

## Proton Magnetic Resonance of Thiophenes

### III. Splittings of Side-chain Resonance Peaks

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Splittings of the aldehydic hydrogen resonance lines of the order of 1 c/s have been observed in certain thiophenealdehydes and oximes. This has been shown to be due to spin-spin coupling with the 5-hydrogen. No splittings have been observed when this position is blocked.

In connection with our work on the NMR-spectra of thiophenes<sup>1,2</sup>, we have studied the splitting of side-chain hydrogens in methylthiophenes, thiophenealdehydes and thiophenealdoximes.

In the present paper we wish to communicate some of our results. These findings may provide a foundation for a discussion of some remarkable features in the NMR spectra of these compounds.

In an earlier communication<sup>1</sup> we discussed the NMR spectra of the ring hydrogens in several monosubstituted thiophenes. In this connection we observed the splittings ( $\sim 1$  c/s) of the resonance lines of the aldehydic hydrogens in 2- and 3-thiophenealdehyde.

These splittings could possibly be due to restricted rotation of the aldehyde group; conjugation between the aldehyde group and the thiophene ring giving rise to C—C double bond character<sup>3\*</sup>. The aldehydic hydrogen might have different chemical shifts in the two possible rotational isomers thus giving rise to two hydrogen lines. The splittings then should be field as well as temperature dependent. Such chemical shifts due to hindered rotation have been observed, *e.g.* in amides and nitroso compounds<sup>5</sup>.

Another possible explanation of the splittings is that they are caused by spin-spin coupling of the aldehyde proton to one or more of the ring protons. In 2-thiophenealdehyde the ring hydrogen spectrum was not well enough

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\* We obtained no splittings of the aldehyde resonance line in benzaldehyde or 1-naphthaldehyde, but this fact might be explained by the greater conjugation in the thiophene compounds as compared to the benzene analogues<sup>4</sup>.

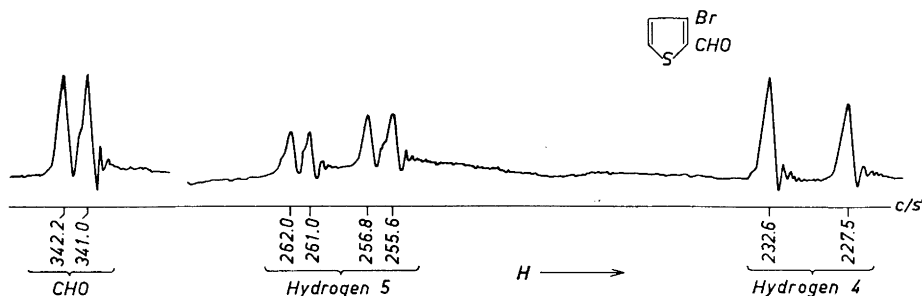


Fig. 1. NMR-spectrum of 3-bromo-2-thiophenealdehyde in *cyclohexane* (internal reference) at 40 Mc/s.

resolved to make a definite choice between the two alternative explanations possible. However, some preliminary experiments indicated that the splittings were temperature independent. In disubstituted thiophenes the ring hydrogen spectra are simpler, and therefore such spin-spin splittings should be observed in the ring hydrogen resonance band as well.

This was the case in 3-bromo-2-thiophenealdehyde. The spectrum of this compound with *cyclohexane* as the internal reference (Fig. 1) has the aldehydic hydrogen resonance at 342 c/s. This consists of a doublet with a splitting of 1.2 c/s. The two ring hydrogens give rise to a quartet and a doublet. The splittings in the quartet are 5.3 c/s and 1.1 c/s and in the doublet 5.1 c/s. This latter is the known  $J_{45}$  coupling constant for thiophenes<sup>1,2</sup>. The lower field quartet lies in the same region as the 5-hydrogen resonance in 2-thiophenealdehyde and the doublet has a shift similar to that of the 4-hydrogen of 2-thiophenealdehyde<sup>1</sup>. These results thus show that coupling occurs between the 5-hydrogen and the aldehydic hydrogen of this compound. Splittings of the aldehydic hydrogen in doublets were also observed in 4-substituted 2-thiophenealdehydes such as 4-bromo-2-thiophenealdehyde (0.9 c/s) and 4-methyl-2-thiophenealdehyde (1.3 c/s). In the first mentioned compound, however, the chemical shift between the 3- and 5-hydrogens is so small, (*cf.* 2-thiophenealdehyde<sup>1</sup>), that splittings due to coupling with the aldehydic hydrogen could not be observed in the ring spectrum. In the second compound the spectrum was complicated through additional coupling of the ring hydrogens with the methyl group.

No splitting of the aldehydic hydrogen resonance was however observed in 5-substituted 2-thiophenealdehydes such as 5-bromo-2-thiophenealdehyde and 5-methoxy-2-thiophenealdehyde.

These facts show that the splitting of the aldehydic hydrogen resonance line is caused by a coupling with the 5-hydrogen. These observations are quite remarkable since the coupling hydrogens are separated by as much as five bond distances, but consistent with Leane and Richards' interpretation<sup>6</sup> of the spectrum of furfural at 30 Mc/s. We have obtained a well resolved spectrum of furfural at 40 Mc/s and obtained a splitting of the aldehydic hydrogen equal to 0.8 c/s. Since they obtained a splitting of 0.9 c/s it is clear that these

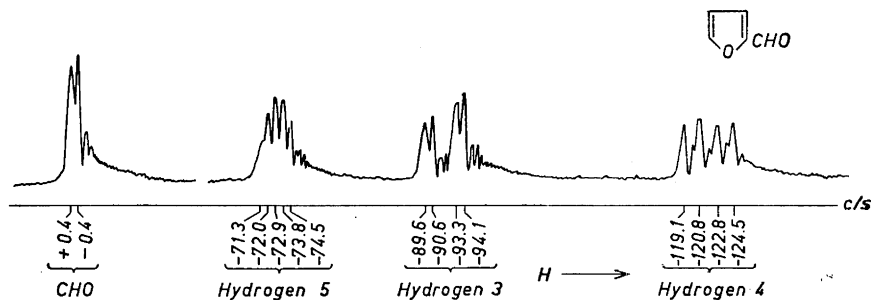


Fig. 2. NMR-spectrum of furfural at 40 Mc/s. The shifts are given relative to the aldehyde proton resonance line. The assignments are those of Refs.<sup>6,7</sup>

splittings are caused by spin-spin interactions. A chemical shift should have given a splitting at 30 Mc/s equal to 3/4 of that at 40 Mc/s.

The spectrum of the ring proton, which occurs at the lowest magnetic field (Fig. 2), consists of a quintet. This could be interpreted as a superposition of the patterns arising from three spin-spin couplings, two of which are nearly equal, and about half the magnitude of the third. This additional splitting of the lowest field ring proton resonance was also observed by Leane and Richards. They assign this multiplet to the five hydrogen as did Corey *et al.*<sup>7</sup> Apparently these assignments were based solely on the observed chemical shifts. If correct, it should then be pointed out that the relative magnitudes of  $J_{45}$  and  $J_{34}$  in furans are opposite to those in thiophenes. (In furans  $J_{34} > J_{45}$  in thiophenes  $J_{34} < J_{45}$ <sup>1,8</sup>). Leane and Richards<sup>6</sup> assumed that  $J_{34} > J_{45}$  for thiophenes. Their interpretations of the spectra of 2-nitrothiophene and 2-thiophenecarboxylic acid thus would seem to be incorrect. This difference in relative magnitudes of the coupling constants in thiophenes and furans, if correct, is of considerable theoretical interest. It should be of great value therefore to obtain spectra of 2,3-disubstituted and 2,5-asymmetrically

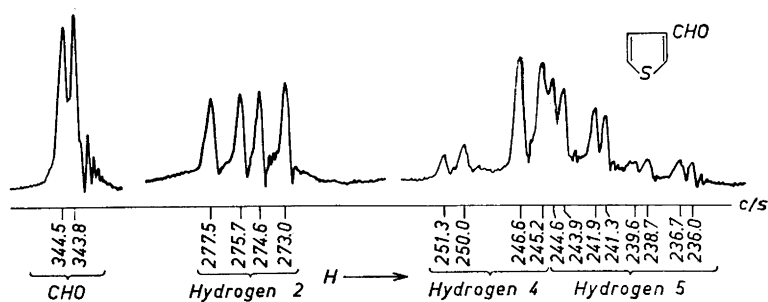


Fig. 3. NMR-spectrum of 3-thiophenealdehyde in cyclohexane (internal reference) at 40 Mc/s.

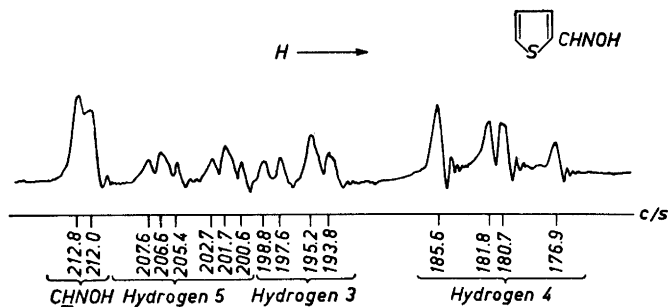


Fig. 4. NMR-spectrum of 2-thiophenealdoxime in dimethyl sulphoxide (internal reference) at 40 Mc/s.

disubstituted furans in order to confirm the assignments of coupling constants in furans.\*

The observed splitting of the aldehydic hydrogen resonance in 3-thiophenealdehyde (Fig. 3) may be caused by spin-spin interaction with the five hydrogen since the resonance lines in the  $2 \times 2 \times 2$  multiplet have splittings equal to 2.7, 5.2 and 0.7 c/s, respectively<sup>1</sup>. We intend to confirm this interpretation by studying the spectra of substituted 3-thiophenealdehydes. We have shown through a study of several substituted 3-methylthiophenes<sup>9</sup> that the splitting of the methyl resonance in 3-methylthiophene is caused by coupling with the 2-hydrogen. This indicates that the mechanism of the spin-spin coupling between side-chain protons and protons of the ring is different in thiophenealdehydes and methylthiophenes.\*\*

An investigation of the aldoxime hydrogen splitting in aromatic aldoximes is complicated by the fact that those compounds exist in *syn* and *anti* isomers. We have investigated a sample of 2-thiophenealdoxime, m.p. 130–131°, which was predominantly the *anti* form<sup>10</sup>. Its spectrum in dimethyl sulphoxide (Fig. 4) showed a doublet at 212 c/s from the solvent peak with a splitting of 0.8 c/s. Because of its shift<sup>5</sup> and because it is absent in the spectrum of 2-acetothienone oxime, this doublet is assigned to the aldoxime hydrogen. The spectrum of its ring hydrogens is well resolved; consisting of one sextet and two quartets. The hydrogen causing the high field quartet has couplings to the other ring hydrogens equal to 3.8 and 4.9 c/s and is thus<sup>1</sup> hydrogen 4. The next quartet has splittings equal to 1.3 and 3.7 c/s and is therefore assigned<sup>1</sup> to hydrogen 3. The band from the 5-hydrogen at the lowest field consists of two triplets. This can be interpreted as arising from a proton coupled to three other hydrogens with two couplings being nearly equal and much smaller than the third. Thus the aldoxime hydrogen in 2-thiophenealdoxime

\* The NMR spectrum of 5-chloromethyl furfural has been obtained by R. J. Abraham and H. J. Bernstein. *Canad. J. Chem.* **37** (1959) 1056.

\*\* Smaller spin couplings ( $\approx 0.4$  c/s) between the methyl group and the 4- and 5-hydrogens in 3-methylthiophene have been observed by P. L. Corio and I. Weinberg. *J. Chem. Phys.* **31** (1959) 569.

is coupled to the 5-hydrogen as is the aldehydic hydrogen in 2-thiophenealdehyde. The aldoxime hydrogen as well as the ring hydrogens in 3-thiophenealoxime gave complex spectra probably due to small relative shifts of the ring hydrogens. The splittings of the aldehyde and oxime hydrogen resonances are listed in Table 1.

Table 1. Observed splittings of aldehyde and oxime hydrogen resonance lines.

Compound	B.p./M.p.	Ref.	Splitting c/s
Furfural	63—64° (20 mm)		0.8
2-Thiophenealdehyde	85° (20 mm)	11	0.9
3-Thiophenealdehyde	86—87° (20 mm)	12	0.7
5-Bromo-2-thiophenealdehyde	105—107° (11 mm)	13	≈ 0
5-Methoxy-2-thiophenealdehyde	79—81° (0.9 mm)	14	≈ 0
3-Bromo-2-thiophenealdehyde	109—110° (10 mm)	9	1.2
4-Bromo-2-thiophenealdehyde	114—115° (11 mm)	9	0.9
	44—45° (m. p.)		
4-Methyl-2-thiophenealdehyde	95—96° (11 mm)	15	1.3
2-Thiophenealoxime	130—131° (m. p.)	16	0.8

We note that long-range splittings of aldehydic hydrogen resonance lines have not as yet been observed in either the benzene or the  $\alpha,\beta$ -unsaturated aldehyde series<sup>9</sup>. It is suggested that there might be a connection between the magnitude of the splittings and the degree of conjugation in the aldehydes. This would, however, require some interaction between the extended  $\pi$ -orbitals and the  $\sigma$  type C—H bond in the aldehyde group which is rather unexpected. We are continuing our studies in this field.\*

#### EXPERIMENTAL

The spectra were obtained with a Varian Associates Model V-4300 B high resolution Spectrometer and a flux-stabilized 12" magnet model V-4012-HR from the same company. The magnet sweep was calibrated by the familiar modulation side-band technique and the shifts from the internal standard were obtained by interpolation on the recorder chart. The modulation frequency obtained from the power line was 50 c/s.

References to the methods of preparation of the compounds investigated are given in Table 1. 4-Bromo-2-thiophenealdehyde and 3-bromo-2-thiophenealdehyde have been obtained from 4-bromo-2-lithiothiophene and 3-bromo-2-lithiothiophene, respectively, through the reaction with N,N-dimethyl formamide. Details of the preparation of these new compounds will be given later.

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\* Splittings of the aldehyde peak in ortho-substituted benzaldehydes ( $\sim 0.5$  c/s) have recently been observed in these laboratories by Drs. D. and V. J. Kowalewsky (private communication).

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