

Long-range Proton-proton Spin Coupling Constants in Thienothiophenes

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The cross-ring coupling constants in thieno[2,3-*b*]thiophene and a number of bromo substituted thieno[2,3-*b*]thiophenes and thieno[3,2-*b*]thiophenes have been determined. The largest couplings are observed between protons separated by six bonds placed in a straight zig-zag path, this coupling constant being +1.5 Hz in the thieno[3,2-*b*]thiophenes and +1.2 Hz in the thieno[2,3-*b*]thiophenes. The coupling *via* five bonds in thieno[3,2-*b*]thiophene is +0.7 Hz. Cross-ring coupling constants between protons not situated in a straight zig-zag configuration are small.

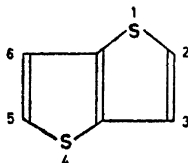
Proton-proton spin coupling constants in aromatic systems have been extensively studied, both the dependence on the heteroatoms in heteroaromatic systems, as well as the dependence on the substituents in substituted aromatic compounds.¹⁻³ Long-range interactions between protons situated on different rings in polycyclic aromatic systems have been observed in some instances. Most of the couplings observed are between protons separated by five bonds placed in a straight zig-zag structure.

Additional cross-ring interactions were observed in the spectrum of thieno[3,2-*b*]thiophene, which was studied in a previous investigation of perturbation methods for the analysis of AA'BB' spectra.^{4,5} In order to determine the assignment of the long-range couplings we have studied a number of substituted thieno[3,2-*b*]thiophenes. We have also extended the investigation to thieno[2,3-*b*]thiophenes, where similar cross-ring interactions are to be expected.

RESULTS

Thieno[3,2-*b*]thiophenes

*Thieno[3,2-*b*]thiophene.* The AA'BB' spectrum of this compound has been analysed previously using the (AB)₂ approximation as a basis for the analysis as well as by exact treatment.^{4,5}



The coupling constants were found to be $J_{23}=J_{56}=5.25$ Hz, $J_{26}=J_{35}=-0.20$ Hz, $J_{AA'}=1.55$ Hz and $J_{BB'}=0.75$ Hz. The signs are based on the assumption of a positive value for the vicinal coupling constant J_{23} .¹⁻³ The parameters $J_{AA'}$ and $J_{BB'}$ cannot be assigned to definite couplings in the molecule.

2,6-Dibromothieno [3,2-b]thiophene. The spectrum of this compound appears as two well separated doublets, belonging to the 5- and 3-hydrogens, respectively. In thiophene the α -proton resonance is known to be displaced towards lower field, due to the deshielding effect of the sulphur atom. The Br substituent cannot be expected to reverse this order in the thienothiophenes⁶ and we assign the 5-hydrogen to the low field doublet. The observed splitting is $|J_{35}|=0.15$ Hz. The sign of a coupling constant in a two spin system cannot be determined. However, it is well established that couplings are fairly insensi-

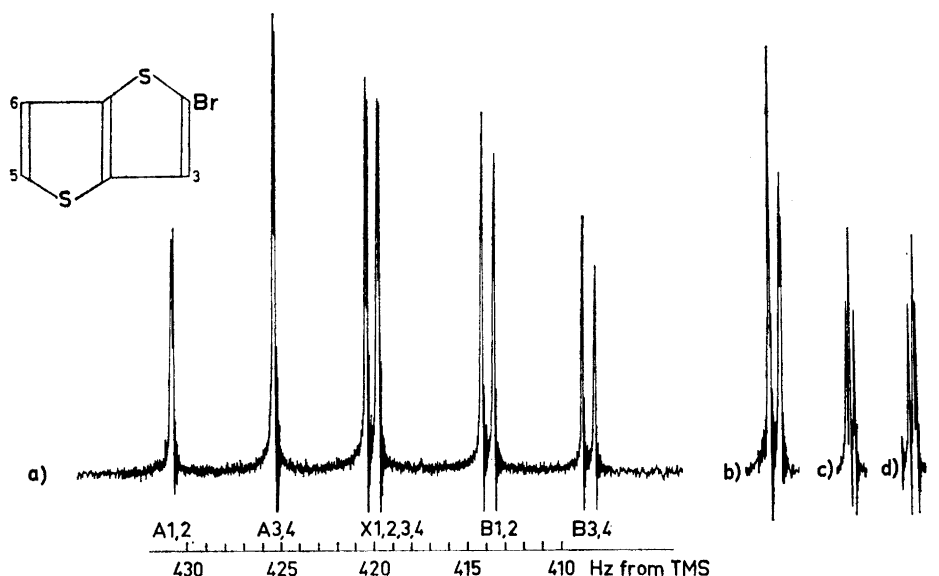


Fig. 1. (a) The single resonance spectrum at 56.444 MHz of 2-bromothieno[3,2-b]thiophene in ca. 15% acetone solution. (b-d). The results of the double irradiation experiments; (b) shows the X region in the presence of an irradiating field centred on the A1, A2 doublet; c) shows the A3,A4 region in the presence of a weak irradiating field centered on B3; d) shows the same region when the weak irradiating field is centered on B4.

tive to substituents ^{2,3} and we can therefore set J_{35} negative to obtain agreement with the corresponding coupling in thieno[3,2-b]thiophene.

2-Bromothieno[3,2-b]thiophene. The spectrum of this compound is reproduced in Fig. 1. Hydrogen 5 is assigned to the low field quartet and hydrogen 6 to the high field quartet. An ABX analysis of the spectrum gives the coupling constants $J_{56}=5.30$ Hz, $J_{36}=0.69$ Hz, and either $J_{35}=-0.12$ Hz or $J_{35}=0.06$ Hz. To distinguish between the two assignments double irradiation experiments were performed to determine the relative signs of the coupling constants. The decoupling of the J_{35} coupling by selective irradiation of the A1, A2 doublet in the 5-hydrogen band leads to a collapse of the X1, X2 doublet in the 3-hydrogen band, see Fig. 1 b. This proves that J_{56} and J_{36} are of equal sign.⁷

The results of the selective irradiation (tickling) of the B3 and B4 lines respectively are shown in Figs. 1 c and 1 d. From the asymmetries in the observed patterns of the A3,A4 band it is clear that transition B3 is connected with A4, and transition B4 with A3 in the energy level diagram. This proves that J_{35} is of opposite sign to J_{36} , *i.e.* also of opposite sign to J_{56} . This confirms the signs of the coupling constants determined in the unsubstituted thieno[3,2-b]thiophene.

The assignment of the cross-ring coupling constants in thieno[3,2-b]thiophene is then clear, the largest cross-ring coupling is over six bonds, J_{25} . This is in agreement with conclusions from the study of thieno[3,2-b]thiophene-2-carboxylic acid by Bugge⁸ and by Litvinov and Fraenkel.⁹

3-Bromothieno[3,2-b]thiophene. The spectrum of 3-bromothieno[3,2-b]thiophene is shown in Fig. 2. The spectrum is of ABC type, where the low field

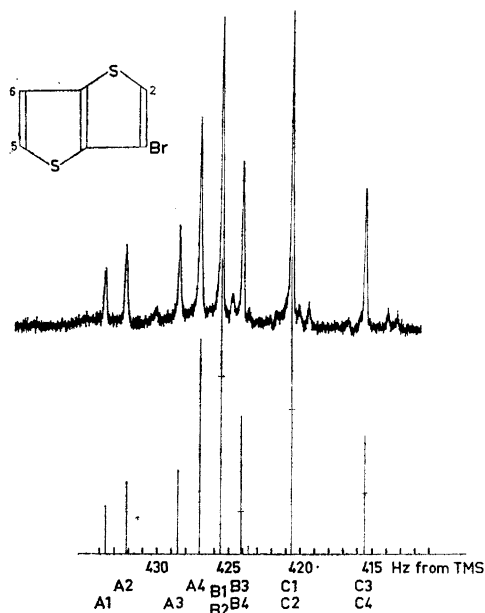


Fig. 2. The NMR spectrum at 56.444 MHz of 3-bromothieno[3,2-b]thiophene in *ca.* 15% acetone solution. The theoretical spectrum is calculated with the parameters (in Hz) $\nu_A=429.54$, $\nu_B=424.89$, $\nu_C=418.68$, $J_{AB}=1.55$, $J_{AC}=5.25$ and $J_{BC}=-0.20$.

A quartet is assigned to hydrogen 5. No coupling between the B and C protons, *i.e.* the 2 and 6 protons, respectively, is directly discernible as a splitting in the spectrum. All the lines are equally sharp, which implies that the B and C lines consist of two almost exactly degenerate transitions. A least square fit of observed and theoretical transition frequencies, calculated by an exact ABC treatment, gives $J_{56}=5.25$ Hz, $J_{25}=1.55$ Hz, and $J_{26}=-0.20$ Hz. These values are in excellent agreement with those observed in the unsubstituted compound. The theoretical spectrum is included in Fig. 2. The spectrum depicted in Fig. 2 illustrates the fact, that the absence of a splitting in a spectrum does not necessarily mean that the corresponding coupling constant is equal to zero.

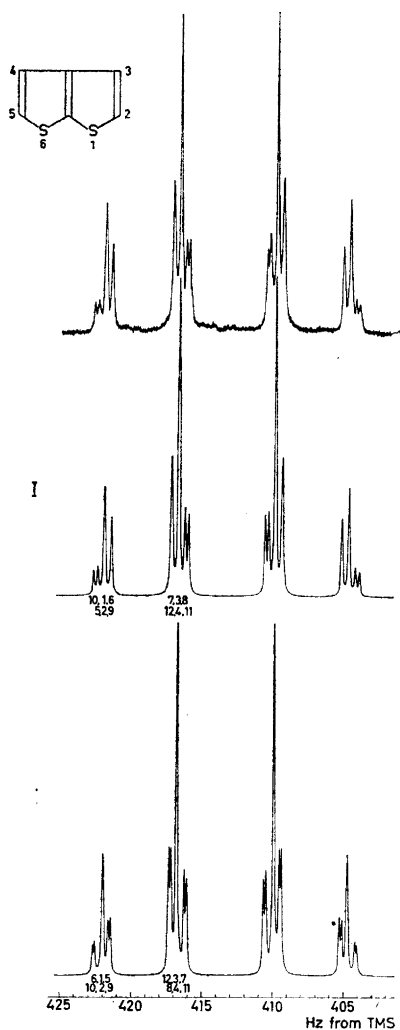
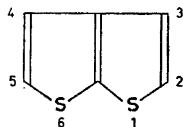


Fig. 3. The NMR spectrum at 56.444 MHz of thieno[2,3-b]thiophene in *ca.* 20 % acetone solution. The upper part shows the experimental spectrum. The middle part (I) shows the computer simulated spectrum calculated with the parameter set (in Hz) $|v_A - v_B| = 10.88$, $J_{AB} = 5.23$, $J_{AB}' = -0.02$, $J_{AA}' = -0.18$, $J_{BB}' = 1.20$ and assuming a Lorentzian line shape of width 0.12 Hz at half height. The lower part (II) shows the computer simulated spectrum calculated with the parameter set (in Hz) $|v_A - v_B| = 10.89$, $J_{AB} = 5.23$, $J_{AB}' = 0.04$, $J_{AA}' = -1.20$, $J_{BB}' = 0.18$ with the same line shape as in (I).



Thieno[2,3-b]thiophenes

Thieno[2,3-b]thiophene. The unsubstituted thieno[2,3-b]thiophene gives rise to an AA'BB' spectrum similar to that of the isomeric thieno[3,2-b]thiophene previously studied. The spectrum is reproduced in Fig. 3. Approximate values for the NMR parameters can be obtained from the (AX)₂, A₂X₂, or (AB)₂ approximations.^{5,10} However, an unambiguous analysis was found to require an exact AA'BB' treatment.

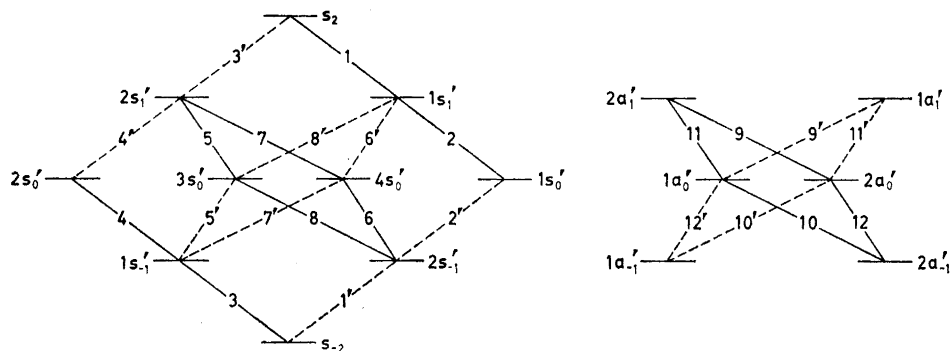


Fig. 4. Schematic diagram of energy levels and transitions in an AA'BB' spectrum. The numbering of levels and transitions are according to Pople, Schneider and Bernstein.¹¹

The energy level diagram for an AA'BB' system is given in Fig. 4, the numbering of levels and transitions being according to the convention of Pople, Schneider and Bernstein.¹¹ The overlapping pair of transitions 1,2 and 3,4, respectively, are easily recognized as the strongest lines in the inner and outer bands of the spectrum. This assignment defines the separation between levels $2s_1'$ and $2s_{-1}'$. Due to the almost equal spacing between the lines in the inner and outer bands, respectively, one is still left with several conceivable assignments of line pairs 5,8 and 6,7.

The number of possible assignments is substantially reduced by first identifying the transitions between the antisymmetric set of energy levels. This can be done by studying the double quantum spectrum which is reproduced in Fig. 5. The double quantum transitions at ± 0.62 Hz from the centre can only be attributed to transitions in the antisymmetric set ($1a_{-1}' \longleftrightarrow 2a_1'$,

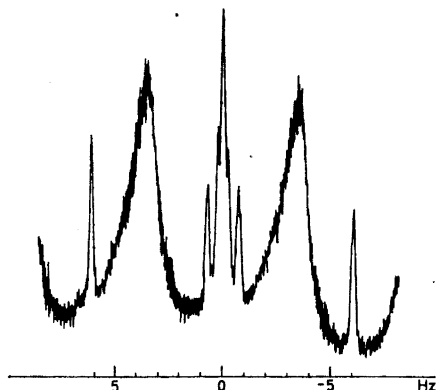


Fig. 5. Double quantum transitions in the AA'BB' spectrum of thieno[2,3-b]thiophene. The original single quantum transitions are severely saturated.

and $2a_{-1}' \longleftrightarrow 1a_{-1}'$. This shows that transitions 11 and 12 should be assigned to the high and low field lines in the inner band, which are separated by 1.21 Hz. Lines 9 and 10 are then given as the high and low field lines in the outer band. A reversal of the assignment of 11 and 12 only leads to a change of sign of the parameter $M (=J_{AA'} - J_{BB'})$, the sign of which cannot be determined in an AA'BB' spectrum.

This leaves us with two possible assignments of the progressive transition pair 5 and 8, which both are in agreement with the double quantum spectrum and accords with the separation between levels $2s_{-1}'$ and $2s_{-1}$. These two assignments essentially differ in the sign of the parameter $K (=J_{AA'} + J_{BB'})$. The sign of K cannot be determined in the weakly coupled AA'XX' case. However, the spectrum of thieno[2,3-b]thiophene is sufficiently strongly coupled to enable a determination of the sign of K , *i.e.* a distinction between the discussed assignments.

A least square fit of observed and theoretical transition frequencies based on these assignments gives a considerably better fit for assignment I (see Fig. 3) the root mean square deviation being less than 0.03 Hz as compared to 0.06 Hz for assignment II (see Fig. 3). Even more crucial is the comparison of theoretical and experimental intensities based on computer simulated spectra. The theoretical spectra reproduced in Fig. 3 have been calculated assuming a Lorentzian line shape of width 0.12 Hz at half height. It is clear that parameter set II can be excluded.

The coupling constants derived from assignment I are $J_{23} = J_{45} = 5.23$ Hz, $J_{24} = J_{35} = -0.02$ Hz, $J_{AA'} = -0.18$ Hz, and $J_{BB'} = 1.20$ Hz. From the AA'BB' analysis it is impossible to assign $J_{AA'}$ and $J_{BB'}$ to definite couplings in the molecule.

3,5-Dibromothieno[2,3-b]thiophene. The spectrum of this compound appears as two sharp single lines, *i.e.* we have no resolvable coupling between the 2 and 4 hydrogens. This is in agreement with the result from the unsubstituted thieno[2,3-b]thiophene.

2-Bromothieno[2,3-b]thiophene. This compound gives an ABX type spectrum, where the AB part can be assigned to the 5 and 4 hydrogens. These

hydrogens are coupled by $J_{45}=5.26$ Hz. An additional splitting in the 3 and 4 hydrogen bands reveals a coupling $|J_{34}|=0.13$ Hz. The sign of this coupling constant cannot be determined, but a comparison with the results from the unsubstituted thieno[2,3-b]thiophene indicates that it is negative.

The assignment of cross-ring couplings in thieno[2,3-b]thiophene is then clear, the largest coupling $J_{25}=1.20$ Hz is due to an interaction over six bonds, while the smaller $J_{34}=-0.18$ Hz is over four bonds.

3-Bromothieno[2,3-b]thiophene. This assignment of cross-ring couplings is confirmed by a study of the spectrum from 3-bromothieno[2,3-b]thiophene. This compound gives an ABC spectrum as shown in Fig. 6. The B and C lines (hydrogens 2 and 4, respectively) at first appear to be doubly degenerate. A close inspection of the line widths shows that the B1, B2 *etc.* transitions are

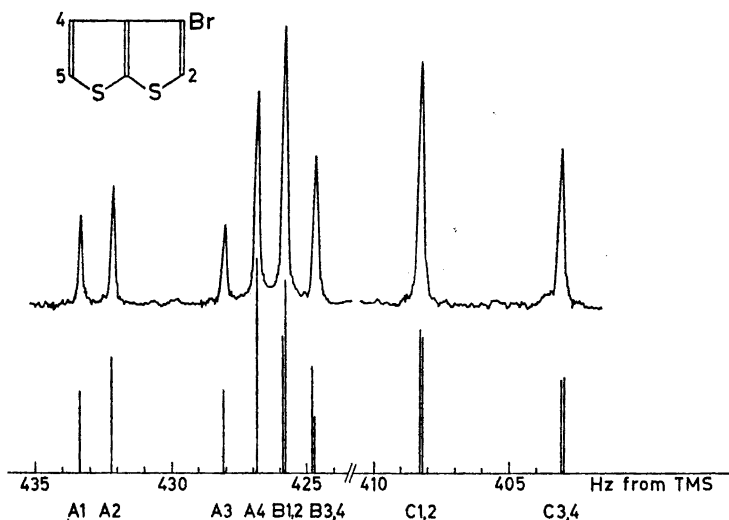


Fig. 6. NMR spectrum at 56.444 MHz of 3-bromothieno[2,3-b]thiophene in *ca.* 20% acetone solution. The theoretical spectrum is calculated with the parameters (in Hz) $\nu_A=429.83$, $\nu_B=425.57$, $\nu_C=405.90$, $J_{AB}=1.17$, $J_{AC}=5.29$, and $J_{BC}=-0.04$.

not completely degenerate; these lines are broader than the single A lines. On estimating this unresolved splitting to be 0.08 ± 0.04 Hz one obtains a coupling of $J_{24}=-0.04 \pm 0.04$ Hz as a result of a least square fit of observed and theoretical spectral frequencies. The other coupling constants are $J_{45}=5.29$ Hz and $J_{25}=1.17$ Hz.

An equally good fit to the experiment spectral frequencies can be obtained by assuming a negative sign for the $J_{AB}=J_{25}$ coupling constant. This will only give rise to very minor differences in the theoretical line intensities, too small to be observable experimentally.

Several methods to determine the relative signs of the spin coupling constants in three spin systems with only two observable couplings employing

Table 1. Chemical shifts^a and coupling constants in thienothiophenes.

	ν_2	ν_3	ν_5	ν_6	J_{23}	J_{35}	J_{26}	J_{35}	J_{36}	J_{56}
Thieno[3,2-b]thiophene ^b	421.94	411.78	421.94	411.78	5.25	1.55	-0.20	-0.20	0.75	5.25
2,6-Dibromothieno[3,2-b]thiophene ^c	429.02	432.82	432.82					-0.15		5.30
2-Bromothieno[3,2-b]thiophene ^d	420.13	427.61	427.61	411.77		1.55	-0.20	-0.12	0.69	5.25
3-Bromothieno[3,2-b]thiophene ^e	424.89	429.54	429.54	418.68						
	ν_2	ν_3	ν_4	ν_5	J_{23}	J_{34}	J_{35}	J_{34}	J_{35}	J_{45}
Thieno[2,3-b]thiophene ^e	419.07	408.19	408.19	419.07	5.23	-0.02	1.20	-0.18	-0.02	5.23
3,5-Dibromothieno[2,3-b]thiophene ^e	427.96	408.74	408.74			0.0		-0.13	0.0	5.26
2-Bromothieno[2,3-b]thiophene ^d	417.22	409.26	409.26	427.96		-0.04	1.17			5.29
3-Bromothieno[2,3-b]thiophene ^e	425.57	405.90	405.90	429.83						

^a The shifts are given at 56.444 MHz relative to TMS as internal reference.^b ca. 12 % in acetone^c < 1 % in acetone^d ca. 15 % in acetone^e ca. 20 % in acetone

multiple resonance techniques have been developed.¹²⁻¹⁴ This information can in principle also be obtained from the double quantum spectrum, if only the protons are sufficiently strongly coupled to render possible the observation of the double quantum lines.

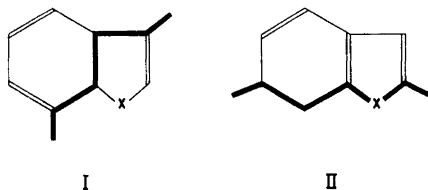
In the ABC spectrum in Fig. 6 a double quantum transition should be observed midway between lines C1 and B2 if J_{AB} and J_{AC} are of equal sign. In case J_{AC} and J_{AB} are of unequal sign C1 and B4 will constitute a progressive pair of transitions, giving a double quantum transition midway between these lines. These two cases differ in the predicted position of the double quantum transition by 0.6 Hz.

Experimentally a double quantum transition was observed centred between C1 and B2, showing that $J_{AB}=J_{25}$ is of the same sign as $J_{AC}=J_{45}$, i.e. positive. This corroborates the assignment of coupling constants in the unsubstituted thieno[2,3-b]thiophene.

The observed spin coupling constants and chemical shifts are summarized in Table 1. The uncertainty in the parameters determined in this study is generally less than 0.04 Hz.

DISCUSSION

The majority of reported cross-ring couplings have been observed between protons separated by five bonds placed in a zig-zag structure (see Ref. 15 and references given therein). A typical structure is shown below (I).



The magnitude of this coupling is ≤ 1 Hz, its sign being in general unknown. The coupling constant $J_{36}=0.75$ Hz in thieno[3,2-b]thiophene can be classified as falling in this category. Its sign has been determined to be positive, a result which can probably be carried over to similar structures (I).

In a few instances a long-range cross-ring interaction over six bonds has also been observed, the coupling following a zig-zag path as in structure II.^{15,16} In benzothiophene this coupling is smaller than the five-bond coupling (I).

The J_{25} couplings in thieno[3,2-b]thiophene and thieno[2,3-b]thiophene both fall in this category. They are both much larger than the corresponding five-bond coupling constant, however. Their sign is positive.

Gutowsky *et al.*¹⁷ observed the same anomaly in *N*-benzylthieno[3,2-b]pyrrole where the cross-ring coupling over six bonds was found to be twice as large as the coupling over five bonds. They suggested this as being due to the larger weight of canonical structures with a crossring charge transfer over six bonds than over five bonds.

The suggestion of a π -electron transmitted interaction could be tested by the substitution of a ring proton with a methyl group. The corresponding spin coupling should then only change its sign but not its magnitude.^{18,19} Methyl substitutions in structures like I, however, have extinguished the long-range cross-ring couplings.¹⁵

It has been suggested that only polynuclear heterocyclic systems with highly asymmetric charge distributions will exhibit the cross-ring interactions.¹ The symmetric molecules thieno[3,2-b]thiophene and thieno[2,3-b]thiophene both exhibit these interactions, the J_{25} coupling in thieno[3,2-b]thiophene being the largest one reported.

Takahashi²⁰ has suggested a correlation between the size of the long-range couplings and the number of paths over which the interaction can take place. The relative importance of the number of bonds over which the protons interact and the number of possible paths is not clear, however.

The $J_{26}=J_{35}$ coupling in thieno[3,2-b]thiophene is over five bonds and is small and negative. The $J_{24}=J_{35}$ coupling in thieno[2,3-b]thiophene is vanishingly small. In contrast to the previously discussed couplings, these do not follow a straight zig-zag path. The same is the case for the four-bond coupling J_{34} in thieno[2,3-b]thiophene, which is small and negative. This seems to confirm the importance of a straight zig-zag path for long-range cross-ring interactions in polyring aromatic systems.

The results given here for thieno[2,3-b]thiophene are in marked contrast to the parameters assigned by Olsen and Snyder²¹ for the structurally similar molecule *N*-benzylthieno[2,3-b]pyrrole. Whereas the coupling over the heteroatoms J_{25} in thieno[2,3-b]thiophene is the largest one, it is negligible in the thienopyrrole. The cross-ring coupling $J_{24}=J_{35}$ in the thieno[2,3-b]thiophene is negligible, while Olsen and Snyder assign $J_{35}=1$ Hz and $J_{24}=0$ Hz for the *N*-benzylthieno[2,3-b]pyrrole. A reversal in the assignment of α - and β -hydrogens in the thiophene part of the spectrum of *N*-benzylthieno[2,3-b]pyrrole would give agreement in coupling constants with those given here for thieno[2,3-b]thiophene. This reversal is, however, difficult to reconcile with the known order of the resonance frequencies of the α and β hydrogens in thiophene itself.^{2,6}

EXPERIMENTAL

The NMR spectra were obtained using a Varian HA-60 spectrometer operating at 56.444 MHz. All spectra were recorded in the frequency sweep mode, where TMS served as lock signal for the internal stabilization. In the decoupling experiments the second rf field was obtained by amplitude modulation of the magnetic field. The modulation frequency was produced by a Philips oscillator PP 6050. The compounds were prepared according to Ref. 22.

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