# Long-Range-Spin Coupling in Benzo[b] Thiophenes, Benzo[b] Furans and Quinolines

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**Summary:** Proton NMR spectra of ethyl acetate derivatives of benzo[b] thiophenes, benzo[b] furans and quinolines show that there is a strong long range coupling between $H_3$ and $H_7$ ($^5J$). The coupling magnitude in benzo[b] thiophenes and benzo[b] furans was 0.73 ± 0.1 Hz. The observed coupling values between $H_4$ and $H_8$ ($^5J$) $H_2$ and $h_7$ ($^6J$) in quinolines were 0.73 ± 0.1 and 0.36 ± 0.1 Hz respectively. Long range spin-spin coupling of ca. 0.73 ± 0.1 Hz over four bonds between ring proton and adjacent methine proton of ethylacetate group is observed for a wide variety of the title compounds.

## Introduction

Appreciable long-range spin-spin coupling (ca. 0.4 to 1.3 Hz) has been reported for a number of fused ring systems. Thus the parent or substituted benzo[b] furan[1,2,3] benzo[b] thiophene[2,4], quinoline[5-8], purines[9], pteridines[9], benzophenone[10], indole[2,11,12,13], indene[1,14], indazol[15], thienothiophen[16], isoquinoline[2], anthracene[11], acridine[17], acridon[17] ring protons coupling has received considerable investigations.

The present study provides further examples of long-range coupling between $H_3$ and $H_7$ in benzo [b] thiophenes and benzo[b] furans derivatives as well as the long-range coupling between the ring protons and the methine proton of ethylacetate group which was introduced in different positions as ring substituent on benzo[b] thiophene benzo[b] furan rings. This study also, discusses the long-range proton coupling of quinolines having ethylacetate substituent at different positions. The inter-range couplings and ring-chain couplings is also described with discussion of the possible mechanisms of the long-range couplings.

Further $^1H$ NMR study of the various ethyl acetate of benzo[b] thiophenes, benzo[b] furans and quinolines have been achieved in different solvents to work out the additivity of their chemical shifts[18]. The 1 'H NMR; shift reagent effect; and $^{13}C$ NMR of the title compounds will be reported separately.

The final spectral parameters are given in Table 1, with a comparison of other long-range coupling discussed by several authors.

## Results and Discussion

The NMR spectrum of 1-(2-benzo[b] thienyl) ethyl acetate in benzene-$d_6$ consists of a doublet of doublets of doublets at 7.53 and 7.45 δ with splitting of 8.8, 2.4 and 0.73 Hz, [$H_7$] $J_{6,7}$ = 8.8; $J_{5,7}$ = 2.4 ; $J_{3,7}$ and $J_{4,7}$ = 0.73 Hz, and doublet of doublets appears as a triplets with splittings of 0.73 Hz. The signal assigned to $H_3$ ($J_{3,7}$ = 0.73 Hz) and coupling between $H_3$ and the proton of ethylacetate group is 0.73 Hz. A complicated overlapping specturm is observed in dimethylsulfoxide-$d_6$, acetone -$d_6$, deuterochloroform, methanol-$d_4$. Similarly, $H_7$ in 1-(3-benzo[b] thienyl)ethyl acetate in deutero-chloroform at 7.8 δ also gives rise to a doublet of doublets of doublets with smallest splitting of 0.73 Hz (due to $J_{4,7}$ in absent of $H_3$). The $H_2$ signal appears as a doublet with splitting of 0.73 Hz ($J_{23}$).

Unsubstituted benzo[b] furan, in deuterchloroform shows that $H_2$ signal arise at 6.62 δ as doublet of doublet with splitting of 2.2 and 0.73 Hz which is assigned to $J_{2,3}$ and $J_{3,7}$ respectively. The $^1H$ NMR spectra of 1-(benzofuran 2-yl) ethyl acetate in acetone-$d_6$ and benzene-$d_6$ show the signal assigned to $H_3$ as triplet (doublet of doublets) at 7.46 δ with splitting in acetone-$d_6$ of 0.73 Hz, ($J_{3,2}$ and $J_{3,7}$) and –CH signal of ethyl acetate appears as double quartets. Double irradiation at CH of ethyl acetate proton, leads to a doublet for the $H_3$ signal with splitting of 0.73 Hz. On the other hand, double irradiation of the $H_3$ signal gave quartet for the CH proton with splitting of 0.73 Hz, signals of $H_7$ and $H_4$ overlap as a result of incident solvent effect. Similarly

Table 1. Long-range Coupling Costants in Hz for Benzo[b] thiophenes and Related Heterocyclic Compounds

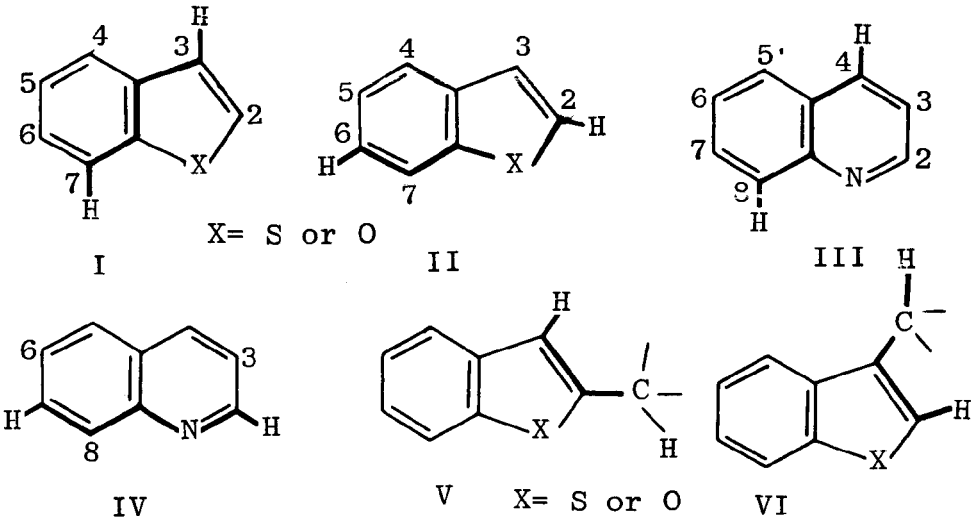
| Compound | J in Hz | Reference |
|---|---|---|
| Benzo[b] thiophene unsubst. | $J_{3,7} = 0.7 \pm .1$ ; $J_{3,7} = 0.73$ | 35, p.w. |
| 2-benzo[b] thienyl ethyl acetate | $J_{3,7} = 0.73$; $J_{4,7} = 0.73$; $J_{3,2} = 0.73$ | 35, p.w. |
| 3-methylbenzo[b] thiophene | $J_{2,3} = 1.1$ | 35 |
| 2,3-dimethylbenzothiophene | $J_{2,3} = 0.75$ | 35 |
| 1-(3-benzo[b] thienyl)ethyl acetate | $J_{4,7} = 0.73$; $J_{2,3} = 0.73$ | p.w. |
| 2-methylbenzo[b] thiphene | $J_{3,7} = 0.9$ | 2 |
| 5-methylbenzo[b] thiophene | $J_{3,7} = 0.7$ | 35 |
| 5-bromobenzo[b] thiophene | $J_{3,7} = 0.8$; $J_{2,6} = 0.6$ | 35 |
| Benzo[b] furan, Unsubst. | $J_{3,7} = 0.73$ | p.w. |
| | $J_{3,7} = 0.90$ | 1 |
| 1-(benzofuran-2-yl)ethyl acetate | $J_{3,7} = J_{3,2} = 0.73$ | p.w. |
| 2-methylbenzofuran | $J_{3,7} = 1.0$ | 2 |
| 1-(benzofuran-3-yl)ethyl acetate | $J_{4,7} = 0.73$; $J_{2,3} = 0.73$ | p.w. |
| 4-methylbenzo[b] furan | $J_{3,7} = 0.8$ | 2 |
| 6-methylbenzo[b] furan | $J_{3,7} = 1.0$ | 2 |
| quinoline, unsubst. | $J_{4,8} = 1.0$ | 5 |
| | $J_{4,8} = 0.73$ (in acetone-$d_6$) | p.w. |
| 1-(6-quinolyl) ethyl acetate | $J_{4,8} = 0.73$; $J_{2,7} = 0.36$ | p.w. |
| 1-(7-quinolyl)ethyl acetate | $J_{4,8} = 0.73$ | p.w. |
| 5,7-dichloroquinoline | $J_{4,8} = 0.8$ | 5 |
| 7-ethylquinoline | $J_{4,8} = 0.8$ | 8 |
| 5,7-dimethylquinoline | $J_{4,8} = 0.8$ | 5 |
| indoles unsubst. | $J_{3,7} = 0.7$ | 2 |
| 4-methyl indole | $J_{3,7} = 0.8$ | 2 |
| 5-methyl indole | $J_{3,7} = 0.6$ | 2 |
| 6-methyl indole | $J_{3,7} = 1.0$ | 2 |
| indene, unsubs. | $J_{3,7} = 0.7$ | 1 |
| 4-methylindene | $J_{3,7} = 0.7$ | 1 |

p.w. = present work

$H_7$ in 1-(3-benzofuryl-3-yl)ethyl acetate also gives rise to a doublet of doublets of doublets centered at 7.60 δ in acetone-$d_6$ with small splitting of 0.73 Hz ($J_{4,7}$ in absence of $H_3$). The signal of $H_2$ appears as a doublet at 7.80 δ with splitting of 0.73 Hz ($J_{2,3}$). The side chain C-H signal appears as quartet of doublets with splitting of 0.73 Hz. Double irradiation at –CH of ethyl acetate of at $H_2$, indicate the coupling is due to $H_2$ and CH proton.

The $^1$H NMR spectra of 1-(6-quinolyl)ethyl acetate in acetone-$d_6$, methanol-$d_4$ and dimethylsulphoxide-$d_6$, show the signal assigned to $H_4$ at 8.30 δ in acetone-$d_6$ as a doublet of doublets of doublets with splitting of 8.40, 1.83 and 0.73 Hz ($J_{3,4}$, $_{2,4}$ and $_{4,8}$) respectively. The signal due to $H_8$ at 8.00 δ is a broad doublet with splittings of 8.42 Hz $J_{7,8}$). The broadness of $H_8$ signal may be due to a very small additional splitting by $H_4$ and $H_5$. The signal assigned to $H_2$ is a doublet of doublets of doublets centered at 8.87 δ ($J_{2,3} = 4.39$ Hz; $J_{2,4} = 1.83$ Hz and small splitting of 0.36 Hz interpreted for $J_{2,7}$). The signal of $H_7$ gives rise to a doublet of doublets of small splitting doublets at 7.75 δ ($J_{7,8} = 8.42$ Hz, $J_{5,7} = 1.83$ Hz and $J_{2,7} = 0.36$ Hz).

Similarly the $^1$H NMR spectra of 1-(7-quinolyl) ethyl acetate in acetone-$d_6$ or deutereochloroform show that $H_4$ signal also gives rise to a doublet of




doublets of doublets at 8.30 δ in acetone-$d_6$ with smallest splitting of 0.73 Hz for $J_{4,8}$. The signals due to $H_2$ is a doublet of doublets at 8.89 δ with splittings of 4.39 Hz ($J_{2,3}$ and 1.83 Hz $J_{2,4}$). The signal assigned to $H_8$ is a broad doublet of doublets at 8.00 δ with splitting of 1.46 ($J_{6,8}$) and 0.73 Hz ($J_{4,8}$), the broadness is due to additonal splitting by $H_4$.

The long-range inter-ring coupling ($^5J_{3,7}$), in the benzo[b]thiophenes I(X=S) and benzo[b] furans I(X=O) disappears on replacement of either the $H_3$ or the $H_7$ by an ethylacetate group. The inter-ring coupling were considered to involve the π-electrons system[19]. In valence bond terms, there must be conjugation between those positions to which the coupled protons are attached. Consider canonical forms for benzo[b]furan and benzo[b]thiophen, there is a conjugated path between the 3 and 5-position, yet 3,5-coupling is not detectable. It appears that the cojugated path must usually be over bonds which are disposed in a near perfect zig-zag or all trans configuration (I to VI). This leads to best overlap not only of π orbitals but also of the σ orbitals. The spin-spin coupling constant depends mainly on the number and type of the interacting chemical bonds and on the stereochemical relations of the groups involved[20].

The values of the spin-spin coupling constants through five bonds ($^5J_{HH}$) are all 0.73 ± 0.1 Hz (see Table 1). The same results was observed in substituted quinoline II (Table 1). There was appreciable $H_2$, $H_7$ coupling(IV) ($^6J_{2,7}$ = 0.36 Hz ± 0.1 Hz) This may be a general feature in quinolines spectra. As analogous interaction have also been tentatively proposed in benzo[b]thiophens[21], indolizines[22] and diazanaphthalenes[23] and may correspond to those established in thienopyrroles[19,24-28]. It is likely that long-range coupling along the path indicated in IV is in general like the one along the path indicated in I to III. It is noteworthy that $H_2$ and $H_7$ in IV are connected by a "Straight zig-zag path"[29] which is conjugated in a number of canonical forms[2]. The coupling between $H_2$ and $H_6$ (II) in benzo[b]thiophenes has been noted by Takahashi[30]. In this study $H_2$ and $H_6$ couplin in I (X=S, X=O) was not observed due to the broadening of $H_2$ and $H_6$ peaks. This may be due to the splitting with adjacent ring C - H protons with expected small value of $J_{2,6}$.

The couping between C-H ethyl group and the ring proton in 1-(2 or 3-benzo[b]thienyl)ethyl acetate and 1-(benzofuran-2 or 3-yl) ethyl acetate is of great interest. Thus the coupling between the protons of $H_2$, $H_3$ or $H_3$, $H_2$, ($J_{2\text{-H},3\text{-CH}}$ and $J_{3\text{-H}\ 2\text{-CH}}$ respectively) which are four bonds apart, is 0.73 Hz. Large values were recorded for different heterocyclic compounds of different substituents (see Table 1). The main difference (ca. 0.37 Hz) could be due to the size of the ethyl acetate. The bulkiness of ethylacetate group compared with methyl group could in fact prevent any "through-space" couplings mechanism associated with the proximity of the hydrogen atoms in the two C-H bonds.

This effect has been recently explained theoretically by Barfield et al[10,31,32]. Similar results have been reported for coupling between N-methyl and adjacent ring C-H protons of purines and pteridines ($^4J_{N\text{-}CH_3,\ C\text{-}H}$ = 0.5 Hz)[9]. It is interesting to point out that when ethylacetate group is attached to (4-7) position in the benzene ring of benzothiophene, benzofuran and quinoline (5-8) positions, a broad quartet for methine proton has been notices, recorded in different solvents. The broadness in the quartet could be due to a very small additonal splitting by the proton of the benzeneoid ring, compared with the heterocyclic proton ring.

## Experimental

The proton NMR spectra were measured on a JEOL JNM FX-100 instrument, operating at 100 MHz. Chemical shifts and coupling constants were obtained by JEC 980 B computer with an accuracy of ± 0.1 Hz. The samples concentration was 0.1 M.

Heterocyclic compounds of the title were prepared by known methods[33,34].

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