	111 (20)
2-CH$_2$Ph-5-Me-3-Ph (**18b**)	264 (100)	263 (21)	187 (64)
5-OMe-2-Me-3-Ph (**17c**)	204 (100)	189 (64)[b]	161 (79)[c]
diphenylmethane[d]	168 (100)	167 (90)	91 (18)
2-methylbiphenyl[d]	168 (75)	167 (100)	91 (6)

[a] Substituted thiophenes unless full name is given. [b] M – Me. [c] M – Me – CO. [d] NBS Library of Standard Mass Spectra.

Phenylthiophenes, the formal insertion products of benzyne + thiophenes, were detected above the trace level only with the α-halo- (**1h,j,l**) and the alkyl-substituted thiophenes (**1b–d,g**). With the first category of compounds the complexity and composition of the products as shown in Table III, as well as the detection of halobenzenoid species such as **12–15**, indicate that extensive cleavage of the carbon–halogen bond occurs, possibly induced by electrophilic species generated during the decomposition of the benzyne precursor **7**.[2,34] With each of the alkylthiophenes, however, no more than two phenylated compounds are observed, and their mass spectra (Table IV)



12a: X=Cl
12b: X=Br



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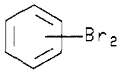

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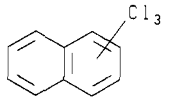

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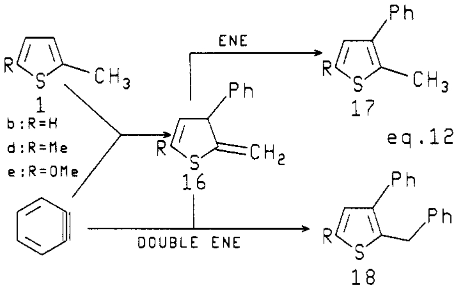
show molecular ions consistent with 1:1 (**17**) and 1:2 benzyne adducts (**18**) and fragmentation patterns with prominent M − H and M − Ph peaks. The relative intensities of the latter are much greater for the 1:2 adducts, suggesting that they may contain a benzyl moiety. This hypothesis is supported in the mass spectra (Table IV) of the isomeric pairs 2-methylbiphenyl vs diphenylmethane and the product **17a** vs an authentic sample of 2-benzylthiophene, the expected[35] insertion product of benzyne and 2-methylthiophene.

Although insertion reactions of benzyne are known they are relatively rare compared to the ene reactions,[36] which with alkylbenzenes and benzyne gives only *o*-benzylbiphenyls, the double ene (1:2) condensation products.[37] While not as exclusive, this same preference is observed with the alkylthiophenes and suggests, along with the mass spectral data cited above, the ene and double ene structures for the adducts as shown in Table III. The predominance of double ene products such as **18** probably has its origin in the preference of the initial adduct **16** to react with a second molecule of benzyne rather than undergo a disallowed, concerted 1,3-hydrogen migration to give **17** (eq 12). The fact that *any* single ene products are observed with the alkylthiophenes, but not with the alkylbenzenes, is probably due to the higher temperatures (220 °C vs 45 °C) required to generate benzyne from precursor **7** compared to benzenediazonium 2-carboxylate.[37] With the methylmethoxythiophene **1g** only the single ene product **17c** was detected. Apparently with this trap the effectiveness of the [4 + 2] cycloaddition reaction (eq 6, Table I) lowers the benzyne concentration sufficiently to permit the initial ene adduct **16c** to rearomatize completely before reaction with a second molecule of benzyne is likely to occur.



eq.12

Conclusion

The above results demonstrate that with regard to [4 + 2] cycloaddition, [2 + 2] cycloaddition, and the ene reaction the reactivity of thiophenes toward benzyne is much the same as the analogous benzene compounds. The [3 + 2] cycloaddition leading to benzo[*b*]thiophenes is related to reactions of less aromatic heterocycles and suggests the intervention of dipolar intermediates in the reactions of thiophenes with benzyne. This question will be examined in more detail in a subsequent publication.[12]

Experimental Section

Materials. The following known reactants or authentic samples were synthesized by the cited literature procedures or, where modified procedures were used, the physical and spectral properties (melting point, NMR, MS) were identical with literature values or were consistent with the assigned structures: 2-methoxythiophene (**1e**),[38] 2,5-dimethoxythiophene (**1f**),[21] 2-methoxy-5-methylthiophene (**1g**),[38] 1,4-dimethoxynaphthalene (**3f**),[39] 1,2-dimethoxynaphthalene (**3o**),[40] 1-methoxy-4-methylnaphthalene (**3g**),[41] 1-methoxy-2-methylnaphthalene (**3p**),[42] 1,2-dibromonaphthalene (**3q**),[43] 1,4-dichloronaphthalene (**3l**),[2] diphenyliodonium 2-carboxylate (**7**),[44] 2-methylbenzo[*b*]thiophene (**8b**),[45] 3-bromobenzo[*b*]thiophene (**8c**),[46] 2-phenylthiophene,[47] 2-benzylthiophene,[48] 2-(*o*-bromophenyl)thiophene.[49]

Standard Conditions. A mixture of 3 mL of the distilled and dried (4-Å molecular sieves, 24 h) thiophene **1** and 50 mg of the anhydrous (P_2O_5, vacuum) benzyne precursor **7** was heated in an evacuated (1 mm), ca. 13 mL, thick-walled glass vial (12 mm i.d., 16 mm o.d.) for 15 min at 220 ± 20 °C as described in ref 2. The products were identified as indicated in the tables using for GC/MS analyses a Finnigan 1020 OWA quadrupole mass spectrometer containing a 1.8-m glass column with a 3% OV-1 liquid phase. Quantitation was performed with an appropriate internal standard as previously described[2] on either the above GC/MS or on a Perkin-Elmer Sigma 3 instrument[50] with flame ionization detection (FID) and the following 1.6 mm i.d. nickel columns packed on Gas-Chrom Z 80-100M: A, 10% Carbowax 20M, 3 m; B, 7% same, 2 m; C, 3% same, 1.8 m; D, 7% Bentone-34 plus 5% SE-52, 3 m. Complete analysis of a reaction mixture usually required several columns and, in the case of **1h** and **1i**, a tandem arrangement of columns B and D.[51]

Acknowledgment. This research was supported by grants from the TCU Research Foundation and The Robert A. Welch Foundation. The hospitality of the Department of Chemistry of the University of British Columbia and especially Professor James P. Kutney during the preparation of a portion of this manuscript is gratefully acknowledged.

Registry No. 1 (R^2 = CH_2Ph, R^3 = R^4 = R^5 = H), 13132-15-5; 1 (R^2 = Ph, R^3 = Me, R^4 = R^5 = H), 14300-30-2; 1 (R^2 = Ph, R^3 = CH_2Ph, R^4 = R^5 = H), 119566-90-4; **1a**, 110-02-1; **1b**, 554-14-3; **1c**, 616-44-4; **1d**, 638-02-8; **1e**, 16839-97-7; **1f**, 58386-20-2; **1g**, 31053-55-1; **1h**, 1003-09-4; **1i**, 872-31-1; **1j**, 3141-27-3; **1k**, 3141-26-2; **1l**, 3172-52-9; **3a**, 91-20-3; **3b**, 90-12-0; **3c**, 91-57-6; **3d**, 571-58-4; **3e**, 2216-69-5; **3f**, 10075-62-4; **3g**, 24821-54-3; **3h**, 90-11-9; **3i**, 580-13-2; **3k**, 13214-70-5; **3l**, 1825-31-6; **3m**, 573-98-8; **3q**, 5438-13-1; **3r**, 2050-69-3; **7**, 78610-84-1; **12a**, 41998-16-7; **12b**, 1989-22-6; **17a**, 16939-16-5; **17b**, 5682-08-6; **17c**, 119566-91-5; **18a**, 119528-97-1; **18b**, 119566-92-6.

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