Chloromethoxypropoxychloropropanols.—The reaction mixture from chlorination of allyl alcohol (1.0 mol) in methanol (10 mol) containing Na_2CO_3 (0.5 mol) was filtered and stripped of solvent. The residue was vacuum distilled through a 12-in. glass helices packed column giving 96 g of a mixture of chloromethoxypropanols and dichloropropanol [bp 65° (5 mm)–45° (0.5 mm)]. The pot residue was extracted with ether to eliminate salt. After stripping, it was refluxed in acidified 1:1 MeOH–H_2O to hydrolyze acetals. The mixture was stripped of solvent and the residue vacuum distilled giving an additional 5 g of chlorohydrins and 8 g of a higher boiling fraction (140–145° at 0.5 mm). Chromatographic analysis (220°, 5-ft 15% CW20M/Anakrom ABS) showed two peaks in the ratio 9:1 at retention times of 8 and 12.5 min. The first (major) peak was trapped and identified (ir, mass spectrum, and nmr) as an isomeric mixture of chloromethoxypropoxychloropropanol. The four possible isomers are: $CH_2ClCH[OCH_2CH(OCH_3)CH_2Cl]CH_2OH$, $CH_2ClCH(OCH_2CHClCH_2OCH_3)CH_2OH$, $CH_2ClCH(OCH_3)CH_2OCH_2CHClCH_2OH$, and $CH_3OCH_2CHClCH_2OCH_2CHClCH_2OH$. Mass spectral analysis showed a molecular ion at mass 216 and indicated a compound containing two chlorine atoms. The cracking pattern was consistent with the proposed structures. Nmr (60 MHz) showed a complex region (3.50–4.30 ppm) assigned to the methylene and methine protons, two singlets for methoxy at 3.48 and 3.43 ppm, and a broad absorption due to hydroxyl at 2.88 ppm. At 90 MHz the methoxy protons were resolved into six singlets (3.478, 3.474, 3.467, and 3.417, 3.408, 3.404 ppm). Since each positional isomer contains two asymmetric centers a total of eight singlets is possible. Assigning the higher field group to primary methoxy and the lower field group to secondary methoxy gives values of 73% primary and 27% secondary.

Anal. Calcd for $C_7H_{14}O_3Cl_2$: C, 38.7; H, 6.5; Cl, 32.7. Found: C, 38.9; H, 6.4; Cl, 32.7.

Dichloropropoxychloropropanols.—Peak number two from the higher boiling fraction in the isolation of chloromethoxypropoxychloropropanols was trapped and identified (ir, mass spectrum, and nmr) as an isomeric mixture of $CH_2ClCH(OCH_2CHClCH_2Cl)CH_2OH$ and $CH_2ClCHClCH_2OCH_2CHClCH_2OH$.

Anal. Calcd for $C_6H_{11}O_2Cl_3$: C, 32.5; H, 5.0; Cl, 48.0. Found: C, 32.5; H, 5.0; Cl, 47.6.

Registry No.—3-Chloro-2-(2-hydroxyethoxy)propanol, 15045-14-4; 2-chloro-3-(2-hydroxyethoxy)propanol, 29908-10-9; 2-hydroxymethyl-1,4-dioxane, 29908-11-0; 3-methoxy-2-chloropropanol, 26438-92-6; $H_2CClCH[OCH_2CH(OCH_3)CH_2Cl]CH_2OH$, 29908-13-2; $CH_2ClCH(OCH_2CHClCH_2OCH_3)CH_2OH$, 29908-14-3; $CH_2ClCH(OCH_3)CH_2OCH_2CHClCH_2OH$, 29908-15-4; $CH_3OCH_2CHClCH_2OCH_2CHClCH_2OH$, 29908-16-5.

Acknowledgment.—The author are indebted to Dr. R. C. Rittner, Mr. J. Culmo, and Mr. J. Giunta for microanalyses; to Mr. H. Hoberecht and Dr. F. J. Preston for mass spectral analyses; to Mr. G. D. Vickers and Dr. T. Groom for nmr analyses; and to Mr. W. A. Nichols for performing some of the chromatographic analyses.

Cyclopropylthiophenes. Syntheses, Reactions, and Ultraviolet Spectra

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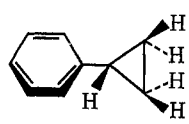
Synthetic routes to 2- and 3-cyclopropylthiophenes are described. Electrophilic deuteration, bromination, formylation, and iodination occur exclusively at the 5 position of 2-cyclopropylthiophene and at the 2 position of 3-cyclopropylthiophene. Nitration is less selective, proceeding at the 3 and 5 positions of 2-cyclopropylthiophene (40 and 60%, respectively) and at the 2 and 5 positions of 3-cyclopropylthiophene (88 and 12%, respectively). The cyclopropyl ring does not open during electrophilic substitution. Upon irradiation in benzene the iodo substituents of 2-cyclopropyl-5-iodothiophene and 3-cyclopropyl-2-iodothiophene are replaced by phenyl. The effect of cyclopropyl on the uv spectra approximates that of phenyl contrasting strongly the behavior of simple cyclopropyl-substituted aryl systems where only modest bathochromic shifts are found. The larger effect in thiophenes is attributed to a relatively larger decrease in electron density upon excitation at the carbon to which cyclopropyl is attached thereby making a greater demand upon the conjugative abilities of cyclopropyl. Comparisons with literature data are made.

Discussions of the effect of a cyclopropyl group on an aromatic ring have generally concentrated on the degree and type of conjugative interaction existing between the two bonded rings. Strong *ground-state* conjugative interaction in cyclopropyl aromatics may occur[2] providing that significant electronic demands are made on the cyclopropyl group[3] and providing that a conformation can be attained allowing maximum overlap between



the Walsh[4] orbitals for cyclopropyl and the aryl π system. The latter condition is best satisfied with the bisected conformation illustrated for cyclopropylbenzene.

Evidence for conjugative interaction in the excited state is less clear-cut. A modest bathochromic shift of 5 mμ (740 cm^{-1}) of the 0–0 band of cyclopropylbenzene over that for isopropyl benzene is indeed found,[5,6] but, as judged from bathochromic shifts, the degree of interaction seems not to be a sensitive function of cyclopropane geometry.[7] The reasonable suggestion has been made recently that significant conjugative interaction (and thereby geometrical influence) in the excited state (as in the ground state) will only occur if the aromatic moiety has "sufficient electron-attracting power to make .....demand on the conjugative ability of the cyclo-

(1) To whom inquiries should be addressed.

(2) For leading references, see (a) R. C. Hahn, T. F. Corbin, and H. Shechter, *J. Amer. Chem. Soc.*, **90**, 3404 (1968); (b) H. C. Brown and J. D. Cleveland, *ibid.*, **88**, 2051 (1966); T. Sharpe and J. C. Martin, *ibid.*, **88**, 1815 (1966). For examples of cyclopropylinteraction in aliphatic systems, see (d) R. C. Bingham, W. F. Sliwinsky, and P. v. R. Schleyer, *ibid.*, **92**, 3471 (1970); (e) C. D. Poulter, E. C. Friedrich, and S. Winstein, *ibid.*, **92**, 4274 (1970).

(3) R. Fuchs, C. A. Kaplan, J. J. Bloomfield, and L. F. Hatch, *J. Org. Chem.*, **27**, 733 (1962); R. Fuchs and J. J. Bloomfield, *ibid.*, **28**, 910 (1963).

(4) A. D. Walsh, *Trans. Faraday Soc.*, **45**, 179 (1949).

(5) W. W. Robertson, J. F. Music, and F. A. Matson, *J. Amer. Chem. Soc.*, **72**, 5260(1950).

(6) A molecular orbital model for interaction has been proposed: H. H. Jaffé, *Z. Elektrochem.*, **59**, 823 (1955).

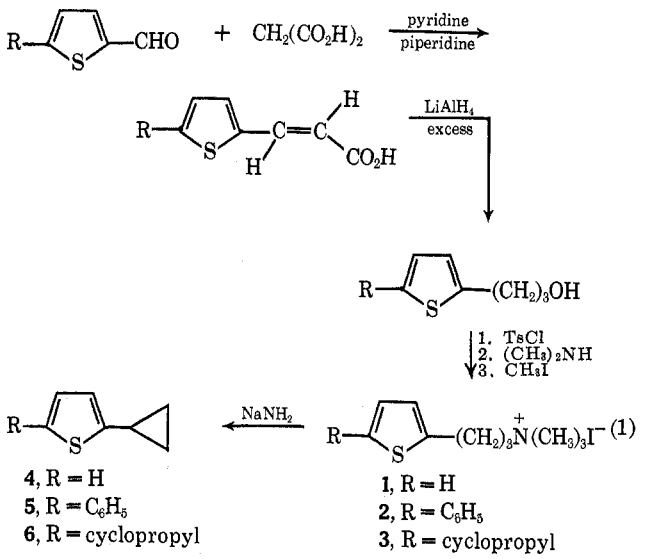
(7) A. L. Goodman and R. H. Eastman, *J. Amer. Chem. Soc.*, **86**, 908 (1964); see also J. C. Bourmanne, G. Leroy, and J. Weiler, *Tetrahedron*, **26**, 2281 (1970).

propyl group."[8] In support of this contention, the magnitudes of the relative bathochromic shifts in para-nitro-substituted arylcyclopropanes are larger than those of the nonnitrated compounds and, in addition, the magnitude becomes a spectroscopically detectable function of cyclopropane geometry.

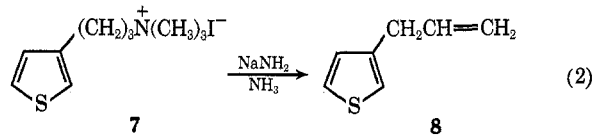
This concept provides a viable qualitative tool with which to rationalize substituent effects on the spectra of arylcyclopropanes but gives only limited help in estimating the effects of an intrinsic change of the aryl system itself. Consider the replacement of phenyl by thienyl. The thiophene system is unquestionably aromatic as evidenced by reactions,[9] nmr spectral data,[10] ^{13}C nmr coupling constants,[11] and resonance energy.[12] However, it is inductively more strongly electron-withdrawing than phenyl (2-thienylcarboxylic acid has a pK_a of 3.53 in water, benzoic acid has pK_a of 4.17).[13] Resonance interaction with a positive center seems to be significantly greater than for phenyl.[14] The appreciable dipole moment, 0.54 D,[15] and greater reactivity in electrophilic substitution with selective activation of positions adjacent to the sulfur atom[16] further accent the difference with phenyl.[17] On the other hand, the effectiveness of transmission of inductive (and presumably also resonance) effects from the 2 to the 5 position is nearly the same as in benzene.[16] Using the guideline of "increased electron-attracting ability" we might predict an increase in the auxochromic effect of cyclopropyl as a substituent on thiophene, but no intelligent guess as to the magnitude can be made. In an effort to probe further into this problem we have synthesized a number of cyclopropylthiophenes and have studied their ultraviolet spectra.

Results

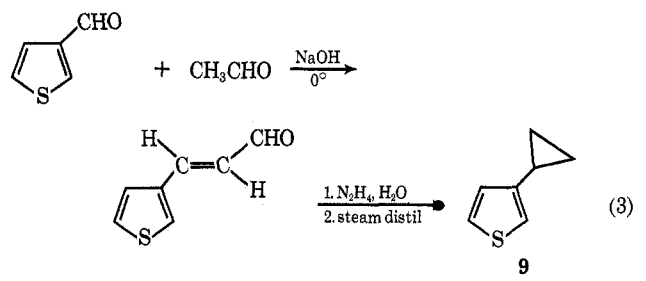
A facile synthesis of 2-cyclopropylthiophene (**4**) is achieved from the sodium amide induced cyclization of the requisite quaternary ammonium iodide (**1**) (eq 1). This procedure was developed by Bumgartner[18] for the synthesis of cyclopropylbenzene and has also been used for the synthesis of 4-cyclopropylpyridine.[19] Its application to the synthesis of **4** has been described briefly in Russian literature.[20,21] This approach, although a trifle lengthy, gives good yields and may be scaled up readily. No difficulties were experienced in adaptation to the synthesis of 2-cyclopropyl-5-phenylthiophene (**5**) and 2,5-dicyclopropylthiophene (**6**).



An alternative route had to be sought for 3-cyclopropylthiophene (**9**) since sodium amide induced ring closure of the quaternary ammonium iodide (**7**) gave chiefly the E2 elimination product, 3-(3-thienyl)-1-propene (**8**) (eq 2).[22] This demonstrates well (but unhappily) the difference in acidity of α-methylene groups in 2- compared with 3-thenyl derivatives. A successful synthesis of **9** was obtained by appropriate modification (eq 3) of a well-known route to cyclopropylbenzene.[23]



(2)



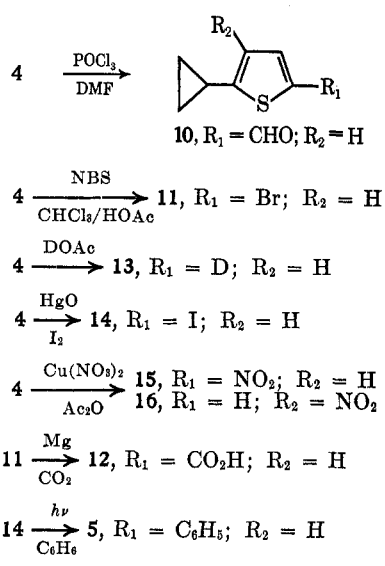
(3)

Yields are not exceptional (overall 30%), but nevertheless this procedure is sufficiently simple as to justify recommendation.

The reactions carried out on **4** are presented in Scheme I. Electrophilic bromination,[24] deuteration,[24] formylation, and iodination[25] proceed exclusively in the 5 position as is expected for 2-substituted thiophenes.[26] Electrophilic nitration is, however, less selective giving both 3- and 5-substituted products paralleling the situation with 2-phenylthiophene.[27] Irradiation of 2-cyclopropyl-5-iodothiophene (**14**) in benzene gives 2-cyclo-

(8) R. C. Hahn, P. H. Howard, S.-M. Kong, G. A. Lorenzo, and N. L. Miller, *J. Amer. Chem. Soc.*, **91**, 3558 (1969).
(9) S. Gronowitz, *Advan. Heterocycl. Chem.*, **1**, 1, (1963).
(10) H. A. P. de Jongh and H. Wynberg, *Tetrahedron*, **21**, 515 (1965).
(11) T. F. Page, Jr., J. T. Alger, and D. M. Grant, *J. Amer. Chem. Soc.*, **87**, 5333 (1965).
(12) See, *e.g.*, M. J. S. Dewar and N. Trinajstić, *ibid.*, **92**, 1453 (1970).
(13) A. R. Butler, *J. Chem. Soc. B*, 867 (1970).
(14) E. A. Braude and J. S. Fawcett, *J. Chem. Soc.*, 4158 (1952).
(15) Taken from V. Schomaker and L. Pauling, *J. Amer. Chem. Soc.*, **61**, 1769 (1939).
(16) See for recent quantitative studies of this phenomenon (a) A. R. Butler and J. B. Hendry, *J. Chem. Soc. B*, 848 (1970); (b) A. R. Butler and J. B. Hendry, *ibid.*, 852 (1970); (c) G. Marino, *Tetrahedron*, **21**, 843 (1965).
(17) A popular molecular orbital picture for thiophene is that given by H. C. Longuet-Higgens, *Trans. Faraday Soc.*, **45**, 173 (1949).
(18) C. L. Bumgartner, *J. Amer. Chem. Soc.*, **83**, 4423 (1961).
(19) A. P. Gray and H. Kraus, *J. Org. Chem.*, **31**, 399 (1966).
(20) E. G. Treshchova, D. Ekkhardt, and Yu. K. Yur'ev, *Zh. Fiz. Khim.*, **38**, 295 (1964); *Chem. Abstr.*, **60**, 14027*d* (1964); and earlier references.
(21) The synthesis of carboalkoxy substituted cyclopropylthiophenes by addition of diazo esters to vinylthiophenes has been described: A. Burger, D. G. Markess, W. R. Nes, and W. L. Yost, *J. Amer. Chem. Soc.*, **71**, 3307 (1949).
(22) We are grateful to Miss Karon Armstrong for this experiment.
(23) R. J. Petersen and P. S. Skell, *Org. Syn.*, **47**, 98 (1967).
(24) NBS has been shown to be an extremely effective electrophilic bromination agent for activated thiophenes: R. M. Kellogg, A. P. Schaap, E. T. Harper, and H. Wynberg, *J. Org. Chem.*, **33**, 2902 (1968). Selective deuterium exchange with alkyl- and arylthiophenes in refluxing deuterioacetic acid is also described.
(25) Assumed to involve electrophilic mercuration as the initial step.
(26) Orientational factors in thiophenes are discussed in detail in ref 9.
(27) S. Gronowitz and N. Gjøs, *Acta Chem. Scand.*, **21**, 2823 (1967).

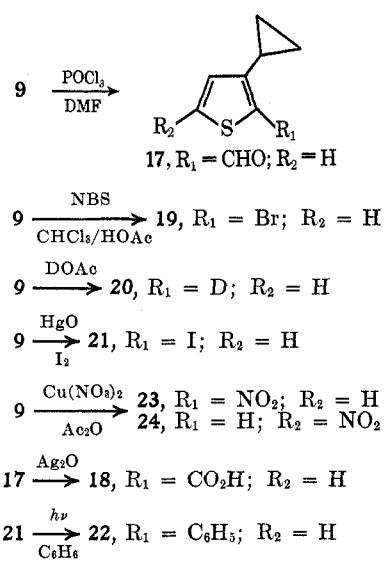
SCHEME I



propyl-5-phenylthiophene[28] (**6**) [also synthesized by an alternative route (eq 1)].

With 3-cyclopropylthiophene (**9**) electrophilic bromination, deuteration, formylation, and iodination take place within the limits of detectability only in the 2 position (Scheme II). Electrophilic nitration also occurs chiefly in the 2 position giving 2-nitro-3-cyclopropylthiophene (**23**) along with some 2-nitro-4-cyclopropylthiophene (**24**) the presence of which can be deduced from the nmr spectrum. Again the cyclopropyl ring is not opened. Irradiation of 3-cyclopropyl-2-iodothiophene (**21**) in benzene gives 3-cyclopropyl-2-phenylthiophene (**22**).

SCHEME II



Discussion

Electrophilic Substitution.—In cyclopropylbenzene both bromination and acylation are known to go exclusively in the para position at −75°.[29] Attack on the cyclopropyl ring is also a possibility as witnessed by ring opening during sulfonation[30] and during bromination in acetic acid–sodium acetate.[31] With cyclopropylthiophenes under mild conditions no attack on the cyclopropyl group is observed and substitutions are highly selective. For 2-cyclopropylthiophene attack at the 5 position is completely predictable. The exclusive reaction at the 2 position of 3-cyclopropylthiophene, while at first sight surprising, follows the pattern found with analogous aryl and alkylthiophenes.[24] Most likely this orientation arises from the capability of the cyclopropyl substituent to stabilize directly the positively charged intermediate formed during electrophilic substitution. Formylation of 3-cyclopropylthiophene is more selective than with 3-methylthiophene which gives a 4:1 mixture of 2- and 5-formylated products[32] or with 3-isopropylthiophene which gives a 1:1 mixture of isomers (Experimental Section); with 3-phenylthiophene a 94:6 ratio of 2- to 5-substituted products is found.[33]

Electrophilic nitration in benzenoid systems is usually less selective than most other types of electrophilic substitution[34] and the same holds in thiophenes.[9] Nitration of 2-phenylthiophene gives a 6:4 mixture of 5-nitro- and 3-nitro-2-phenylthiophenes (in addition to dinitrated products) and 3-phenylthiophene gives a 9:1 mixture of 2-nitro- and 5-nitro-3-phenylthiophenes.[27] This parallels closely the isomer distribution obtained from the cyclopropylthiophenes. There appears to be no need to invoke any special stabilization factors such as suggested for nitration of cyclopropylbenzene in which a decided preference for ortho substitution is found.[2]

Ultraviolet Spectra.—The extent of the putative conjugative interaction of a cyclopropyl group with an excited chromophore depends strongly on the system. An unambiguous example of interaction occurs with certain cyclopropyl ketones where the cyclopropyl group lowers the energy of the $\pi-\pi^*$ transition some 7–8 kcal/mol providing that the preferred bisected geometry can be attained.[35,36] This clear-cut case is contrasted by the behavior of vinylcyclopropanes where the cyclopropyl group, although behaving as a fairly strong auxochrome relative to isopropyl, surprisingly appears to have no geometric preference for conjugative interaction.[37] On the other hand, closely related cyclopropylacrylic esters (carboalkoxy substituted vinylcyclopropanes) exhibit bathochromic shifts relative to their isopropyl analogs as well as a clear preference for bisected geometry for maximum conjugative interaction.[38]

For the specific case of aryl-substituted cyclopropanes one finds that a cyclopropyl group in simple benzenoid aromatics causes only modest to negligible shifts compared with isopropyl. Some pertinent spectra are col-

(28) Technique of W. Wolf and N. Kharasch, *J. Org. Chem.*, **30**, 2493 (1965).

(29) Ya. Levina and P. A. Gembitskii, *Zh. Obshch. Khim.*, **31**, 3480 (1961); *Chem. Abstr.*, **57**, 701*f* (1962).

(30) Yu. S. Shabarov, R. Ya. Levina, and V. K. Potapov, *Zh. Obshch. Khim.*, **32**, 3184 (1962); *Chem. Abstr.*, **58**, 11241*h* (1963).

(31) A product of incompletely determined structure is formed.[2a]

(32) S. Gronowitz, P. Moses, A. B. Hörnfeldt, and R. Håkansson, *Ark. Kemi*, **17**, 165 (1961).

(33) S. Gronowitz, N. Gjøs, R. M. Kellogg, and H. Wynberg, *J. Org. Chem.*, **33**, 463 (1967); N. Gjøs and S. Gronowitz, *Acta Chem. Scand.*, **24**, 99 (1970).

(34) R. O. C. Norman and R. Taylor, "Electrophilic Substitution in Benzenoid Compounds," Elsevier, Amsterdam, 1965, pp 61–91.

(35) E. M. Kosower and M. Ito, *Proc. Chem. Soc.*, 25 (1962).

(36) See also W. G. Dauben and G. H. Berezin, *J. Amer. Chem. Soc.*, **89**, 3449 (1967).

(37) C. H. Heathcock and S. R. Poulter, *ibid.*, **90**, 3766 (1968).

(38) M. L. Jorgenson and T. Leung, *ibid.*, **90**, 3769 (1968).

lected in Table I. The long wavelength $^1B_{2u} \rightarrow {}^1A_{1g}$ transition is bathochromically shifted only 7 mμ in

TABLE I

ULTRAVIOLET SPECTRA OF SOME SELECTED CYCLOPROPYL SUBSTITUTED AROMATIC COMPOUNDS

Compounds	λ_{max} (log ε)
Cyclopropylbenzene	275 (2.26)[a,b]
Isopropylbenzene	268 (2.57)[a,b]
4-Nitro-*n*-propylbenzene	265.5[c,d] (....)[e]
4-Nitrocyclopropylbenzene	283 (4.05)[b,f]
α-Cyclopropylnaphthalene	224.5 (4.86), 283 (3.82)[f,g]
α-Methylnaphthalene	224 (4.99), 282 (3.69)[f,g]
β-Cyclopropylnaphthalene	227.5 (4.90), 277 (3.72)[f,g]
β-Methylnaphthalene	224 (4.94), 275 (3.68)[f,g]
2-Cyclopropylpyridine	268.5 (3.60)[h,i]
2-Isopropylpyridine	261.5 (3.58), 267.8 (3.48)[h,i]
4-Cyclopropylpyridine	259 (3.38)[i,g]
4-Isopropylpyridine	255 (3.32), 261 (3.20)[i,g]

[a] Reference 5. [b] Cyclohexane. [c] Heptane. [d] W. M. Schubert and J. Robins, *J. Amer. Chem. Soc.*, **80**, 559 (1958). [e] Not given. [f] Reference 8. [g] 95% EtOH. [h] Reference 39. [i] 0.1 *N* NaOH. [j] Reference 19.

cyclopropylbenzene compared with that in isopropylbenzene and in α- and β-substituted naphthalenes the long wavelength absorption is shifted only 1–2 mμ relative to alkyl.[8] For a heterocyclic system closely resembling benzene, *i.e.*, pyridine, cyclopropyl causes negligible bathochromic shifts in 2-[39] and 4-substituted[19] compounds (although protonation causes considerable enhancement of the long wavelength band of 4-cyclopropylpyridine).[19] On the other hand, the long wavelength absorption of 4-nitrocyclopropylbenzene, where the electronic demand made on cyclopropyl is greatly increased, is shifted some 2330 cm^{-1} (17.5 mμ) over that of the isopropyl derivative. Moreover, the magnitudes of the bathochromic shifts decrease steadily as the cyclopropyl group is twisted away from the preferred bisected geometry.[8]

The spectral properties of thiophene must be considered before attempting to apply the electron-withdrawing ability proportional to bathochromic shift concept[8] to cyclopropylthiophenes. Thiophene has in solution a broad, featureless absorption band located at 231 mμ (log ε 3.87) which in the gas phase is resolved into overlapping absorptions at 240, 233, and 220 mμ.[40] A shorter wavelength band with a maximum at 188 mμ is also seen.[41] A recent molecular orbital treatment of thiophene using a five-orbital model, *i.e.*, four carbon 2p orbitals and the sulfur 3p orbital, successfully accounts for the overlapping long wavelength $\pi-\pi^*$ absorptions.[42] Analysis of substituent effects on spectra is complicated by this band overlap which often leads to structureless absorptions. In the present discussion we shall try only to distinguish qualitative features between related sets of thiophenes sufficient to allow an evaluation of the magnitudes of the bathochromic shifts of the major thiophene absorption bands which are thought to reflect the extent of cyclopropyl interaction in the excited state. Since no safely interpretable trend of intensities can be distinguished, this aspect is not treated in any detail.

Pertinent spectroscopic data are listed in Table II. The isopropyl compounds listed were synthesized to provide reference compounds with roughly the same inductive contributions as a cyclopropyl group. Only absorption maxima are given; in several cases overlap of peaks leads to a featureless band undoubtedly embodying more than one transition.[43] Casual inspection would suggest an enormous bathochromic shift of 41 mμ for 2-cyclopropylthiophene (**4**) over 2-isopropylthiophene. Although the effect of cyclopropyl, presumably attributable chiefly to conjugative interaction, must be large, one should note that the 274-mμ band of **4** is much less intense than the 239 mμ band which suggests that, rather than a simple shift phenomenon, a new band having some degree of "intramolecular charge-transfer character," is being formed.[44]

Particularly valuable and more easily interpretable information can be gained from the 5-substituted 2-cyclopropylthiophenes. Particularly the long wavelength absorption bands as well as a second shorter wavelength band in CHO, CO_2H, and NO_2 derivatives display appreciable bathochromic shifts over the isopropyl reference compounds. Inspection of spectra indicates clear similarities between the spectra for the cyclopropyl compounds and analogous 5-substituted 2-*phenyl*thiophenes. The 2-phenylthiophenes have two well-developed bands of the same general form as observed in the cyclopropyl compounds;[43] the third band seen for 5-CHO or $-CO_2H$ derivatives at 231 and 222 mμ, respectively, may be hypsochromically shifted in the cyclopropyl derivatives and therefore not observable. The phenyl derivatives have absorption maxima shifted bathochromically with respect to the cyclopropyl compounds. If cyclopropyl participation is indeed sensitive to the electron-withdrawing capacities of the aryl ring to which it is attached, maximum shifts (indicative of conjugative interaction) would be expected with 2-cyclopropyl-5-nitrothiophene (**15**) with a steady decrease in interaction as the electron-attracting ability of the 5 substituent is varied in the order NO_2 > CHO > CO_2H > halogen. This hypothesis can be tested. To a first approximation, the degree of inductive and resonance interaction by phenyl in 5-substituted 2-phenylthiophenes will be roughly the same in all compounds or at least more constant than in the analogous 2-cyclopropyl compounds. In Table III the relative bathochromic shifts of the longest wavelength absorption bands for 2-phenyl compared with 2-cyclopropyl compounds are compiled. The ratio of bathochromic shifts for phenyl compared with cyclopropyl increases steadily from NO_2 through CHO through CO_2H consistent with strongest cyclopropyl

(39) R. P. Mariella and K. H. Brown, *J. Org. Chem.*, **34**, 3191 (1969). Note that this is a correction of an earlier report of the synthesis of 2-cyclopropylpyridine: R. P. Mariella, L. F. A. Peterson, and R. C. Ferris, *J. Amer. Chem. Soc.*, **70**, 1494 (1948).

(40) E. Milazzo, *Gazz. Chim. Ital.*, **78**, 835 (1948).

(41) W. C. Price and A. D. Walsh, *Proc. Roy. Soc.* (*London*), **A179**, 201 (1941).

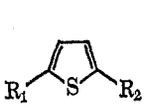
(42) M. J. Bielefeld and D. D. Fitts, *J. Amer. Chem. Soc.*, **88**, 4804 (1966). For pioneering work on the electronic structure of thiophene, see ref 15 and for an original MO description ref 17 as well as A. J. H. Wachters and D. W. Davies, *Tetrahedron*, **20**, 2841 (1964).

(43) Drawings of the spectra of **4**, **15**, **9**, and **23** (in 95% EtOH) along with appropriate reference compounds will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Reprint Department, ACS Publications, 1155 Sixteenth Street, N. W., Washington, D. C. 20036. Remit $3 for photocopy or $2 for microfilm.

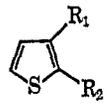
(44) (a) S. Nagakura and J. Tanaka, *J. Chem. Phys.*, **22**, 236 (1954); (b) S. Nagakura, *ibid.*, **23**, 1441 (1955); (c) S. Nakakura, *J. Mol. Phys.*, **3**, 105 (1960); (c) K-K. Cheong, Y-C. Fu, R. K. Robins, and H. Eyring, *J. Phys. Chem.*, **73**, 4219 (1969), and references therein; (d) this point was stressed by a referee.

TABLE II

COMPARISON OF ULTRAVIOLET SPECTRA OF SOME THIOPHENE DERIVATIVES[a]



A



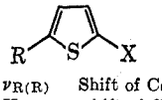
B

R_2	R_1 = $CH(CH_3)_2$	R_1 = H	R_1 = C_6H_5	R_1 = C_3H_5
		λ_{max} (log ϵ)		
		Thiophene A		
H (a[b])	233 (3.86)	215 (3.80), 231 (3.87)[c,d]	252 (3.86), 282 (4.16)	239 (3.88), 274 (3.05)
CHO (b)	265 (3.96), 296 (4.04)	260 (4.04), 286 (3.86)[c,d]	231 (3.98), 286 (3.83), 328 (4.33)	268 (3.87), 308 (4.15)
CO_2H (c)	254 (3.95), 277 (4.04)	246 (3.96), 260 (3.84)[c,d]	222 (4.00), 280 (sh), (4.00), 310 (4.31)	233 (2.85), 258 (3.49), 285 (3.72)
NO_2 (d)	290 (sh) (3.64), 329 (3.99)	270 (3.80), 296 (3.78)[c,d]	248 (3.99), 366 (4.21)[d,e]	222 (3.64), 345 (4.26)
Br (e)	242 (3.88)	236 (3.90)[c,d]	293 (4.22)	254 (3.93)[f]
I (f)	254 (4.00)		293 (4.28)	260 (4.04)[f]
C_6H_5	291 (4.19)[d,g]		230 (4.08), 324 (4.45)[f]	297 (3.98)
C_3H_5				256 (3.94), 290 (3.29)
		Thiophene B		
H (g)	235 (3.78)		227 (4.16), 258 (4.12)	232 (3.26), 243 (3.64)
CHO (h)	276 (4.05)		229 (4.10), 295 (4.08)	290 (4.08)
CO_2H (i)	257 (4.02)		224 (4.11), 276 (4.06)	265 (4.16)
NO_2 (j)	307 (3.91)		250 (3.55), 319 (3.95)[d,e]	240 (sh) (3.39), 319 (4.03)
C_6H_5	267 (3.96)[d,g]		238 (4.31), 278 (4.60)[d,g]	233 (3.89), 273 (4.08)
Br (k)	238 (3.89)		229 (4.22), 253 (4.05)	241 (3.88)[f]
I				248 (3.96)[f]

[a] Compounds cited without reference are from this work and spectra are in 95% EtOH. [b] Registry numbers: a [R_1 = $CH(CH_3)_2$], 4095-22-1; a (R_1 = C_6H_5), 825-55-8; b (R_1 = $CH(CH_3)_2$], 29481-40-1; b (R_1 = C_3H_5), 19163-21-4; c [R_1 = $CH(CH_3)_2$], 29481-42-3; c (R_1 = C_6H_5), 19163-24-7; d [R_1 = $CH(CH_3)_2$], 29481-18-3; d (R_1 = C_6H_5), 18150-93-1; e [R_1 = $CH(CH_3)_2$], 29488-23-1; e (R_1 = C_6H_5), 29488-24-2; f [R_1 = $CH(CH_3)_2$], 29488-25-3; f (R_1 = C_6H_5), 13781-37-8; g [R_1 = $CH(CH_3)_2$], 29488-27-5; g (R_1 = C_6H_5), 2404-87-7; h [R_1 = $CH(CH_3)_2$], 29488-29-7; h (R_1 = C_6H_5), 26170-85-4; i [R_1 = $CH(CH_3)_2$)], 29488-31-1; i (R_1 = C_6H_5), 10341-88-5; i (R_1 = C_3H_5), 29488-33-3; j [R_1 = $CH(CH_3)_2$], 29488-34-4; j (R_1 = C_6H_5), 18132-94-0; k [R_1 = $CH(CH_3)_2$], 29488-36-6; k (R_1 = C_6H_5), 10341-87-4. [c] S. Gronowitz, *Ark. Kemi*, **13**, 239 (1958). [d] 95% EtOH. [e] S. Gronowitz and N. Gjøs, unpublished results. [f] Identical λ_{max} (log ϵ) in C_6H_{12}; likely a long wavelength band is buried. [g] From ref 45d with methyl instead of isopropyl.

TABLE III

SHIFTS OF LONG WAVELENGTH BANDS AS A FUNCTION OF SUBSTITUENT X OF COMPOUNDS



Shift (cm^{-1}) = $\nu_{R(C_3H_7)} - \nu_{R(R)}$ R = C_6H_5	R = C_3H_5	Shift of C_6H_5/ shift of C_3H_5	X
3070	1410	2.18	NO_2
3300	1320	2.50	CHO
3850	1020	3.78	CO_2H
7200	1950	3.70	Br

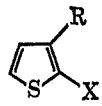
interaction for the 5-nitro-substituted compounds but with the extent of participation relative to phenyl becoming progressively less as the electron-withdrawing ability of the 5 substituent decreases.

A further demonstration that the magnitude of conjugative interaction is proportional to electronic demand is obtained on comparison of the spectrum of 2,5-divinylthiophene,[45a] λ_{max} 315 mμ (log ϵ 4.70) and 328 (3.69), with that of 2,5-dicyclopropylthiophene (**6**) which absorbs at some 25-mμ shorter wavelength (Table II). Obviously, since less strong electronic demands are made on the cyclopropyl substituents in **6**, the magnitude of interaction is lessened. The extent of cyclopropyl participation should not be underestimated, however, since even in **4** the fluorescence maximum is found at 335 mμ compared with 319 mμ for 2-phenylthiophene.[45]

Important trends are found from the spectra of the 2-substituted 3-cyclopropylthiophenes. First, these derivatives consistently absorb at shorter wavelength than the corresponding 2-cyclopropyl 5-substituted derivatives. The effect of cyclopropyl substitution in 3-cyclopropylthiophene (**9**) compared with that in the isopropyl compound is much less drastic than that observed for **4**. Second, the similarities between the 2-NO_2-, CHO-, CO_2H-, and Br-substituted derivatives and the corresponding *phenyl* derivatives are particularly striking as is seen from comparison of data in Table II.[43] The same trend of decreasing degree of interaction with decreasing electron-withdrawing ability of the 2 substituent is apparent from Table IV where the same arguments are invoked as used for the 5-substituted 2-cyclopropylthiophenes. Direct comparison of the data of Tables III and IV is unwarranted since the degree of interaction of either a cyclopropyl *or phenyl* substituent in the 3 position will necessarily be different from that in the 2 position. Finally, expected steric effects in the 2,3-substituted compounds come into play. This point is made obvious on observing the hypsochromic shifts of the long wavelength bands in the 3-isopropyl 2-substituted reference compounds compared with those of the 2-isopropyl 5-substituted compounds. The shifts are too great to be at-

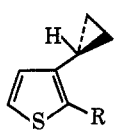
(45) (a) J. W. van Reijendam, Thesis (Groningen), 1968; (b) J. W. van Reijendam, G. J. Heeres, and M. J. Janssen, *Tetrahedron*, **26**, 1291 (1970); (c) J. W. van Reijendam and M. J. Janssen, *ibid.*, **26**, 1303 (1970); (d) H. Wynberg, H. van Driel, R. M. Kellogg, and J. Buter, *J. Amer. Chem. Soc.*, **89**, 3487 (1967); R. M. Kellogg and H. Wynberg, *Tetrahedron Lett.*, 5895 (1968).

TABLE IV
SHIFTS OF LONG WAVELENGTH BANDS AS A FUNCTION OF SUBSTITUENT X OF COMPOUNDS

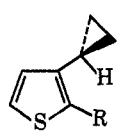


Shift (cm^{-1}) = $\nu_{R(C_6H_7)} - \nu_{R(R)}$ R = C_6H_5	R = C_6H_5	Shift of C_6H_5/ shift of C_6H_5	X
1230	1230	1.00	NO_2
2340	1750	1.34	CHO
2680	1180	2.27	CO_2H
2490	520	4.78	Br

tributed to different inductive contributions. Rather, twisting of the 2 substituent from coplanarity owing to steric interaction with the isopropyl group is more likely responsible for this effect. Similar steric interactions would be expected to hold for the cyclopropyl derivatives in view of the bulk similarities of isopropyl and cyclopropyl. For cyclopropyl, steric effects will likely again be reflected chiefly in deviation of the 2 substituent from coplanarity with the ring; the cyclopropyl group, although it may be crowded, still has a readily accessible bisected conformation available with the methine hydrogen directed away from the 2 substituent (conformation **25**). Conformation **25** should be of lower energy than **26** or intermediate twisted conformations.



25



26

The various bromo- and iodocyclopropylthiophenes listed in Table II exhibit very slight hypsochromic shifts relative to the unsubstituted cyclopropylthiophenes contrary to the usual effect of a halogen substituent[46] and also contrary to what is usually found in simple thiophenes.[9] An economical explanation is that any bands which have been bathochromically shifted are buried as shoulders and are simply not resolved; the resolution could not be improved by changing solvents.

Obviously, a cyclopropyl group may induce large bathochromic shifts of various thiophene bands, the effect being most pronounced for 2-cyclopropylthiophenes.[47] *A priori*, the cause could be either destabilization of the ground state relative to the excited state or greater stabilization of the excited state relative to the ground state. Since there is no good reason to postulate ground-state destabilization, the latter must pertain. Any factors which intrinsically lower the electron density of the carbon to which cyclopropyl is attached should enhance cyclopropyl participation both in the ground and excited states. In this light the trends with 5-substituted 2-cyclopropylthiophenes and 2-substituted 3-cyclopropylthiophenes are entirely reasonable. The relatively large shifts in 2-cyclopropylthiophene (**4**) itself, and to a lesser extent with 3-cyclopropylthiophene (**9**), are more puzzling if interpreted by extension of the above rationalizations. The important, and thus far overlooked, factor here, however, is the appreciable charge redistribution in thiophene upon excitation wherein the electron density increases on sulfur at the expense of chiefly the 2 and, to a lesser extent, the 3 position. This can be best illustrated in terms of the charge density q defined as in eq 4. Using

$$q_r = \sum_j n_j c_{jr}^2 \qquad (4)$$

the five-orbital model of Bielefeld and Fitts[42] for thiophene and taking as an example the $\varphi_4 \leftarrow \varphi_3$ transition, it is seen that particularly the charge density at the 2 and 5 carbons decreases significantly on excitation (Table V). The effect is even more pronounced if the

TABLE V
CHANGE IN CHANGE DENSITY q FOR $\varphi_4 \rightarrow \varphi_3$ TRANSITION IN THIOPHENE FOR A FIVE-ORBITAL MODEL

	Ground state[a]	Excited state (φ_4 occupied)
S	1.793	1.896
$C_{2,5}$	1.064	0.861
$C_{3,4}$	1.040	1.020

[a] From ref 42.

3d orbitals on sulfur are included in the orbital picture for thiophene (data of ref 42). This situation is, of course, exactly what is required for effective cyclopropyl participation in the excited state.

In summary, we believe that good support for the general idea of cyclopropyl participation in the excited state has been provided by the present examples. Moreover, the concept of increasing conjugative interaction with increasing electronic demand has been not only supported but also modified in the sense that any factors causing a significant electronic redistribution in the excited state will enhance cyclopropyl participation so long as the effect operates in an electron-withdrawing sense relative to cyclopropyl.

Experimental Section

Melting points were determined on a calibrated melting point block and boiling points are uncorrected. Ultraviolet (uv) spectra were recorded on a Zeiss PMQ II spectrophotometer. Infrared spectra (ir) were obtained with a Perkin-Elmer Model 125 infrared spectrophotometer. Nuclear magnetic resonance (nmr) spectra were taken on a Varian A-60 instrument using TMS as the internal standard. Fluorescence spectra were taken in cyclohexane solution at room temperature using an Aminco-Bowman spectrophotofluorometer. Analytical gas chromatography (glpc) was done on a F & M Model 810 gas chromatograph equipped with flame detectors and preparative work was done with a F & M Model 700 unit with thermal conductivity detectors. Irradiations were carried out using a Hanau TQ-81 medium pressure lamp equipped with quartz jackets. Many of the uv, ir, and nmr spectra were taken by Mrs. K. S. Rozema. Microanalyses were done by the analytical section of this laboratory under the direction of Mr. W. Hazenberg.

Syntheses of the various phenyl- and isopropylthiophenes used for comparison purposes were carried out along the lines detailed in Schemes I and II. Formylation and iodination of 3-isopropylthiophene produced *ca.* 50:50 mixtures of 2,3- and 2,4-substituted isomers; bromination, however, was completely-selective to the 2 position. The aldehyde derivative was therefore prepared from 2-lithio-3-isopropylthiophene prepared from the 2-bromo derivative; the carboxylic acid was obtained by oxidation of the aldehyde. All reference compounds were shown to be isomerically pure by nmr spectroscopy as well as glpc.

2-Cyclopropylthiophene (**4**) was prepared following the general synthesis for cyclopropylbenzene described by Bumgartner.[18]

(46) H. H. Jaffé and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy," Wiley, New York, N. Y., 1962, pp 242–259.

(47) For favorable cases the conjugative ability of cyclopropyl has been calculated to be similar to that of phenyl and vinyl: R. Hoffmann, *Tetrahedron Lett.*, 3819 (1965).

Since some modifications have been made, important details of the procedure are given. Condensation of 2-thienylaldehyde with malonic acid in pyridine gave 3-(2-thienyl)acrylic acid.[48] This compound (28.5 g, 0.185 mol) was placed in the thimble of a Soxhlet extractor attached to a flask containing $LiAlH_4$ (11.0 g, 0.29 mol) in 1200 ml of ether.[49] The acid was completely transferred to the ether solution after 30–60-min refluxing; after refluxing 15 min more, the solution was cooled and water (or ethyl acetate) was added slowly to decompose the excess $LiAlH_4$. A solution of 300 ml of 10% H_2SO_4 was added, whereupon a clear solution resulted which was separated in a separatory funnel. The ether layer was neutralized with $NaHCO_3$ solution, washed once with water, and dried over $MgSO_4$. Distillation gave 18.7 g (0.132 mol, 71%) of 3-(2-thienyl)-1-propanol:[50] bp 88° (0.6 mm); ir (neat) 3350 cm^{-1}; nmr (CCl_4) δ 1.84 (quint, 2, J = ~6.5 Hz, CH_2), 2.86 (t, 2, J = 8.0 Hz, CH_2OH), 3.57 (t, 2, J = 8.0 Hz, $ThCH_2$), 3.80 (s, 1, OH), and 6.60–7.12 (m, 3, Th), no vinyl protons observable.

Anal. Calcd for $C_7H_{10}OS$: C, 59.12; H, 7.09; S, 22.54. Found: C, 58.91; H, 6.95; S, 22.58.

The above alcohol (17.1 g, 0.12 mol) was converted to 3-(2-thienyl)-1-propyl tosylate by treatment with *p*-toluenesulfonyl chloride in pyridine[51] to give 34.5 g (0.116 mol, 96.5%) of product, mp 63.5–64.5°.

Anal. Calcd for $C_{14}H_{16}O_3S_2$: C, 56.73; H, 5.44; S, 21.63. Found: C, 56.62; H, 5.43; S, 21.55.

The above tosylate (30 g, 0.107 mol) in 120 ml of benzene containing dimethylamine [25 g (0.55 mol, excess)] was sealed in a heavy-walled glass tube and heated (with shaking) at 65–70° for 3 days. The reaction mixture was washed successively with 10% $NaHCO_3$ solution and water and dried over $MgSO_4$. Distillation gave 15.0 g (0.90 mol, 84%) of 3-(2-thienyl)-*n*-propyldimethylamine: bp 104–106° (14 mm); $n^{20.5}D$ 1.5090.

Anal. Calcd for $C_9H_{15}NS$: C, 63.86; H, 8.93; N, 8.27; S 18.94. Found: C, 63.85; H, 8.98; N, 8.27; S, 19.13.

The above amine (22 g, 0.13 mol) was treated with excess MeI in ether to give 39 g (0.125 mol, 96%) of the quaternary salt (**1**), mp 186–186.5°.

Anal. Calcd for $C_{10}H_{19}NSI$: C, 38.59; H, 5.84; N, 4.50; S, 10.30; I, 40.78. Found: C, 38.74; H, 5.91; N, 4.49; S, 10.23; I, 40.75.

A 2-l. three-necked flask containing a magnetic stirring bar was fitted with a condenser through which cold MeOH (−15°) was pumped and which was protected with a drying tube. To another neck was attached a piece of Teflon tube connected to an erlenmeyer flask containing the iodide. The apparatus was flame-dried. Ammonia (750 ml) was added followed by Na (5.0 g, 0.22 g-atom) and *ca.* 200 mg $Fe(NO_3)_3$ while the flask was contained in a solid CO_2–acetone bath. After the sodium had dissolved the above quaternary salt (39 g, 0.125 mol) was added portionwise to the solution over a period of *ca.* 20 min. A deep green color immediately developed later turning to black. After the mixture was allowed to stand for 4 hr, NH_4Cl (15.8 g, 0.30 mol) was added followed by 430 ml of ether. The ammonia was allowed to evaporate overnight. Water was added to the solution, the layers were separated, and the ether layer was washed once with dilute HCl solution, once with water, once with 10% $NaHCO_3$ solution, and once again with water and finally dried over $MgSO_4$. Distillation gave 13.38 g (0.108 mol, 86%) of 2-cyclopropylthiophene (**4**): bp 58° (10 mm); $n^{20.5}D$ 1.5473; ir (neat) 1045 cm^{-1} (cyclopropyl); nmr (CCl_4) δ 0.5–1.20 (complex multiplet, 4, cyclopropylmethyl), 1.80–2.30 (complex multiplet, 1, *tert*-H), and 6.40–7.00 (complex multiplet, 3, thiophene).

Anal. Calcd for C_7H_8S: C, 67.69; H, 6.49; S, 25.82. Found: C, 67.45; H, 6.46; S, 25.87.

2-Bromo-5-cyclopropylthiophene (**11**) was obtained when 2-cyclopropylthiophene (1.000 g, 0.08 mol) was allowed to react with NBS (1.500 g, 0.008 mol) in 30 ml of a 1:1 $CHCl_3$–HOAc solution. Distillation provided 1.45 g (0.007 mol, 87.5%) of **11**: bp 106° (14 mm); nmr (CCl_4) δ 0.6–1.1 (multiplet, 4, cyclopropylmethylene), 1.75–2.20 (multiplet, 1, *tert*-H), 6.47 (q, 1, J = 4.0 Hz, 1.0 Hz, 4 proton), 6.76 (d, 1, J = 4.0 Hz, 3 proton), no vinyl absorption was observable even at high attenuation.

Anal. Calcd for C_7H_7SBr: C, 41.40; H, 3.47; S, 15.79; Br, 39.34. Found: C, 41.86; H, 3.47; S, 15.84; Br, 39.39.

Deuterium exchange with 4 was carried out with **4** (287 mg, 1.93 mmol) in a refluxing solution of acetic anhydride (5 ml) and D_2O (3 ml). After 6 hr the mixture was worked up.[24] The product **13** had a nmr spectrum (CCl_4) identical with that of **4** except that in the aromatic region a set of doublets (J = 4.0 Hz) at δ 6.46 and δ 6.56 were seen indicating 100% exchange at the 5 position.

5-Cyclopropylthiophene-2-carboxylic acid (**12**) was obtained from the Grignard reagent obtained from **11** (650 mg, 3.2 mmol) with Mg (80 mg, 3.5 g-atoms) in ether. The Grignard reagent was poured on to solid CO_2, the resulting solution was acidified and extracted with ether, the ether layer was extracted with dilute NaOH solution, and the water layer was acidified whereupon crude acid precipitated. Recrystallization from petroleum ether (bp 40–60°) gave 240 mg (1.43 mmol, 45%) of **12**: mp 113–114.5°; ir (KBr) 1630 (C=O), 1045 cm^{-1} (cyclopropyl); nmr (C_3D_6O) δ 0.6–1.2 (multiplet, 4, cyclopropylmethylene), 1.90–2.35 (multiplet, 1, *tert*-H), 5.6–6.3 [s (broad), 1, OH], 6.82 (q, 1, J = 4.0 Hz, 1.0 Hz, 4 proton), and 7.55 (d, 1, J = 4.0 Hz, 3 proton).

Anal. Calcd for $C_8H_8O_2S$: C, 57.12; H, 4.79; S, 19.06. Found: C, 57.25; H, 4.90; S, 19.07.

5-Cyclopropylthiophene-2-carboxaldehyde (**10**) was obtained upon slow addition of 2-cyclopropylthiophene (1.0 g, 9 mmol) to a solution of dimethylformamide (900 mg, 9 mmol) containing $POCl_3$ (1900 mg, 9 mmol) with the temperature being held at 10–20°. After addition was complete the magnetically stirred mixture was warmed gently for 1 hr and therafter poured onto ice. The solution was extracted with ether; the ether solution was neutralized with $NaHCO_3$ solution washed with water, and dried over $MgSO_4$. Distillation gave 750 mg (4.9 mmol, 56%)[52] of **10**: bp 135° (18 mm); ir (CCl_4) 1650 (C=O) and 1040 cm^{-1} (cyclopropyl); nmr (CCl_4) δ 0.6–1.3 (multiplet, 4, cyclopropylmethylene), 1.8–2.3 (multiplet, 1, *tert*-H), 6.78 (q, 1, J = 4.0 Hz, ~0.5 Hz, 4 proton), 7.47 (d, 1, J = 4.0 Hz, 3 proton), and 9.67 [s, 1, C(=O)H].

Anal. Calcd for C_8H_8OS: C, 63.13; H, 5.29; S, 21.06. Found: C, 62.82; H, 5.27; S, 21.02.

2-Cyclopropyl-5-iodothiophene (**14**) was prepared using a previously described iodination procedure.[53] Starting from **4** (6.21 g, 50 mmol), iodine (12.8 g, 0.05 g-atom), and mercuric oxide (8.02 g, 0.04 mol) there was obtained after distillation[54] 10.91 g (43.6 mmol, 87%) of **14**: bp 90° (2.5 mm); ir (neat) 1040 cm^{-1} (cyclopropyl); nmr (CCl_4), δ 0.5–1.1 (multiplet, 4, cyclopropylmethylene), 1.7–2.2 (multiplet, 1, *tert*-H), 6.28 (q, 1, J = 3.9 Hz, ~0.5 Hz, 3 proton), and 6.88 (d, 1, J = 3.9 Hz, 4 proton).

Anal. Calcd for C_7H_7SI: C, 33.62; H, 2.82; S, 12.82; I, 50.74. Found: C, 33.56; H, 2.69; S, 12.94; I, 50.78.

Nitration of 4 was carried out in a manner similar to that described for the phenylthiophenes.[27] 2-Cyclopropylthiophene (5.0 g, 0.04 mol) in 65 ml of acetic anhydride was added dropwise to a solution of $Cu(NO_3)_2 \cdot 3H_2O$ (4.88 g, 0.02 mol) in 65 ml of acetic anhydride. The solution was held at 10–12° for 2 hr whereupon the copper salts were removed by filtration and the residue was poured into ice water. Continuous extraction with ether gave a thick oil which consisted of mono- and dinitrothiophenes as determined by nmr. Distillation gave, in addition to a small amount of unreacted **4** and pot residue, 2.1 g (1.24 mmol, 30%) of a mixture consisting, as determined by nmr, of 60% 2-cyclopropyl-5-nitrothiophene (**15**) and 40% 2-cyclopropyl-3-nitrothiophene (**16**): bp 146° (11 mm); ir (neat) 1035 cm^{-1} (cyclopropyl).

Anal. Calcd for $C_7H_7NO_2S$: C, 49.69; H, 4.17; N, 8.27; S, 18.95. Found: C, 49.87; H, 4.18; N, 8.11; S, 18.91.

The individual compounds were obtained pure by preparative glpc (SE-30, 6 ft, 185°): **15**, nmr (CCl_4) δ 0.6–1.3 (multiplet, 4,

(48) M. J. Mihailović and M. Tot, *J. Org. Chem.*, **22**, 682 (1957).

(49) R. F. Nystrom and W. G. Brown, *J. Amer. Chem. Soc.*, **69**, 2548 (1947).

(50) This procedure should be followed rigorously to obtain good yields of alcohol. Minor deviations lead to decreased yield.

(51) L. Fieser and M. F. Fieser, "Reagents for Organic Synthesis," Wiley, New York, N. Y., 1968, p 1180; S. W. Pelletier, *Chem. Ind.*, 1034 (1953).

(52) Scaling up the reaction continually resulted in a lowered yield. We have not, despite repeated efforts, been able to circumvent this difficulty.

(53) W. Minnis, *Org. Syn.*, **12**, 44 (1933).

(54) This material can decompose quite violently above ~100° and care should be exercised in distilling it. We have observed that brominated or iodinated thiophenes have in general an unpredictable tendency to decompose violently even at room temperature. Extra care is therefore strongly recommended in the distillation and storage of these materials.

cyclopropylmethylene), 1.85–2.30 (multiplet, 1, *tert*-H), 6.67 (q, 1, J = 4.0 Hz, ~0.8 Hz, 3 proton), and 7.66 (d, 1, J = 4.0 Hz, 4 proton); **16**, nmr (CCl_4) δ 0.7–1.45 (multiplet, 4, cyclopropylmethylene), 1.7–3.2 (multiplet, 1, *tert*-H), 6.92 [d, 1, J = 5.5 Hz, 4(?) proton], and 7.46 [d, 1, J = 5.5 Hz, 5(?) proton].

Nitration of 2-isopropylthiophene was carried out as described above to yield 50% of a fraction of bp 141–142° (23 mm) consisting of a 80:20 mixture of 2-isopropyl-5-nitro and 2-isopropyl-3-nitrothiophenes as evidenced by nmr absorptions in the aromatic region with J values of 4.0 and 5.5 Hz, respectively.

Anal. Calcd for $C_7H_9NO_2S$: C, 49.11; H, 5.30. Found: C, 49.12; H, 5.31.

Repeated attempts to obtain satisfactory N and S analyses failed; the mass spectrum, however, showed the parent peak at m/e 171.

The 2-isopropyl-5-nitrothiophene was purified by preparative glpc (DEGS, 6 ft, 170°): nmr (CCl_4) δ 1.36 (d, 6, J = 6.5 Hz, CH_3), 3.15 (complex multiplet, 1, methine H), 6.71 [d (slightly split), 1, J = 4.0 Hz, 3 H), and 7.68 (d, 1, J = 4.0 Hz, 4 H).

2-Cyclopropyl-5-phenylthiophene (**5**) was prepared in an analogous manner to that described for **4**. 5-Phenylthiophene-2-carboxaldehyde[55] was obtained from 2-phenylthiophene and condensation with malonic acid yielded 3-(5-phenyl-2-thienyl)-propenoic acid in 91% yield, mp 206.5–207.5° (from ethanol).

Anal. Calcd for $C_{13}H_{10}O_2S$: C, 67.80; H, 4.33; S, 13.92. Found: C, 67.75; H, 4.37; S, 13.83.

Reduction of the acid gave 3-(5-phenyl-2-thienyl)-1-propanol in 81% yield as a crude solid which was not purified further (no alkene absorption in ir). Conversion to the tosylate proceeded in 90% yield, mp 63.5–64.5° (from 40–60° petroleum ether).

Anal. Calcd for $C_{20}H_{20}O_3S_2$: C, 64.49; H, 5.41; S, 17.21. Found: C, 64.80; H, 5.50; S, 17.23.

The above tosylate with excess dimethylamine in benzene at 65° (sealed tube) for 2 days gave dimethyl-*n*-[3-(5-phenyl-2-thienyl)]propylamine in 70% yield, bp 152° (0.7 mm).

Anal. Calcd for $C_{15}H_{19}NS$: C, 73.42; H, 7.81; S, 5.71; N, 13.07. Found: C, 73.46; H, 7.66; S, 5.51; N, 13.46.

The amine was treated with excess methyliodide in ether to give trimethyl-*n*-[3-(5-phenyl-2-thienyl)]propylammonium iodide (**2**) in 78% yield, mp 226.5–227°.

Anal. Calcd for $C_{16}H_{22}NSI$: C, 49.62; H, 5.72; N, 3.61; S, 8.28; I, 32.72. Found: C, 49.57; H, 5.74; N, 3.65; S, 8.22; I, 32.65.

Treatment of **2** (12 g, 0.031 mol) in 250 ml of NH_3 in which sodium (1.3 g, 0.057 g-atom) and a trace of ferric nitrate had been dissolved gave in 50% yield **5**: bp 123–125° (0.75 mm); nmr (CCl_4) δ 0.6–1.0 (multiplet, 4, cyclopropylmethylene), 1.8–2.3 (multiplet, 1, *tert*-H), 6.62 (q, 1, J = 3.8 Hz, <0.5 Hz, 3 proton), 6.99 (d, 1, J = 3.8 Hz, 4 proton), and 6.9–7.6 (multiplet, 5, C_6H_5).

Anal. Calcd for $C_{13}H_{12}S$: C, 77.95; H, 6.04; S, 16.01. Found: C, 77.77; H, 6.07; S, 16.08.

2,5-Dicyclopropylthiophene (**6**) was prepared beginning with the condensation of **10** with malonic acid to give 3-(5-cyclopropyl-2-thienyl)propenoic acid, mp 106–108° (from ethanol), in 81% yield. This was reduced with excess $LiAlH_4$ to 3-(5-cyclopropyl-2-thienyl)-1-propanol which was converted to the tosylate without any purification. The tosylate was an oil which failed to crystallize. Treatment with excess dimethylamine in benzene for 2 days at 65° (sealed tube) gave 55% (based on tosylate) dimethyl-*n*-[3-(5-cyclopropyl-2-thienyl)]-propylamine, bp 102–106° (0.8 mm). Treatment with excess methyl iodide gave trimethyl-*n*-[3-(5-cyclopropyl-2-thienyl)]-propylammonium iodide (**3**) in quantitative yield, mp 88.5–90°.

Anal. Calcd for $C_{13}H_{22}NSI$: C, 44.45; H, 6.31; N, 3.98; S, 9.13; I, 36.13. Found: C, 44.04; H, 6.32; N, 3.92; S, 9.05; I, 36.45.

Treatment of **3** with sodium amide in ammonia gave in 62% yield 2,5-dicyclopropylthiophene: bp 112–114° (10 mm); nmr (CCl_4) δ 0.55–1.05 (multiplet, 8, cyclopropylmethylene), 1.7–2.15 (multiplet, 2, *tert*-H), and 6.42 (s, 2, 3,4 protons).

Anal. Calcd for $C_{10}H_{12}S$: C, 73.12; H, 7.36; S, 19.52. Found: C, 73.20; H, 7.27; S, 19.43.

3-Cyclopropylthiophene (**9**) was prepared by modification of a published procedure.[23] Base-catalyzed condensation of 3-thiophenealdehyde with acetaldehyde at 0° proceeded smoothly to give 3-(3-thienyl)acrylaldehyde.[56] To a refluxing mixture of 85% hydrazine (3.9 ml) in 10 ml of 95% ethanol was added slowly the above aldehyde (3.5 g, 25 mmol). The mixture was refluxed for 1.5 hr after which time distillation was begun. When the head temperature reached 120° (bath 200°) gas evolution began, after which colorless liquid distilled over. Water was added to the distillate which was then extracted twice with ether. The ether layer was backwashed twice with water and dried over $CaCl_2$. Distillation gave **9** (800 mg, 6.35 mmol, 25%): bp 58° (10 mm); ir (neat) 1040 cm^{-1} (cyclopropyl); nmr (CCl_4) δ 0.5–1.0 (complex multiplet, 4, cyclopropylmethylene), 1.6–2.0 (complex multiplet, 1, *tert*-H), and 6.65–7.15 (complex multiplet, 3, aromatic H).

Anal. Calcd for C_7H_8S: C, 67.69; H, 6.49; S, 25.82. Found: C, 67.39; H, 6.41; S, 25.57.

3-Cyclopropyl-2-iodothiophene (**21**) was prepared in a manner analogous to that described for **14**. From **9** (464 mg, 3.74 mmol) was obtained 750 mg (3.0 mmol, 80%) of **21** which was purified by chromatography over Al_2O_3 using benzene. Removal of the benzene left a clear oil (explosion upon distillation) which had ir (neat) 1045 cm^{-1} (cyclopropyl) and nmr (CCl_4) δ 0.4–1.1 (complex multiplet, 4, cyclopropylmethylene), 1.5–2.0 (complex multiplet, 1, *tert*-H), 6.29 (d, 1, J = 5.5 Hz, 4 H), and 7.22 (d, 1, J = 5.5 Hz, 5 H).

Anal. Calcd for C_7H_7SI: C, 33.62; H, 2.82; S, 12.82; I, 50.74. Found: C, 33.79; H, 2.80; S, 12.87; I, 50.69.

2-Bromo-3-cyclopropylthiophene (**19**) was obtained by bromination of 3-cyclopropylthiophene (200 mg, 1.61 mmol) with NBS in HOAc–$CHCl_3$ as described for **11**. There was obtained 262 mg (1.28 mmol, 80%) **19**: bp 97° (10 mm); ir (neat) 1050 cm^{-1} (cyclopropyl); nmr (CCl_4) δ 0.4–1.25 (complex multiplet, 4, cyclopropylmethylene), 1.6–2.2 (complex multiplet, 1, *tert*-H), 6.36 (d, 1, J = 5.6 Hz, 4 H), and 7.03 (d, 1, J = 5.6 Hz, 5 H).

Anal. Calcd for C_7H_7SBr: C, 41.40; H, 3.47; S, 15.79; Br, 39.34. Found: C, 41.49; H, 3.60; S, 15.90; Br, 39.34.

Deuterium exchange with 3-cyclopropylthiophene (200 mg, 1.61 mmol) was carried out at reflux temperature for 5 hr with a mixture of D_2O (2 ml) and acetic anhydride (5 ml). After work-up the product (**20**) had nmr (CCl_4) δ 0.45–1.0 (complex multiplet, 4, cyclopropylmethylene), 1.6–2.1 (complex multiplet, 1, *tert*-H), 6.72 (d, 1, J = 5.0 Hz, 4 H), and 7.08 (d, 1, J = 5.0 Hz, 5 H). This indicates 100% exchange (by nmr) of the 2 hydrogen with undetectable exchange at other positions.

3-Cyclopropylthiophene-2-carboxaldehyde (**17**) was obtained in a manner analogous to that described for **10**. From **9** (1.09 g, 8.79 mmol) there was obtained 1.00 g (6.58 mmol, 75%) **17**: bp 132° (10 mm); ir (neat) 1050 cm^{-1} (cyclopropyl); nmr (CCl_4) δ 0.6–1.3 (complex multiplet, cyclopropylmethylene), 2.2–2.7 (complex multiplet, 1, *tert*-H), 6.59 [d, 1, J = 5.0 Hz, 4(?) H], 7.47 [q, 1, J = 5.0 Hz, ~0.5 Hz, 5(?) H], and 10.08 (d, 1, J = 1.2 Hz, COH).[57]

Anal. Calcd for C_8H_8OS: C, 63.13; H, 5.29; S, 21.06. Found: C, 63.11; H, 5.48; S, 21.07.

Nitration of 9 was carried out in a manner analogous to that described for **4**. From **9** (1.30 g, 10.5 mmol) was obtained a crude mixture of mononitrothiophenes (1.31 g, 7.75 mmol, 74% crude yield), bp 150° (12 mm). This mixture consisted of ~12% 4-cyclopropyl-2-nitrothiophene (**24**) as judged from absorptions at δ 1.6–2.2 (complex multiplet, *tert*-H), 7.06 (J = 2.0 Hz), and 7.54 (J = 2.0 Hz) with the cyclopropylmethylene absorptions buried under those for 3-cyclopropyl-2-nitrothiophene (**23**) which constituted 88% of the mixture. Repeated attempts by glpc, tlc, and column chromatography failed to effect a separation of the nitrothiophenes. The crude mixture was recrystallized three times from absolute methanol to give **23**: mp 48.5–50°; nmr (CCl_4) δ 0.6–1.4 (complex multiplet, 4, cyclopropylmethylene), 2.7–3.2 (complex multiplet, 1, *tert*-H), 6.52 (d, 1, J = 5.8 Hz, 4 H), and 7.32 (d, 1, J = 5.8 Hz, 5 H).

Anal. Calcd for $C_7H_7O_2NS$: C, 49.69; H, 4.17; N, 8.27; S, 18.95. Found: C, 49.74; H, 4.30; N, 8.10; S, 18.74.

Nitration of 3-isopropylthiophene was carried out as described above for **4**. A 73% yield of a fraction of bp 140–150° (20 mm)

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(57) Usually the aromatic protons can be assigned from chemical shift values, *i.e.*, β protons absorb at higher field.[9] With **17** the resonance at δ 7.47 shows long-range, probably allylic coupling. This should come from the methine proton of the cyclopropyl ring but the chemical shifts are inverted from what would be expected.

was obtained which consisted of about 50% 3-isopropyl-2-nitrothiophene and 50% 4-isopropyl-2-nitrothiophene.

Anal. Calcd for $C_7H_9NO_2S$: C, 49.11; H, 5.30; N, 8.18; S, 18.72. Found: C, 49.48; H, 5.35; N, 8.20; S, 18.59.

The isomers were separated by preparative glpc (DEGS, 6 ft, 170°): 2-nitro-3-isopropylthiophene, nmr (CCl_4) δ 1.28 (d, 6, J = 7.0 Hz, CH_3), 3.98 (complex m, 1, methine H), 7.03 (d, 1, J = 5.5 Hz, aromatic H), and 7.38 (d, 1, J = 5 Hz, aromatic H); 2-nitro-4-isopropylthiophene, nmr (CCl_4) δ 1.27 (d, 6, J = 7.5 Hz, CH_3), 2.98 (complex m, 1, methine H), 7.19 [d (slightly split), 1, J = 2.0 Hz, 5 H), and 7.76 (d, 1, J = 2.0 Hz, 3 H), and uv (95% EtOH) 289 mμ (log ϵ 3.76) and 327 (3.80).

3-Cyclopropyl-2-phenylthiophene (22) was prepared by irradiating with a high pressure mercury lamp **21** (500 mg, 2 mmol) in 125 ml of benzene containing 1 mol % anhydrous $Na_2S_2O_3$. After 6 hr irradiation stopped. The benzene solution was washed repeatedly with aqueous $Na_2S_2O_3$ and then dried over $MgSO_4$. After removal of the solvents the residue was chromatographed over Al_2O_3 using benzene to give chiefly **22** (50% yield from glpc) which was purified by preparative glpc (F & M 700, 150°) to give a clear liquid: ir (neat) 1035, 1055 cm^{-1} (cyclopropyl); nmr (CCl_4) δ 0.5–1.0 (complex multiplet, 4, cyclopropylmethylene), 1.7–2.2 (complex multiplet, 1, *tert*-H), 6.55 [d, 1, J = 5.5 Hz, 4(?) H], 7.04 [d, 1, J = 5.5 Hz, 5(?) H], and 7.1–7.6 (complex multiplet, 5, phenyl). Too little sample was obtained for an elemental analysis.

Attempted Synthesis of 9 from Quaternary Iodide 7.—In a manner analogous to that described for **1**, condensation of 3-thiophenealdehyde with malonic acid gave 3-(3-thienyl)acrylic acid.[48] Reduction with $LiAlH_4$ gave 3-(3-thienyl)-1-propanol in 66% yield, bp 141–145° (12 mm). Treatment with tosyl chloride gave an oily tosylate which was not purified but allowed to react with dimethylamine to give 3(3-thienyl)-1-dimethylaminopropene in 32% yield based on alcohol: bp 104–107° (12 mm); $n^{18}D$ 1.5130. Treatment with methyl iodide gave in 90% yield the quaternary iodide (**7**), mp 167–169°.

Anal. Calcd for $C_{10}H_{18}SNI$: C, 38.59; H, 5.84; S, 10.30; N, 4.50; I, 40.78. Found: C, 38.45; H, 5.71; S, 10.30; N, 4.40; I, 40.73.

Attempted cyclization in liquid ammonia with sodium amide gave, after work-up, a liquid (about 30%), bp 60° (10 mm), which, besides some weak signals ultimately attributed to **9**, showed strong absorptions at δ 6.3–6.5 indicating vinyl protons presumed to arise from 3-(3-thienyl)-1-propene (**8**). The reaction mixture was not investigated further.

Registry No.—**1**, 26019-23-8; **2**, 29481-20-7; **3**, 29481-21-8; **4**, 29481-22-9; **5**, 29481-23-0; **6**, 29481-24-1; **7**, 29481-25-2; **9**, 29576-51-0; **10**, 29481-26-3; **11**, 29481-27-4; **12**, 29481-28-5; **14**, 29481-29-6; **15**, 29576-52-1; **16**, 29481-30-9; **17**, 29481-31-0; **19**, 29481-32-1; **20**, 29481-33-2; **21**, 29481-34-3; **22**, 29481-35-4; **23**, 29481-36-5; **24**, 29481-37-6; 4-isopropylpyridine, 696-30-0; 3-(2-thienyl)-1-propanol, 19498-72-7; 3-(2-thienyl)-1-propyl tosylate, 29488-39-9; 3-(2-thienyl)-*n*-propyldimethylamine, 23711-40-2; 2-isopropyl-3-nitrothiophene, 29488-41-3; 3-(5-phenyl-2-thienyl)-propenoic acid, 29488-42-4; 3-(5-phenyl-2-thienyl)-1-propanol tosylate, 29488-43-5; dimethyl-*n*-[3-(5-phenyl-2-thienyl)]propylamine, 29488-44-6; 3-(5-cyclopropyl-2-thienyl)propenoic acid, 29488-45-7; dimethyl-*n*-[3-(5-cyclopropyl-2-thienyl)]-propylamine, 29488-46-8; 4-isopropyl-2-nitrothiophene, 29488-47-9; 3-(3-thienyl)-1-propanol, 20905-98-0; 3-(3-thienyl)-1-dimethylaminopropane, 29488-48-0; 4-cyclopropylpyridine, 4904-21-6.

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Reactions of Phosphorus Compounds. XXVI. Preparation and Reactions of 3- and 4-Substituted 5-Benzoyl-2,2,2,5-tetraphenyloxa-2-phospholanes[1]

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Substituted (1- and 2-) vinylphosphonium salts reacted with the sodium salt of benzoin in DMSO to give 3- and 4-substituted 5-benzoyl-2,2,2,5-tetraphenyloxa-2-phospholanes, respectively. Methyl-substituted oxaphospholanes were separated into diastereoisomers while 3- and 4-phenyl-substituted oxaphospholanes were isolated as single isomers. Diastereomeric mixtures of oxaphospholanes substituted at C_3 tended to isomerize to one stable isomer while those substituted at C_4 did not isomerize. Reaction of 1- and 2-substituted vinylphosphonium salts with the sodium salt of benzoin in acetonitrile gave 2,5-dihydrofurans in all cases except 1-phenylvinyltriphenylphosphonium bromide which gave only the oxaphospholane. Pyrolysis of the oxaphospholanes gave benzil, triphenylphosphine, and an olefin.

In a previous article[2] we described the preparation and reactions of 5-benzoyl-2,2,2,5-tetraphenyloxa-2-phospholane (**5**) formed by attack of the benzoin enolate carbanion **1a** on vinyltriphenylphosphonium bromide (**2**) in dimethyl sulfoxide (DMSO). In contrast, the dihydrofuran **3** was exclusively formed when acetonitrile was used as solvent (Scheme I).[2]

We now wish to report the reactions of **1** with 1- and 2-substituted vinylphosphonium salts which yield oxaphospholanes and dihydrofurans. The basis for the stereochemical assignments of the oxaphospholanes obtained is discussed. The fusion reaction products of the oxaphospholanes are also examined.

Previous workers have had variable success in obtaining products from conjugate additions to propenyltriphenylphosphonium bromide[3] **6**. When **1** was allowed to react with this salt in DMSO, a 40% yield of oxaphospholanes was realized, which was easily separated into two diastereomeric oxaphospholanes **7a,b** by selective extraction with chloroform and fractional crys-

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