Relative Signs of Proton Spin Coupling Constants by Multiple Transitory Selective Irradiation

II. The Sign of the Long-Range Aldehyde Coupling in 2-Thiophenealdehydes

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The multiple transitory selective irradiation technique has been used to show that the sign of the long-range aldehyde coupling, J_{CHO-5}, in 3-bromo-2-thiophenealdehyde is the same as that of the ring coupling constant, J_{45}.

This result is in accordance with the suggestion that the mechanism of the aldehyde coupling is the same in 2-thiophenealdehydes and in 2-furanaldehydes.

The problem of determining the relative signs of nuclear spin coupling constants in three spin systems with only two observable couplings is discussed.

In part one of this series [1] a new method for determining the level arrangement in high resolution NMR spectra was described. The general idea of this method is to produce transitory changes in the level populations by Transitory Selective Irradiation (TSI) of selected lines. These changes are then detected by intensity changes in those spectral lines which have an energy level in common with the irradiated ones.

An attractive feature of this method is that it may readily be applied to systems with degenerate transitions, and as an example we considered the case of a three-spin system in which one coupling constant is negligibly small and where the successive application of three transitory irradiations could be used to determine the relative signs of the two remaining coupling constants. In our initial experiment we applied this technique to the side chain spectrum of *trans*-cinnamaldehyde where the largeness of the two observable coupling constants (7.3 c/s and 15.9 c/s) gave us a favourable latitude in the choice of

the experimental parameters (amplitude and frequency of the rf. irradiation field, and sweep rate).

While this work was in progress an alternative method for determining the relative signs of the coupling constants in three-spin systems with only two observable coupling constants was developed by Cohen, Freeman, McLauchlan and Whiffen.[2] This technique, which employs "double tickling" by the simultaneous application of two perturbing rf. fields, was used to determine the relative signs of the ring coupling constant, J_{45}, and the long-range aldehyde coupling, J_{CHO-5}, in 3-bromo-2-thiophenealdehyde. It was suggested by Cohen et al. that their method should prove particularly useful for relating the signs of long-range spin coupling constants to couplings of known sign. The present authors have for some time been engaged in sign determinations of long-range spin couplings.[3-10] In particular, we have found that the sign of the long-range aldehyde coupling, J_{CHO-5}, in 2-furanaldehyde is the same as that of the ring coupling, J_{45}. Since it has been suggested that the mechanism of the long-range aldehyde couplings is the same in all the five-membered hetero aromatic compounds [11] — and probably in other aromatic compounds [12] as well — it should be of value to obtain the sign of the long-range aldehyde coupling, J_{CHO-5}, in 2-thiophenealdehydes relative to a ring coupling constant. The signs of the ring coupling constants in thiophenes [7,13] and in furans [13,14] are most probably the same as that of the ortho coupling in benzenes which has been shown to be positive.[15]

METHOD

In the present study we have slightly modified the multiple transitory selective irradiation method described in our earlier paper where it was applied to trans-cinnamaldehyde.[1] This modification was undertaken in order to produce intensity changes in one
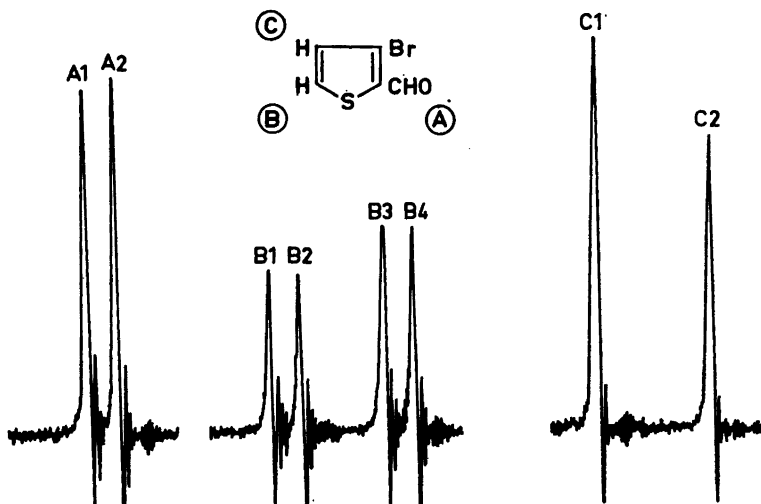

Fig. 1. NMR spectrum at 60 Mc/s of 3-bromo-2-thiophenealdehyde in ca. 20 % CS_2 solution. The line positions relative to the internal tetramethylsilane reference are listed in Table 1.
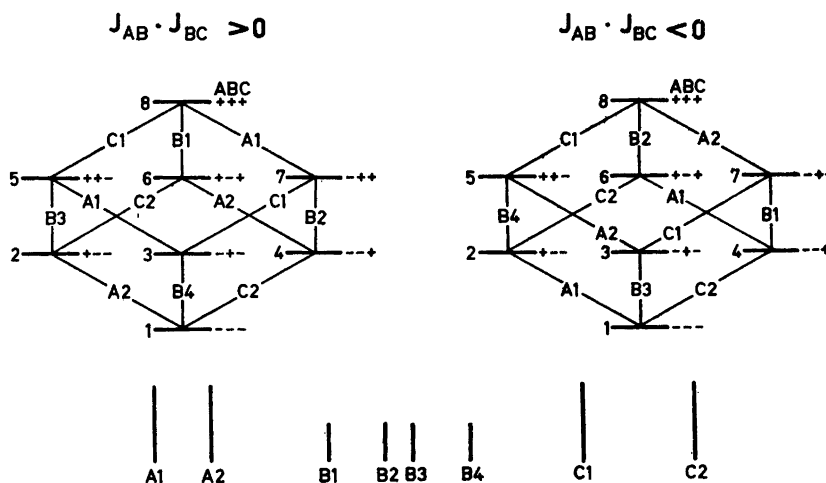
Fig. 2. The two distinct level arrangements and schematic first order NMR spectrum of a three spin system A, B, C, in which one coupling (J_{AC}) is zero. It has been assumed that $|J_{AB}| < |J_{BC}|$.

line only and thus simplify the interpretation of the results. The method is conveniently described with reference to the single resonance spectrum in Fig. 1 and the schematic energy level diagrams in Fig. 2.

The intensity changes of line B4 following transitory irradiations of lines A2, C2, and B1 are studied. It is evident from Fig. 2 that a TSI of A2 will reduce the intensity of line B4 and that the amount of this reduction will be independent of the relative signs of the coupling constants J_{AB} and J_{BC}. For, if these two couplings are of the same sign, the population of the *lower* level (1) of the transition B4 will be *reduced* and if the couplings are of the opposite signs the population of the *upper* level (5) of the transition B4 will be *increased*. Since the intensity of line B4 is proportional to the excess population of the lower level over that of the upper level, the net effect will be independent of the signs of the coupling constants.

Similarly, it may be concluded that the intensity reduction of line B4 caused by a TSI of line C2 will not depend upon the relative signs of J_{AB} and J_{BC}. Nor will the intensity reduction caused by a combined TSI of A2 and C2 be sensitive to the relative signs of J_{AB} and J_{BC}.

The problem may be resolved by an adiabatic fast passage of line B1 preceding that of A2 and C2. If the coupling constants are of the same signs this will cause an intensity reduction of line B4 in addition to that due to the irradiation of A2 and C2. (In the ideal case, the populations of the highest (8) and lowest (1) levels will then be interchanged.)

On the other hand, if the coupling constants are of opposite signs, the population changes caused by an adiabatic fast passage of line B1 will not be further transferred to levels involved in the transition B4 by the subsequent irradiations of A2 and C2. Therefore, the intensity reduction of line B4 in this experiment will be the same as if only A2 and C2 had been irradiated. Accordingly, the decisive part of the experiment is a comparison of the intensity reductions caused by the adiabatic fast passage of lines A2, C2, and B1 on one hand, and that caused by the passage of only A2 and C2 on the other.

In the present study the spectra were recorded by sweeping from low to high field. Precautions were taken to avoid irradiating A1 and C1, and since B4 is the last line in the spectrum of hydrogen B, the experiment could be performed in such a way that only the intensity of line B4 was perturbed (*cf.* below).

EXPERIMENTAL

The 3-bromo-2-thiophenealdehyde was prepared in these laboratories. The sample used in the present study was a ca. 20 % solution in CS_2 to which small amounts of tetramethylsilane were added as internal reference. Dissolved oxygen was removed by bubbling argon through the sample for several minutes before sealing. The relaxation times for the ring protons in our sample were of the order of 20 sec and for the aldehyde proton of about 50 sec, as measured by the recovery of the signals after saturation.

The single resonance spectrum displayed in Fig. 1 was obtained on a Varian A—60 Spectrometer operating at 60.007 Mc/s. The line positions listed in Table 1 were measured

Table 1. Observed line positions in c/s at 60.336 Mc/s of 3-bromo-2-thiophenealdehyde in CS_2 solution relative to tetramethylsilane as internal standard.

Line	Frequency
A1	587.45
A2	586.10
B1	460.70
B2	459.35
B3	455.55
B4	454.20
C1	421.35
C2	416.20

on the Varian 4300 B DP 60 Spectrometer used in the TSI experiments. The operating frequency of the DP 60 spectrometer was measured, and found to be 60.336 Mc/s. The line positions were obtained by superimposing modulation side bands of the internal reference on the line to be measured and searching for optimum overlap by studying the wiggle pattern of the combined signal on the oscilloscope.

The TSI spectra were recorded by the use of phase sensitive detection operating the Varian V 3521 Integrator in the lower sideband mode.[16]

The irradiation fields at A2 and C2 were obtained by audio frequency modulation of the magnetic field (H_0) using two Philips Model GM 2505 B Audio Oscillators. The output from the oscillators was fed to the field modulation coils of the NMR sample probe *via* the simple resistor network shown below.
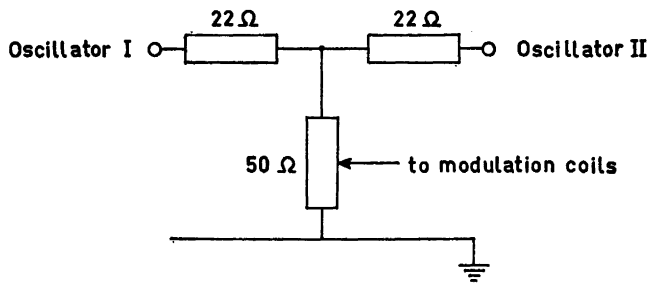
The modulation output was regulated by means of the 50 Ω potentiometer. The irradiation field at B1 was obtained by frequency modulation of the rf. transmitter by use of a Hewlett Packard Model 200 J Audio Oscillator, the output of which was fed to the modulation input of the rf. transmitter *via* a 10 KΩ Helipot potentiometer. The modulation frequencies of the oscillators and of the integrator were measured at repeated intervals by means of a Hewlett Packard Model 5512 A Electronic Counter.

In the TSI experiments the modulation output from the Philips oscillators (at A2 and/or C2) were shortcircuited by means of the 50 Ω potentiometer until the absorption of the line B3 reached its peak value, when the potentiometer was turned up instantane-

ously in order to produce a TSI of A2 and/or C2 immediately before the recording of B4. In the experiments where three transitory irradiations were applied, the Hewlett Packard oscillator (at B1) remained on during the whole experiment.

RESULTS AND DISCUSSION

The spectra obtained in the TSI experiments are displayed in Fig. 3 and the irradiation frequencies used are listed in Table 2.

The five spectra shown in Fig. 3 were all recorded under similar conditions of rf. amplitude, gain, filter bandwidth (0.5 c/s), and sweep rate (0.25 ± 0.02
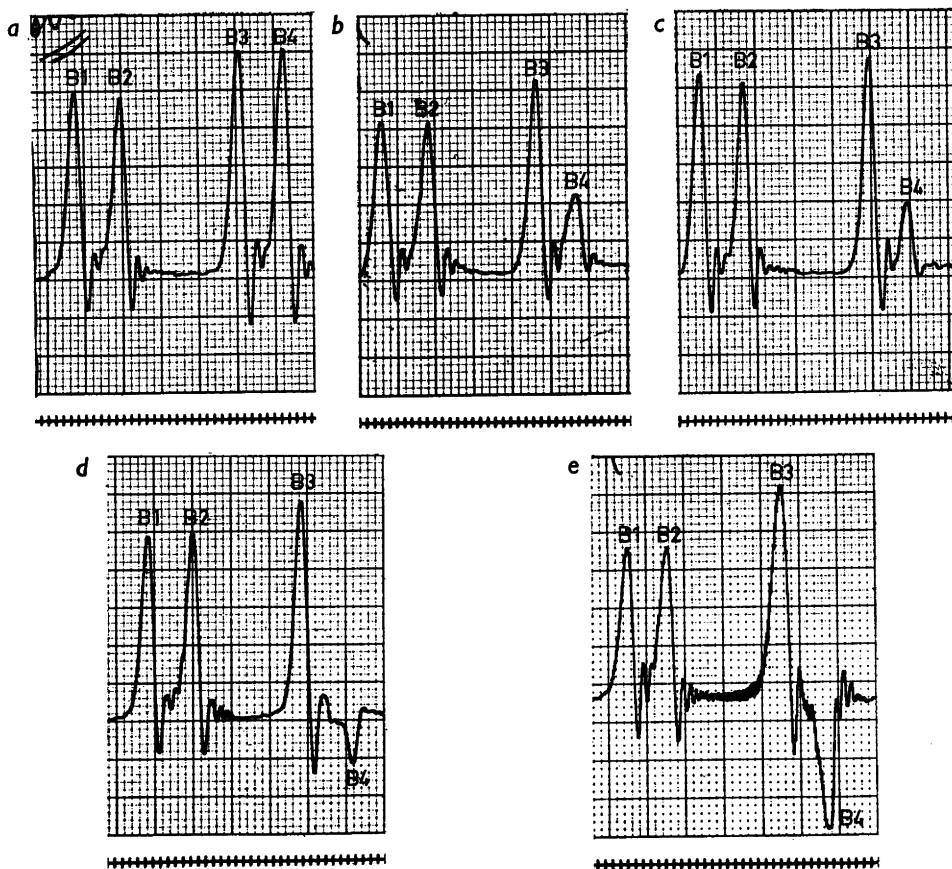

Fig. 3. The results of the TSI experiments. The spectra were recorded under similar conditions of rf. amplitude, gain, filter bandwidth and sweep rate. The markers in the lower part of the figures are second intervals. Only the peaks in the B-hydrogen band are displayed. (a) The unperturbed single resonance spectrum. (b) The spectrum obtained when the line A2 is subjected to TSI 2.8 sec before the recording of line B4. (c) The spectrum obtained when the line C2 is subjected to TSI 2.6 sec before the recording of the line B4. (d) The spectrum obtained when two transitory irradiations were applied, one at C2 as in (c) and the other at A2 as in (b). (e) The spectrum obtained when three transitory irradiations were applied, one at B1 at a time 5.4 sec before the recording of line B4 and the other two at C2 and A2 as in (d).

Table 2. Irradiation frequencies used in the TSI experiments on 3-bromo-2-thiophene-aldehyde. The frequency difference $\nu_i - \nu_0$ between the irradiation and observation rf. fields was offset from the measured value (*cf.* Table 1) of the separation between the transiently irradiated line and line B4 by an amount reported under the heading "Offset". The time elapsed between the TSI and the observation of line B4 ("Delay time") is estimated from the known values of offset and sweep rate.

Line irradiated irradiated	$\nu_i - \nu_0$ c/s	Offset c/s	Delay time sec
A2	+ 131.2	0.70	2.8
C2	− 38.8	0.65	2.6
B1	+ 5.15	1.35	5.4

c/s^2). In order to maintain these parameters as constant as possible and reduce the problem of random drift, the whole experiment had to be performed within a short period of time (about one hour). Likewise the frequency and the output level of each of the audio oscillators used to produce the irradiation fields had to be maintained constant during the whole series of experiments. In the first recording, all the oscillators were disconnected (Fig. 3a). In the second type of experiment, one oscillator is used to produce a TSI of A2 (Fig. 3b) or C2 (Fig. 3c).

In the critical experiment, the effect on the intensity of line B4 produced by TSI of B1, A2, and C2 (Fig. 3e) is compared with the effect produced by TSI of A2 and C2 only (Fig. 3d). It is evident from Figs. 3d and 3e that the additional irradiation of B1 produces a marked effect and thus we may conclude that the signs of J_{AB} and J_{BC} are the same. To check that the additional intensity reduction caused by the TSI of B1 is a genuine effect we repeatedly performed the two types of experiments depicted in Figs. 3d and 3e. No difficulties were encountered in reproducing the results.

It should be noted that in order to obtain unambiguous results one must make sure that the intensity changes observed are not caused by unintentional irradiation of lines other than those considered. Therefore the timing of the different irradiations and of the recordings in the multiple TSI experiments is of great importance. In Fig. 4 we have shown schematically the time relations of the irradiations and line intensity observations in our experiments. Originally, we had intended to apply the irradiations successively such that the TSI of A2 did not occur before the completion of the TSI of C2, since then the theoretical interpretation would be simpler than an analysis of the experiment in which the irradiations of A2 and C2 are applied simultaneously.*

It was found, however, that larger intensity reductions could be obtained if both A2 and C2 were irradiated at the same time with an offset of about $\frac{1}{2} \cdot J_{AB}$. The probable reason for this is that the offset $\frac{1}{2} \cdot J_{AB}$ permits the use of maximum rf. amplitude in the irradiation fields at A2 and C2 without producing unwanted line broadening or line splitting due to "tickling".[17] The offset

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* Since an irradiation field of angular frequency ω_1 and amplitude H_1 may be considered to have an "effective width" of γH_1, two fields H_1 and H_2 irradiating the transitions at ω_r and ω_s may be considered to be non-simultaneous if $\gamma H_1/(\omega_r - \omega_1)$ is negligibly small whenever $\gamma H_2/(\omega_s - \omega_2)$ is not and *vice versa*.

for the TSI of B1 is less critical since the transitions B1 and B2 have no energy levels in common with B3 or B4. Therefore the offset for the TSI of B1 was chosen to be about J_{AB} which means that the TSI of B1 is completed when the lines A2 and C2 are irradiated.
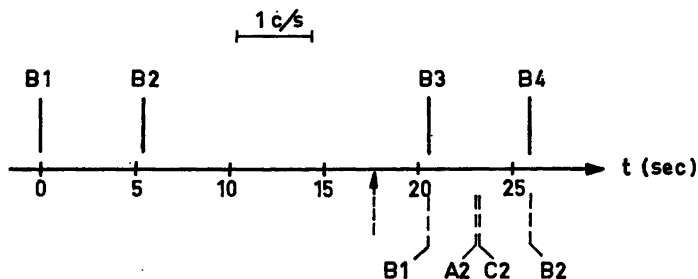

Fig. 4. Schematic diagram illustrating the time relations in the TSI experiments depicted in Fig. 3. The occurrence of the successive peak observations in the B-hydrogen band are indicated above the horisontal time axis and the occurrence of the successive irradiations are indicated below the axis. The arrow indicates the time when the irradiation field used to produce the TSI of A2 fulfils the resonance condition of A1. It is evident from the figure that line A1 was never irradiated since this irradiation field was not turned on until the absorption of line B3 has reached its maximum value. It is also seen that line B2 is irradiated when line B4 is observed but, as discussed in the text, this irradiation will produce no observable effect.

As is evident from Fig. 4 the line B2 is irradiated at the time when B4 is recorded. However, this irradiation cannot change the intensity of line B4 since B2 and B4 have no energy level in common and furthermore by the time B2 is irradiated there is no process (except for the spin relaxation) which can transfer the population changes caused by the TSI of B2 to the levels involved in the transition B4.

CONCLUSION

The present work shows that the TSI technique may be used for the determination of the relative signs of spin coupling constants in three-spin systems with only two observable spin couplings even when one of these couplings is quite small. When applied to this type of problems the method is in principle quite simple to use. In practice, however, the experiment requires the optimization of a large number of experimental settings, the most important of which are the sweep rate and the modulation amplitudes and the frequencies of the three audio oscillators. Although this can to some extent be done in a step by step manner, this procedure is by no means trivial and requires a considerable amount of patience. In this connection it should be pointed out that a negative result may not be taken as sufficient proof of a hypothesis concerning the relative signs of the coupling constants since negative results are most readily obtained by poor experimentation. When a negative result is obtained one should therefore try some other combination of transitory selective irradiations that would prove the hypothesis by a positive result.

The result obtained, *viz.* that the sign of the long-range aldehyde coupling, J_{CHO-5}, in 2-thiophenealdehydes is the same as that of the ring coupling constant, J_{45}, agrees with the result independently arrived at by Cohen *et al.*[2] using a triple resonance method. The result may be taken as a confirmation of the hypothesis that the mechanism of the long-range aldehyde coupling is the same in thiophenes as in furans since in 2-furanaldehydes the sign of J_{CHO-5} is known to be the same as that of J_{45}.[9] The mechanism of these aldehyde couplings has been discussed elsewhere.[9,12]

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