

# Some Observations on the Chemical, Photochemical, and Spectral Properties of Thiophenes

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To many chemists thiophene (**1**) is merely one member of the inexhaustible supply of heteroaromatic com-



pounds.<sup>1</sup> Known for nearly 100 years, thiophene has never found large-scale industrial use, although its successful application in the semisynthetic penicillins is well documented.<sup>2</sup>

It is the purpose of this brief survey to point out certain unique features of the chemistry of thiophene with special emphasis on our own work as it pertains to certain geometrical, photochemical, and optical parameters.

Although thiophene in much of its chemical behavior resembles benzene as an aromatic compound, we will emphasize those structural and chemical features which differ from those of benzene (*vive la différence*): (a) treatment of thiophene and most of its derivatives with Raney nickel causes reductive desulfurization to butane or substituted butanes; (b) as a five-membered ring, substituents on thiophene have a different relation to one another than similar substituents in a six-membered ring; (c) the unsubstituted thiophene ring directs electrophilic substitution to the  $\alpha$  (or 2) position nearly exclusively.

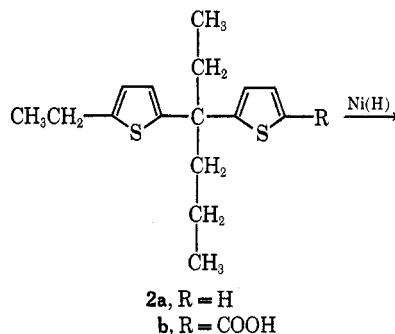
This multifacet nature of the thiophene ring has intrigued us for some time. The chemical phenomena described in this Account may at times seem to be unconnected. In fact the conceptually connecting link is the very nature of the thiophene ring.

## Desulfurization

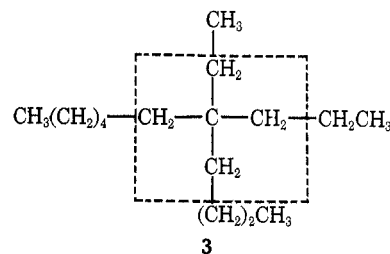
Our early work on the chemistry of thiophene derived from the simple premise that this heteroaromatic compound could undergo virtually all of the normal aromatic substitution reactions, but that the ring system **1** could also be converted smoothly into a four-carbon saturated unit by reductive desulfurization.<sup>3</sup>

In addition to the application of this concept to the synthesis of long-chain compounds,<sup>3</sup> its use in the preparation of asymmetric ethylpropylbutylhexylmethane

(**3**) is illustrative.<sup>4,5</sup> Normal aromatic substitution re-



$[\alpha]_{578} 0.13^\circ$  (neat) for R = H



$[\alpha]_{578} < 0.009^\circ$  (neat)

actions led to the synthesis of **2b**. The latter could be resolved because the enantiomers exhibited optical rotation. The enantiomers exhibit rotation because of the differences between the aromatic thiophene ring and the alkyl substituents. Decarboxylation led to **2a** which still shows significant optical activity.

Desulfurization of optically active **2a** must furnish one enantiomer of **3** since racemization cannot occur.<sup>6</sup> The lack of rotation of **3** thus proves that, with present day instruments, there are limitations to the statement: Optical activity can be observed, between 220 and 578 m $\mu$ , in all compounds of type  $R_1R_2R_3R_4C$  in which  $R_1 \neq R_2 \neq R_3 \neq R_4$ .

## Strains and Stresses

A second simple premise concerns the geometry of an aromatic five-membered ring compared to that of a six-membered ring. Inspection of **4** and **5** shows at once

(1) A. R. Katritzky, *Naturwissenschaften*, **56**, 97 (1969).

(2) M. S. Manhas and A. K. Bose, "Synthesis of Penicillin, Cephalosporin C and Analogs," Marcel Dekker, New York, N. Y., 1969, pp 62, 84, 104.

(3) See J. Smuszkowicz and E. J. Modest, *J. Amer. Chem. Soc.*, **72**, 571 (1950), and H. Wynberg, A. Logothetis, and D. Verploeg, *ibid.*, **79**, 1972 (1957), for some early examples and C. R. Pettit and E. E. van Tamelen, *Org. React.*, **12**, 356 (1962), for a general review.

(4) H. Wynberg, G. L. Hekkert, J. P. M. Houbiers, and H. W. Bosch, *J. Amer. Chem. Soc.*, **87**, 2635 (1965).

(5) R. T. Morrison and R. N. Boyd, "Organic Chemistry," 2nd ed, Allyn and Bacon Inc., Boston, Mass., 1966, p 84.

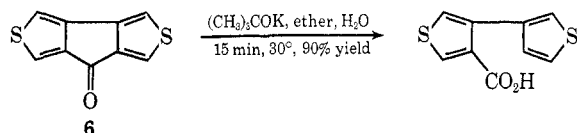
(6) H. J. Monkhorst, *Chem. Commun.*, 1111 (1968). The problem of obtaining an  $sp^3$  carbon in a plane with four surrounding (carbon) atoms has attracted theoretical attention recently; see R. Hoffmann, *J. Amer. Chem. Soc.*, **92**, 4992 (1970).

that: (a) a ring system fused to a thiophene ring will

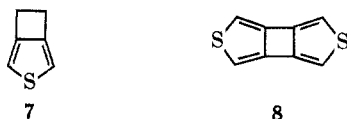


be under *greater* strain than a similar ring fused to benzene,<sup>7</sup> while (b) ortho substituents should experience *less* steric interference in a thiophene ring than in a benzene ring.

The correctness of these premises was shown in a number of positive<sup>8</sup> and negative ways.<sup>9</sup> The unusual reactivity of ketone<sup>10</sup> **6**, for instance, its rapid hydrolysis under exceedingly mild conditions, must be due to



a large extent to ring strain caused by fusion of two thiophene rings to a third five-membered ring.<sup>11</sup> Another indication of this increase in ring strain has been our complete failure over a period of 4 years to prepare the thiophene analogs of either benzocyclobutene or biphenylene, that is **7** or **8**, or any of their isomers, by methods successful for the benzo analogs. One ap-



proach to a mixed system has had some success recently.<sup>12</sup> We predict rich awards in novel chemical and physical properties for the chemists who succeed in preparing these strained systems. We are continuing our attempts.

Proceeding to the corollary of the strain argument, the lower steric requirements of ortho substituents in five-membered aromatic systems is best exemplified by the smooth ortho-*tert*-butylation<sup>13</sup> of 2,5-di-*tert*-butylfuran (**9**) to 2,4,5-tri-*tert*-butylfuran (**10**). In contrast,



*p*-di-*tert*-butylbenzene cannot be converted to an *o*-tri-

(7) The reverse argument: *i.e.*, changes in the chemical and physical properties of the aromatic ring, obviously is an automatic complementary premise. See ref 8 for a detailed discussion and bibliography.

(8) H. Wynberg and D. J. Zwanenburg, *J. Org. Chem.*, **29**, 1919 (1964); A. Kraak, A. K. Wiersema, P. Jordens, and H. Wynberg, *Tetrahedron*, **24**, 3381 (1968).

(9) P. J. A. Frints, J. R. Potoski, E. Jones, O. H. Oldenzel, and H. Wynberg, work in progress.

(10) P. Jordens, G. Rawson, and H. Wynberg, *J. Chem. Soc.*, 273 (1970).

(11) G. Rawson and H. Wynberg, *Recl. Trav. Chim. Pays-Bas*, in press.

(12) P. J. Garratt and K. P. C. Vollhardt, *Chem. Commun.*, 109 (1970).

(13) H. Wynberg and U. E. Wiersum, *ibid.*, 1 (1965).

*tert*-butylbenzene by direct tertiary butylation. Instead acetylenic<sup>14</sup> or photochemical<sup>15</sup> routes are necessary. The differences between furan and thiophene are sufficiently significant, however, both in geometrical parameters as well as in chemical properties, that the successful ortho-*tert*-butylation of furan cannot be extrapolated to thiophene. As a matter of fact thiophene is unique in that *no o*-di-*tert*-butyl derivative has been reported to date. This is not due to a lack of effort.<sup>16,17</sup>

In addition to the intrinsic interest in preparing stable but sterically hindered compounds, the possibility of obtaining photochemical intermediates in valence bond isomerizations<sup>15</sup> gives the work added allure. Thus van Tamelen<sup>18</sup> has isolated ring-opened products by irradiating **10** while tetrakis(trifluoromethyl)thiophene has, on gas-phase photolysis, also furnished what appears to be an intermediate in the valence bond isomerization of this highly substituted thiophene.<sup>19</sup>

## Heterohelicenes

Of recent interest is the preparation,<sup>20</sup> resolution,<sup>20,21</sup> racemization,<sup>22</sup> structure determination,<sup>23</sup> and absolute configuration determination<sup>24</sup> of the heterohelicenes. Better than any single example this work exemplifies the many advantages which are inherent when thiophene is chosen as a building block in the solution of selected problems.

The pioneering work of Newman and his students<sup>25</sup> on hexahelicene (**11**) is well documented.<sup>26,27</sup> Martin and his coworkers have made crucial and major contributions in opening up improved synthetic routes to hexa-, hepta-, octa-, and even higher helicenes, in resolution techniques, and in a careful analysis of the spectral, especially nmr, properties of helicenes.<sup>28-33</sup>

(14) C. Hoogzand and W. Hubel, *Tetrahedron Lett.*, 637 (1961).

(15) E. E. van Tamelen, *Angew. Chem.*, **77**, 759 (1965), for leading references.

(16) H. Wynberg and Ae. de Groot, *Chem. Commun.*, 171 (1965); Ae. de Groot, Ph.D. Dissertation, Groningen, 1967; H. Wynberg and U. E. Wiersum, *J. Org. Chem.*, **30**, 1058 (1965); U. E. Wiersum, Ph.D. Dissertation, Groningen, 1968; G. J. Visser, A. Vos, Ae. de Groot, and H. Wynberg, *J. Amer. Chem. Soc.*, **90**, 3253 (1968); E. H. Wiebenga and E. Bouwhuis, *Tetrahedron*, **25**, 453 (1969).

(17) See R. M. Kellogg, J. K. Dik, H. van Driel, and H. Wynberg, *J. Org. Chem.*, **35**, 2737 (1970), for another unsuccessful attempt to prepare 3,4-di-*tert*-butylthiophene by photochemical means.

(18) E. E. van Tamelen and T. H. Whitesides, *J. Amer. Chem. Soc.*, **90**, 3894 (1968).

(19) H. A. Wiebe and J. Hecklen, *Can. J. Chem.*, **47**, 2965 (1969); S. Braslavsky, H. A. Wiebe, and J. Hecklen, Canadian Atomic Energy Society Publication No. 164-70.

(20) H. Wynberg and M. B. Groen, *J. Amer. Chem. Soc.*, **90**, 5338 (1968); R. H. Martin and M. Deblecker, *Tetrahedron Lett.*, 3597 (1969).

(21) H. Wynberg and M. B. Groen, submitted for publication.

(22) H. Wynberg and M. B. Groen, *Chem. Commun.*, 964 (1969).

(23) G. Stulen and G. J. Visser, *ibid.*, 965 (1969).

(24) M. B. Groen, G. Stulen, G. J. Visser, and H. Wynberg, *J. Amer. Chem. Soc.*, **92**, 7218 (1970).

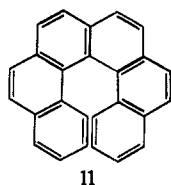
(25) (a) M. S. Newman, W. B. Lutz, and D. Lednicer, *ibid.*, **77**, 3420 (1955); (b) M. S. Newman and D. Lednicer, *ibid.*, **78**, 4765 (1956); (c) M. S. Newman, R. S. Darlak, and L. Tsai, *ibid.*, **89**, 6191 (1967).

(26) A. Moscowitz, *Tetrahedron*, **13**, 48 (1961).

(27) M. B. Groen, Ph.D. Dissertation, Groningen, 1970.

(28) M. Flammang-Barbieux, J. Nasielski, and R. H. Martin, *Tetrahedron Lett.*, 743 (1967).

(29) R. H. Martin and D. Bogaert-Verhogen, *ibid.*, 3045 (1967).



For those uninitiated to the mysteries and delights of helicene chemistry, brief mention of some of the salient features and problems is in order. Helicenes, a name introduced by Newman, refers to ortho-condensed aromatic hydrocarbons in which all benzene rings are angularly anellated such as to give helically shaped molecules. Optically active helicenes exhibit very high specific optical rotations since the chromophore itself—in this case the entire aromatic molecule—is inherently dissymmetric (in the case of all benzene ring helicenes) or inherently asymmetric (in the case of the heterohelicenes). We will use helicenes to denote the benzenoid class and heterohelicenes for compounds containing the helicene framework in which one or more of the benzene rings have been replaced by heterocyclic rings.

**Synthesis of Helicenes.** The synthesis of racemic helicenes remains a laborious process<sup>25c</sup> involving at certain crucial stages the possibility of isomer formation which cannot be avoided. Thus the key step in the synthesis of helicenes introduced by Martin<sup>32</sup> is the photochemical cyclodehydrogenation of substituted stilbenes.<sup>34</sup> In the example<sup>32</sup> shown in Figure 1, the double cyclization can, in principle, lead to a total of ten isomers due to the facts that the positions ortho to the ethylene moiety are not identical and that the differences in reactivity in the ground and excited states are small.<sup>35</sup> In some cases deuterium-labeling studies<sup>32</sup> have aided the assignment of the helical structures.

**Resolution of Helicenes.** Resolution of helicenes has thus far proven to be both exciting and frustrating. Newman<sup>25</sup> resolved hexahelicene by selective complexation with one of the enantiomers of 2-(2,4,5,7-tetra-nitro-9-fluorenylideneaminoxy)propionic acid (TA-PA). This reagent has also been tried in Martin's and our laboratory in solution<sup>26</sup> as well as in conjunction with column and thin-layer chromatographic techniques.<sup>33</sup> The results are merely fair. Martin<sup>30</sup> introduced a crystal-picking technique which has worked in some, but not all, cases examined.<sup>27,33</sup> Enantiomor-

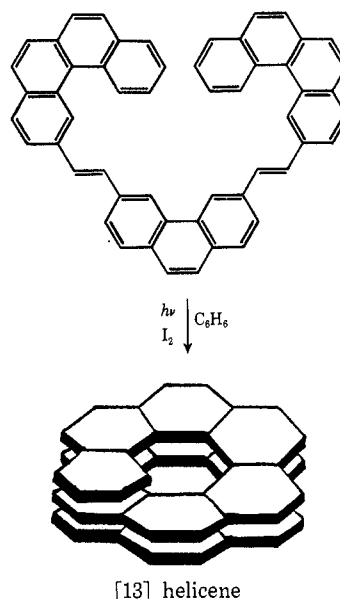


Figure 1.

phous surfaces cannot be recognized by this technique (Pasteur, 1848), and every crystal has to be dissolved and measured before one can be certain whether it is optically active. Levorotatory as well as dextrorotatory crystals are found in the mixture, and optical purity may vary from 0 to 100%. Clearly other techniques need to be introduced, for instance, transformation of a helicene *via* a suitable functional group to a mixture of diastereomeric derivatives or enzymatic destruction of one enantiomer of a racemate. The key-word here is "suitable functional group." Although Martin has a facile route to hexahelicene-carboxylic acid,<sup>29,33</sup> the helicene skeleton itself is clearly unsuited for the unambiguous preparation of substituted derivatives.<sup>36</sup>

**Geometry, Structure, and Racemization of Helicenes.** Helicenes are inherently dissymmetric chromophores<sup>37</sup> having a twofold symmetry axis,  $C_2$ , perpendicular to its cylindrical helix (see Figure 2). The nature of the benzene ring allows no variation in the pitch of the helix. X-Ray structure studies are a bit more difficult because no heavy atom is present.<sup>38</sup> Racemization can be studied to a limited extent only.<sup>39</sup>

**Spectra and Absolute Configuration of Helicenes.** Of critical importance in determining the structure of the helicenes is a correct interpretation of the nmr spectrum. This difficult problem has been studied using computer simulation.<sup>31</sup> Although large differences in shielding and deshielding are evident and aid in inter-

(30) R. H. Martin, M. Flammang-Barbieux, J. P. Cosyn, and M. Gelbeke, *Tetrahedron Lett.*, 3507 (1968).

(31) R. H. Martin, N. Defay, A. P. Figeys, M. Flammang-Barbieux, J. P. Cosyn, M. Gelbeke, and J. J. Schurter, *Tetrahedron*, **25**, 4985 (1969).

(32) R. H. Martin, G. Morren, and J. J. Schurter, *Tetrahedron Lett.*, 3683 (1969).

(33) We acknowledge with pleasure and gratitude the continued free exchange of information between the laboratory of Professor Martin and our laboratory and many personal communications.

(34) See C. O. Parker and P. E. Spoerri, *Nature (London)*, **166**, 603 (1950), and E. V. Blackburn and C. J. Timmons, *Quart. Rev., Chem. Soc.*, **23**, 482 (1969), for a recent survey. See also S. D. Cohen, M. V. Mijovic, and C. A. Newman, *Chem. Commun.*, 722 (1968), for a discussion of anthracene formation from stilbenes.

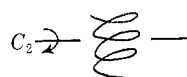
(35) W. H. Laarhoven, Th. J. H. M. Cuppen, and R. J. F. Nivard, *Recl. Trav. Chim. Pays-Bas*, **87**, 687 (1968); H. Güsten, L. Klasinc, and O. Volkert, *Z. Naturforsch. B*, **24**, 12 (1969); M. Scholz, F. Dietz, and M. Mühlstadt, *Tetrahedron Lett.*, 2835 (1970).

(36) To our knowledge no chemical reactions with optically active helicenes have been reported.

(37) K. Mislow, "Introduction to Stereochemistry," W. A. Benjamin, New York, N. Y., 1965, p 28.

(38) See I. R. Mackay, J. M. Robertson, and J. G. Sime, *Chem. Commun.*, 1470 (1969), for the X-ray structure determination of a complex of hexahelicene.

(39) D. M. Hall, *J. Chem. Soc.*, 3674 (1956), and more recently Ch. Goedicke and H. Stegemeyer, *Tetrahedron Lett.*, 937 (1970), have measured the racemization rates of 9,10-dihydro- and pentahelicene, respectively. The statement by the latter authors that hexahelicene racemizes at the melting point has no basis in fact.



dissymmetric cylindrical helix



asymmetric conical helix

Figure 2.

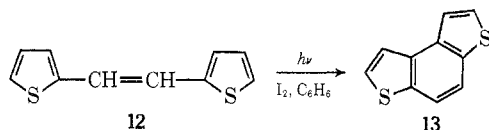
preparing these spectra,<sup>31</sup> it is evident that the extensive spin-spin coupling normal for aromatic hydrocarbons results in complex spectra.

For a determination of the absolute configuration, several theoretical and experimental approaches are possible. The theoretical approach<sup>26,40</sup> is dependent upon the choice of a few critical parameters. These parameters can only be obtained from the detailed structure and geometry of the helicene and from an accurate assignment of those absorption bands whose rotational strengths dominate the direction of rotation. Lacking these data, it is not surprising that authors<sup>26,40</sup> have alternately assigned right- and left-handed helicity to (+)-hexahelicene.

Experimental approaches to the absolute configuration problem involving X-ray techniques are facilitated by the presence of a heavy atom. Although bromo-substituted hexa-, hepta-, and nonahelicenes have been prepared by Martin,<sup>33</sup> the lack of good crystals of one antipode has impeded progress.

**The Heterohelicenes in Prospect.** It would be a miracle indeed if the inclusion of one or more thiophene rings in aromatic helical molecules would solve all of the intriguing problems posed above. Nevertheless it appears that most ambiguities typically arising from an all-benzene helix are removed by the introduction of one sulfur atom for a C=C. In many respects the hetero- and benzenoid helicenes complement one another.

**Synthesis of Heterohelicenes.** Simultaneous with Martin's early work we had established that dithienylethylenes cyclize uniquely and in high yield to benzodithiophenes<sup>41</sup> without rearrangement (see below). Since



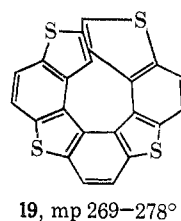
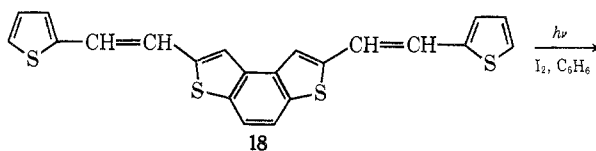
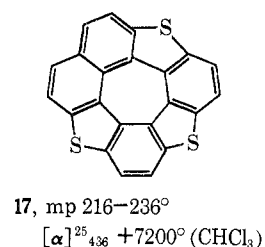
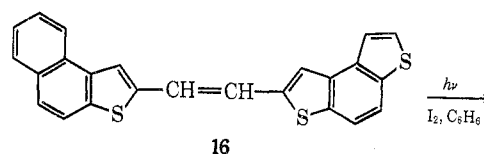
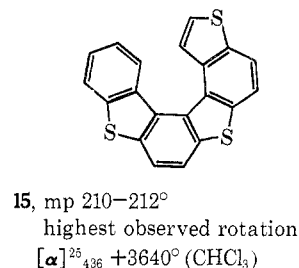
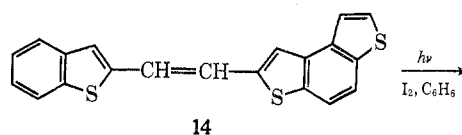
one, and only one, position in the thiophene ring is available for ring closure, no isomers can be formed, regardless of the dissymmetrical nature of the starting olefin. Three further examples suffice.<sup>20,42a</sup>

The fact that ring closure occurs in a unique manner obviates the need for structure proof *via* deuterium labeling. The "building blocks" for the synthesis of

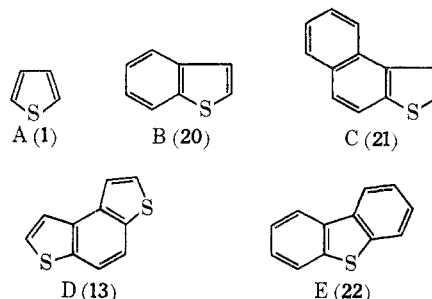
(40) C. M. Kemp and S. F. Mason, *Tetrahedron*, **22**, 629 (1966); R. Brewster, *Top. Stereochem.*, **2**, 40 (1967); I. Tinoco and R. W. Woody, *J. Chem. Phys.*, **40**, 160 (1964); D. D. Fitts and J. G. Kirkwood, *J. Amer. Chem. Soc.*, **77**, 4940 (1955); O. E. Weigang, J. A. Turner, and P. A. Trouard, *J. Chem. Phys.*, **45**, 1126 (1966); H. Looyenga, Ph.D. Dissertation, Leiden, 1955.

(41) R. M. Kellogg, M. B. Groen, and H. Wynberg, *J. Org. Chem.*, **32**, 3093 (1967).

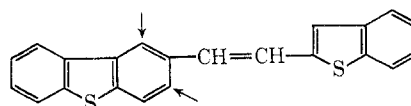
(42) (a) M. B. Groen, H. Schadenberg, and H. Wynberg, work in progress. (b) M. B. Groen, J. M. Pal, and H. Wynberg, work in progress.



heterohelicenes are readily accessible. Using units A, B, C, D, and E<sup>42b</sup> in simple combinations allows the



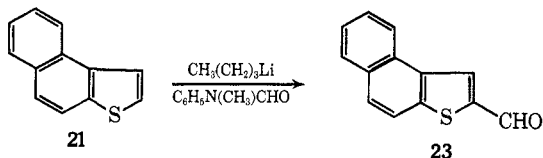
We have used dibenzothiophene (unit E) in one helicene synthesis and find as expected that ring closure of



yields the two possible isomers.

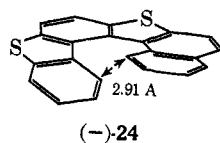
preparation of 15 different olefins and, after photocyclization, 15 different helicenes. Among these 15 heterohelicenes we find three different hexahelicenes and six different heptahelicenes.

Although electrophilic substitution of benzo- and naphthothiophenes may lead to mixtures of isomers, the sequence lithiation, followed by formylation, *e.g.*



allows the introduction of a versatile functional group at a predictable site.<sup>42</sup> Note that the same situation obtains with helicenes **15**, **17**, and **19** since these helicenes have a terminal thiophene ring.

**Resolution and Reactions of Optically Active Heterohelicenes.** Our first resolutions of heterohelicenes were performed using Martin's technique of picking the individual crystals of the helicene in question.<sup>20</sup> Since experimental details about this intriguing technique are virtually nonexistent, the results of an actual experiment performed on the helicene benzo[*d*]naphtho[1,2-*b*:4,3-*b'*]dithiophene (**24**) are described in Table I. Only active crystals are recorded. Obviously, many crystals



(sometimes as many as 16) were measured without rotation being observed. It is evident that this technique, though exceedingly valuable for spectral purposes, cannot be used for obtaining sufficient quantities for further studies. To this end two different routes have been studied.

One makes use of those heterohelicenes whose terminal rings are thiophene, allowing the introduction of a suitable functional group. Thus the heptahelicene **17** is converted to the aldehyde **25** in high yield. Alternately<sup>43</sup> ring closure of the olefin **26** furnishes the methylheptahelicene **27**. The latter can be transformed to **25** by any of a number of standard procedures. Progress has already been made in resolving an aldehyde similar to **25** *via* its *l*-menthoxy-carbohydra-zide.<sup>43</sup>

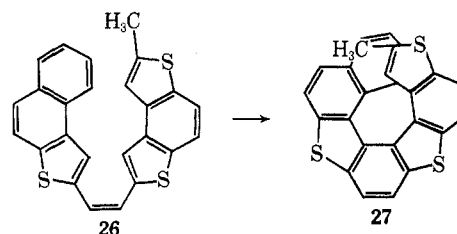
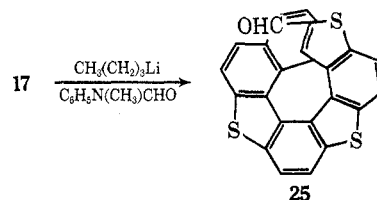
A second approach of considerable intrinsic interest has been partial resolution of **17** by crystallization from (-)- $\alpha$ -pinene.<sup>44</sup> The results are shown in Table II. Each experiment was conducted starting with 50 mg of **17** in 10 ml of (-)- $\alpha$ -pinene. Crystallization from toluene-petroleum ether (bp 30-60°) mixtures resulted in

**Table I**  
Optical Rotation of Some Crystals of **24** at 436  
 $m\mu$  ( $\text{CHCl}_3$ ) at 25°

Weight of the crystal, mg	Measured rotation, $\alpha$ , deg	Specific rotation, $[\alpha]$ , deg
0.59	+0.170	+580
0.47	+0.060	+260
0.53	-0.515	-1950
0.35	-0.385	-2200
0.40	-0.190	-950
0.22	+0.480	+4360

**Table II**  
Resolution of **17** from (-)- $\alpha$ -Pinene

Yield of <b>17</b> , crystals, mg	Conditions of crystallization	Measured rotation, $\alpha_{436}$ , deg	Specific rotation, $[\alpha]_{436}$ , deg
7	-25° (4 days)	+3.60	+1000
13	-25° (1 day)	+2.43	+370
4	-25° (4 hr)	+4.27	+2400
16	+20° (1 day)	+0.27	+34



70% recovery of inactive material. We believe that this resolution is a combination of thermodynamic and kinetic factors.<sup>27,44</sup>

Starting from 15 mg of partially resolved **17** obtained by the method outlined above, optically active di(naphtho[2,1-*b*]thieno)[3,2-*e*:3',2'-*e'*]benzo[1,2-*b*:4,3-*b'*]bis-[1]benzothiophene (**29**), an undecahelicene, was synthesized. The sequence used is important in establishing a general route to different optically active heterohelicenes dependent only on the resolution of one general precursor.

**Geometry, Structure, and Racemization of Heterohelicenes.** The building units A through E furnish heterohelicenes having a varying number of thiophene and benzene rings. Using a 60° internal angle for the benzene ring and a 45° internal angle for the thiophene ring (see Figure 3) a series of helicenes can be constructed having varying degrees of optical stability.

Table III lists some helicenes of increasing size. Details of the racemization studies have been published elsewhere.<sup>22</sup>

The complete X-ray structure of **24** has now been determined<sup>23</sup> and the nearest distance between carbon atoms was found to be 2.91 Å, in excellent agreement

(43) H. Wynberg and P. G. Lehman, work in progress; resolution by the method of Woodward. See R. B. Woodward, T. P. Kohman, and G. C. Harris, *J. Amer. Chem. Soc.*, **63**, 120 (1941).

(44) M. B. Groen and H. Wynberg, manuscript submitted for publication.

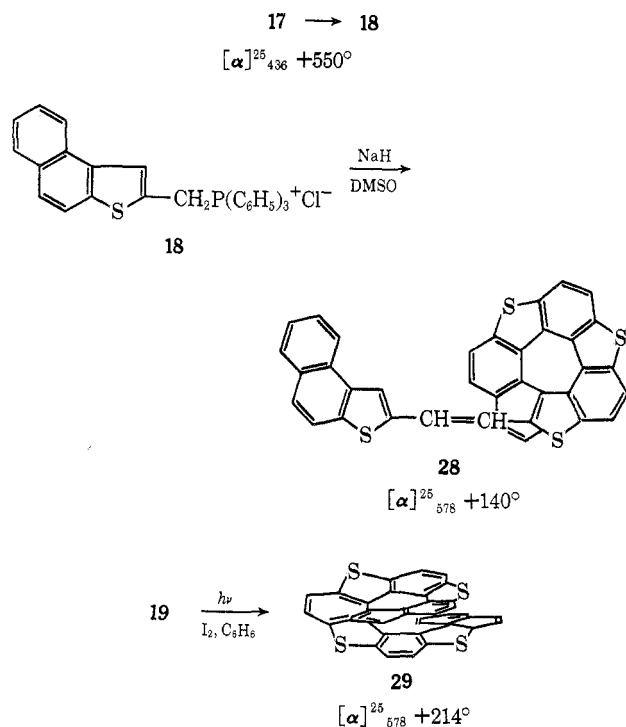


Table III

	Units <sup>a</sup>	Angle <sup>b</sup>	Racemization
 30	B + B	$3 \times 60 = 180^\circ$	Not resolved
		$2 \times 45 = 90^\circ$	
		$270^\circ$	
15	B + D	$3 \times 60 = 180^\circ$ $3 \times 45 = 135^\circ$ $315^\circ$	$\Delta H^\ddagger = 22.0$ kcal/mole $t_{1/2}^{25} = 13.0$ min
24	B + C	$4 \times 60 = 240^\circ$ $2 \times 45 = 90^\circ$ $330^\circ$	$\Delta H^\ddagger = 25.4$ kcal/mole $t_{1/2}^{25} = 241$ min
19	D + D	$3 \times 60 = 180^\circ$ $4 \times 45 = 180^\circ$ $360^\circ$	Optically stable at $25^\circ$
11		$6 \times 60 = 360^\circ$	Optically stable at $25^\circ$
17	C + D	$4 \times 60 = 240^\circ$ $3 \times 45 = 135^\circ$ $375^\circ$	Optically stable at $25^\circ$

<sup>a</sup> Units refer to the structures of thiophene (A), benzothiophene (B), naphthothiophene (C), and benzodithiophene (D) from which the precursors (diarylethylenes) for the heterohelicenes are prepared. <sup>b</sup> The angle refers to the internal angle (see Figure 3).

with calculations.<sup>45</sup> (For a flat molecule, this distance would be 1.12 Å, clearly an impossible situation.) It is evident that the use of a thiophene unit has facilitated study in this area since (a) variation in pitch has allowed several racemization parameters to be measured<sup>22</sup> and (b) the heavy sulfur atom has facilitated accurate X-ray structure determination of an uncomplexed and unsubstituted helicene.<sup>23</sup>

**Spectra and Absolute Configuration of Heterohelicenes.** The insulation of several benzene rings by a

(45) C. A. Coulson and S. Senent, *J. Chem. Soc.*, 1819 (1955); M. A. Herraez Zarza and F. Sanchez, *An. Real Soc. Espan. Fis. Quim., Ser. B*, 61, 953 (1965).

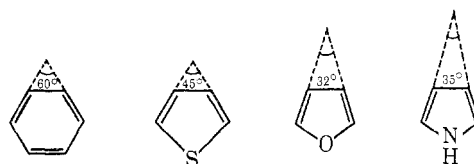


Figure 3.

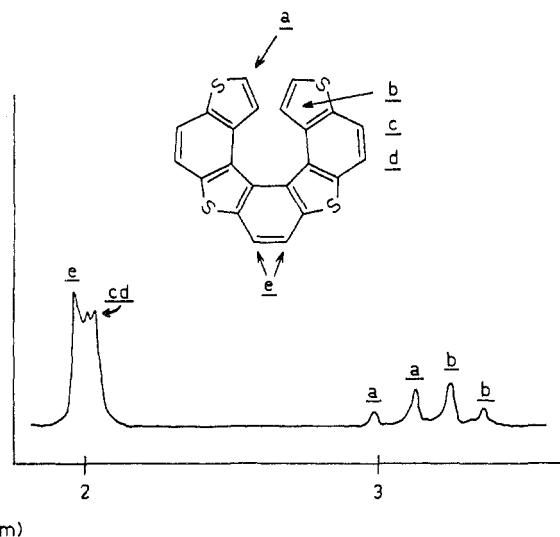


Figure 4.

thiophene ring immediately results in a simplified nmr spectrum, as is evident from inspection of Figure 4. All protons are well resolved; deuteration experiments (thiophene  $\alpha$  proton) confirmed the assignments.

Particularly instructive in Figure 5 is the change in chemical shift of the proton indicated by the letter A (the end thiophene ring  $\beta$  proton) and the proton indicated by the letter Z. The A proton can be seen to shift to *lower* fields up to and including the [5]helicene. This is due to an increase in *deshielding* caused by the approaching aromatic ring. Rapid increase in *shielding* occurs as soon as the true helix is formed resulting in the dramatic upfield shift shown. The total change is more than 3 ppm, a very sensitive measure of changes in shielding conditions. The gradual and steady shift of the Z protons to lower field (*ca.* 5 Hz for every additional ring) is predictable. Martin has also observed end protons at very high fields.<sup>31</sup>

In Figures 6 and 7, selected spectral data showing ORD, CD, and uv curves are shown.<sup>46</sup> The spectra show more fine structure than do the benzo analogs, and appropriate bands can be assigned with reasonable certainty.

Groen,<sup>27</sup> using the theory of Moscovitz<sup>26</sup> and Mason,<sup>40</sup> has calculated the absolute configuration of the heterohelicenes using: (a) the  $\alpha$ ,  $\beta$ , and para band assignments indicated in Figure 6; (b) the structure parameters as determined by Stulen and Visser,<sup>23</sup> and

(46) Mass spectral data<sup>27</sup> are omitted because of lack of space. Ring closure to "hetero" coronene structures is observed with the heptahelicenes, in contrast to coronene formation which occurs with hexahelicene; see R. C. Dougherty, *J. Amer. Chem. Soc.*, 90, 5788 (1968).

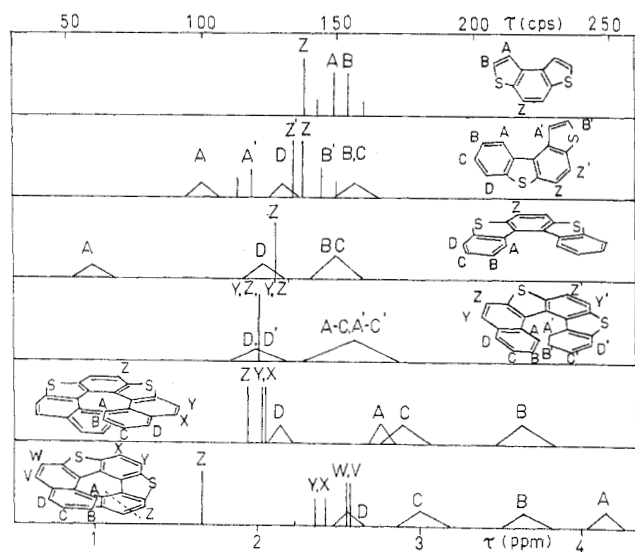


Figure 5. Schematic representation of the nmr spectra of a series of heterohelicenes ( $\text{CDCl}_3$  solutions).

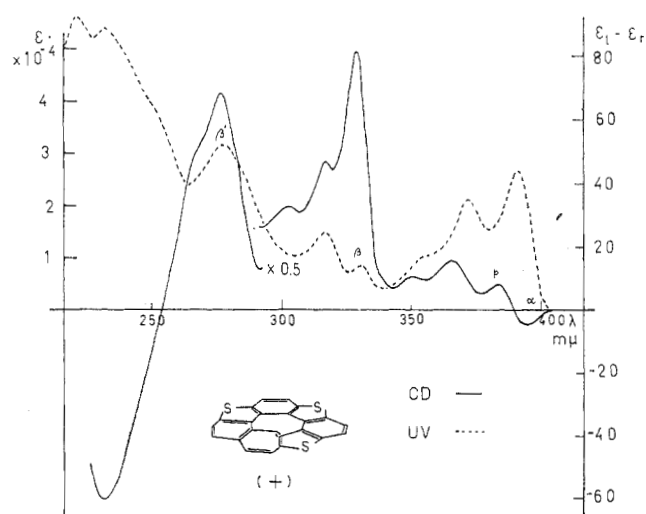


Figure 6. The CD and uv spectra of (+)-**17** in  $\text{CH}_2\text{OH}$  (CD) and  $\text{C}_6\text{H}_{12}$  (uv).

(c) transitional bond order changes (as shown in Figure 8) of benzodithiophene used as a model. His calculations predict that those heterohelicenes which contain the benzodithiophene chromophore and rotate plane-polarized light to the right have right-handed helicity. This prediction,<sup>27</sup> made in April 1970, was verified recently (July 30, 1970) by Stulen and Visser, who determined the absolute configuration of **24** and showed that the (-) isomer had left-handed helicity.<sup>24</sup>

### Photochemical Rearrangements

The final topic which we must mention, albeit briefly, is the quite general photochemically induced valence bond isomerization of substituted thiophenes. The reaction was discovered accidentally,<sup>47</sup> and we have studied it intensively during the past 5 years.<sup>48</sup> Thiophene hereby joined an increasing number of aromatic systems known to undergo valence bond isomeriza-

(47) H. Wynberg and H. van Driel, *J. Amer. Chem. Soc.*, **87**, 3998 (1965).

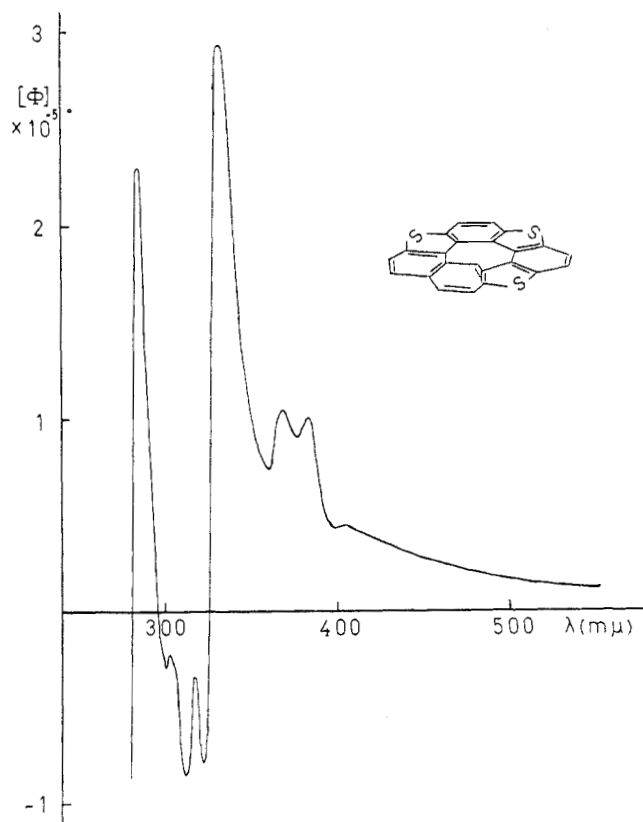


Figure 7. The ORD spectrum of (+)-**17** in  $\text{CHCl}_3$ .

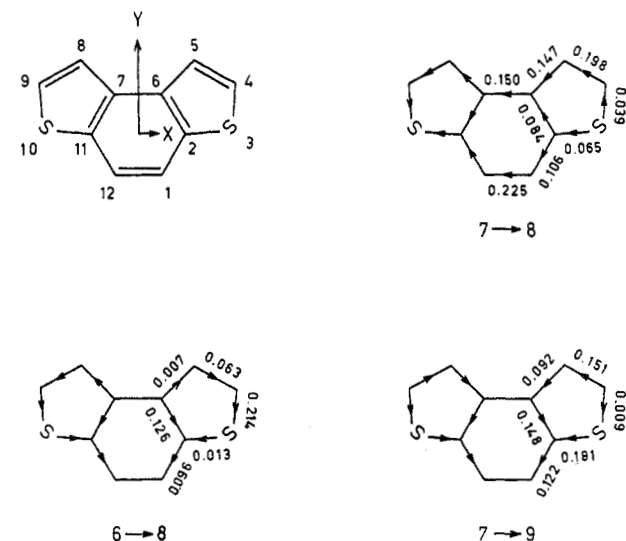


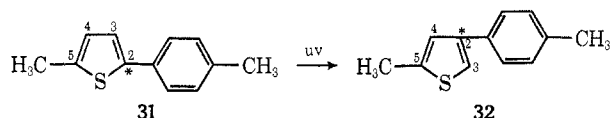
Figure 8. The direction and magnitude of the transitional bond order changes of the three lowest energy transitions of (planar) benzo[1,2-*b*:4,3-*b'*]dithiophene. The coordinate system is right-handed Cartesian ( $z$  axis not shown).

tions.<sup>15,48</sup> With the possible exception of the imidazoles and indazoles,<sup>49</sup> the number of substituted thiophenes shown to rearrange exceeds that of any other aromatic type, not excluding benzenes. A reasonably complete list is shown in Table IV.

(48) For paper IX see R. M. Kellogg, J. K. Dik, H. van Driel, and H. Wynberg, *J. Org. Chem.*, **35**, 2737 (1970). This paper contains a reasonably complete bibliography on photochemically induced aromatic valence bond isomerizations.

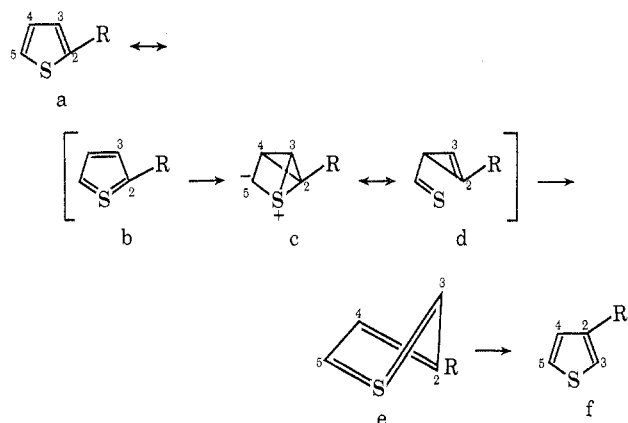
(49) H. Tiefenthaler, W. Dörscheln, H. Göth, and H. Schmidt, *Helv. Chim. Acta*, **50**, 2244 (1967).

The salient features of this rearrangement can be summarized as follows. (1) The rearrangement pro-



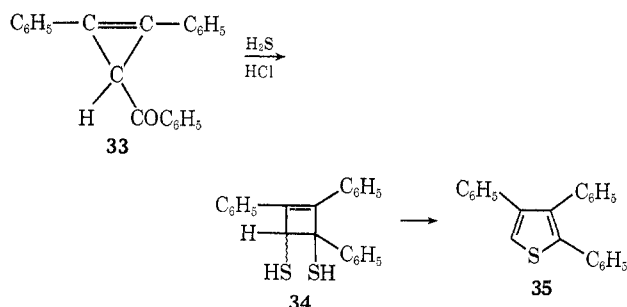
ceeds with mono- and disubstituted alkyl-, aralkyl-, and aryl-substituted thiophenes. Pyridyl, furyl, carbonyl, or olefinic substituents inhibit the rearrangement. No rearrangement of the benzene ring is observed. (2) No ring-carbon to substituent bonds are broken during the rearrangement. (3) Carbon atoms 2 and 3 interchange without concomitant C<sub>4</sub>-C<sub>5</sub> interchange. (4) The reaction proceeds *via* the first excited singlet state.<sup>50</sup> (5) No intermediates have been isolated, although unstable adducts resulting from the reaction of the excited (S<sub>1</sub>) 2-phenylthiophene with singlet quenchers such as perylene have been obtained.<sup>50</sup>

A mechanism involving either a cyclopropene intermediate, or sulfur-valence-expanded structure, seems to fit most of the data and can best be depicted as shown below. Gas-phase photolysis studies of tetra-



kis(trifluoromethyl)thiophene show that such a species (c or d), when properly stabilized,<sup>19</sup> may be capable of existence.

In our laboratory Groen prepared the cyclopropene **33**. When this ketone was treated with H<sub>2</sub>S and HCl at -40° in absolute ethanol an unstable orange oil, probably the triphenylcyclobutene **34**, was formed (no thioketone was detected). This oil was converted to 2,3,4-triphenylthiophene (**35**) in good yield when it was heated.



(50) R. M. Kellogg and H. Wynberg, *Tetrahedron Lett.*, 5895 (1968).

Table IV  
Photoinduced Rearrangement of Substituted Thiophenes<sup>a</sup>

Starting material	Products	Yield, %	Ref
2-Methyl	3-Methyl	9	48
2- <i>tert</i> -Butyl	3- <i>tert</i> -Butyl	27	48
2-Phenyl	3-Phenyl	40	47, b
3-Phenyl	No rearrangement		47, b
2-( <i>p</i> -Tolyl)	3-( <i>p</i> -Tolyl)	42	b
2-( $\alpha$ -Naphthyl)	2-( $\alpha$ -Naphthyl)	40	b
2-(2-Thienyl)	2,3'-Dithienyl	35	47, 48
2-(2-Furyl)	3-(2-Furyl)	5	c
2-(2-Pyridyl)	No rearrangement		d
2-Methyl-5-phenyl	2-Methyl-4-phenyl	20	e
2-Phenyl-4-methyl	3-Methyl-4-phenyl	37	e
2-Phenyl-3-methyl	2-Methyl-3-phenyl	22	e
2,5-Diphenyl	No rearrangement		b
2,3-Diphenyl	Phenanthro[9,10- <i>b</i> ]-thiophene	80	b
2,5-Di- <i>tert</i> -butyl	2,4-Di- <i>tert</i> -butyl	27	e

<sup>a</sup> This list is not complete. Nearly twice as many substituted thiophenes have been shown to rearrange. In general, negatively substituted thiophenes (NO<sub>2</sub>, CHO, COCH<sub>3</sub>) do not rearrange photochemically. <sup>b</sup> H. Wynberg, H. van Driel, R. M. Kellogg, and J. Buter, *J. Amer. Chem. Soc.*, **89**, 3487 (1967). <sup>c</sup> H. Wynberg, H. J. M. Sinnige, and H. M. J. C. Creemers, *J. Org. Chem.*, in press. <sup>d</sup> H. Wynberg, T. J. van Bergen, and R. M. Kellogg, *ibid.*, **34**, 3175 (1969). <sup>e</sup> H. Wynberg, G. E. Beekhuis, H. van Driel, and R. M. Kellogg, *J. Amer. Chem. Soc.*, **89**, 3498 (1967).

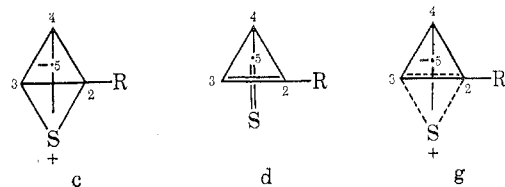


Figure 9.

None of these experiments proves the detailed mechanism. Differences in gas- and liquid-phase photolysis reactions are well documented while even minor changes in substituents can drastically alter the nature of valence bond isomerizations.

In Figure 9 the two disputed entities, valence-shell-expanded closed structure c and cyclopropene open structure d, are shown. They are obviously closely related and might not be distinguishable in the excited state. The frontal view of c and d makes this similarity evident and simultaneously reveals the symmetry about the C<sub>2</sub>-C<sub>3</sub> bond of the original thiophene molecule. It is not unlikely that both drawings represent species at various stages along the reaction coordinate. If there is any merit to this idea, then it seems reasonable that c represents a higher energy state, while d is closer to a ground-state structure. Structure g attempts to show a valence bond hybrid of c and d.

## Conclusions

The aromatic nature of thiophene allows facile substitution reactions while its sulfur atom permits conversion to aliphatic structures under mild conditions. Its pentagon shape provides a template for the study of strain and stresses in organic chemistry. Condensed into helical structures, its reactive  $\alpha$  position facilitates



synthesis, resolution, and chemical studies. The sulfur atom aids X-ray studies while this same atom, acting as it were as an insulator, greatly simplifies the interpretation of spectral data. The absolute configuration of a heterohelicene is reported.

*My collaborators who are named in the references deserve the major credit for the work from my laboratory that is described in this paper. Special thanks are due to Dr. Richard M. Kellogg and Dr. Marinus B. Groen whose loyal and dedicated work and major original contributions can hardly be overestimated.*

## Reactions of Nucleophiles with Ethylenic Substrates

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Intensive work on the mechanisms of nucleophilic substitution at saturated carbon began in the 1930's and at aromatic carbon in the early 1950's. However, it was not until the late fifties and early sixties that thorough scrutiny of nucleophilic substitution at vinylic carbon got under way.<sup>1</sup>

There are well-recognized similarities between aryl halides and vinyl halides. It might therefore be supposed that nucleophilic substitution at vinylic centers would be merely a further chapter of aromatic nucleophilic substitution.

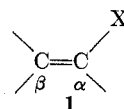
There are similarities, to be sure, but reactions of ethylenic substrates are mechanistically more diverse. Vinyl halides undergo  $\beta$  elimination to acetylenes with greater ease than aromatic compounds form arynes. The competition between substitution and elimination is, indeed, one of the most intriguing features of the reactions of vinylic compounds with nucleophiles. The cis-trans isomerism of substituted ethylenes offers substrates of known configuration for the study of  $\beta$ -elimination mechanisms and also poses obvious questions as to whether configuration is retained or inverted during substitution.

Moreover, a vinylic substrate necessarily carries an  $\alpha$  substituent with respect to the leaving group. The  $\alpha$  substituent may exert steric and electronic effects on the reaction rate and may itself be attacked by the nucleophile, thus opening new reaction pathways.

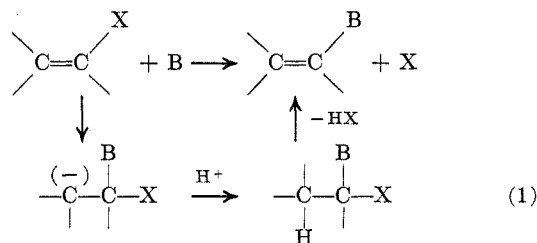
Finally, ethylenic substrates of suitable structure may undergo  $S_N1$ -like reactions even at room temperature.<sup>2</sup> However, this mechanism does not interfere

to any significant extent when strong bases are present.

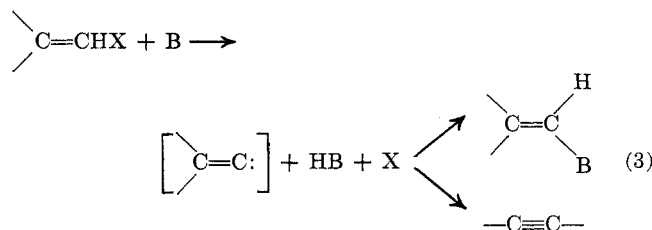
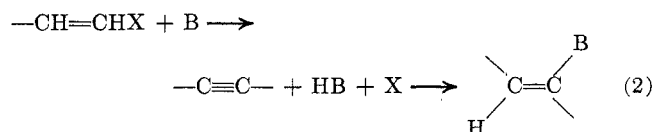
In summary, vinylic substrates (1) may react with a nucleophile B by: (1) attack at the  $\alpha$  carbon<sup>3</sup> to



give either substitution (direct substitution) or addition products (eq 1); the latter may undergo subsequent elimination of HX to give a product of formal substitution (addition-elimination, eq 1); (2) attack



at hydrogen to trigger one of three independent elimination paths involving a  $\beta$  hydrogen ( $\beta$  elimination, eq 2) or the  $\alpha$  hydrogen ( $\alpha$  elimination, eq 3), or a  $\beta'$  hydrogen ( $\beta'$  elimination, eq 4).



(1) (a) D. E. Jones and C. A. Vernon, *Nature*, **176**, 791 (1955); (b) W. E. Truce and M. M. Boudakian, *J. Amer. Chem. Soc.*, **78**, 2748 (1956), and subsequent papers; (c) S. I. Miller and P. K. Yonan, *ibid.*, **79**, 5931 (1957); (d) F. Montanari, *Gazz. Chim. Ital.*, **86**, 406 (1956), and subsequent papers of the series; (e) G. Modena, *Ric. Sci.*, **28**, 341 (1958).

(2) G. Modena, U. Tonellato, and F. Naso, *Chem. Commun.*, 1363 (1968); G. Modena and U. Tonellato, *ibid.*, 1676 (1968); W. M. Jones and D. D. Maness, *J. Amer. Chem. Soc.*, **91**, 4314 (1969).

(3) Throughout this Account  $\alpha$  indicates the carbon to which the leaving group X is linked and  $\beta$  the next one; cis and trans isomers are named on the basis of the relative position of X and the activating group Y.