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Long-range Spin-Spin Coupling in a  $\beta$ -Carboline System (1)

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The importance of long-range spin-spin coupling effects in aliphatic and alicyclic systems has been amply demonstrated in recent publications (2). We now wish to describe an interesting example of long-range spin-spin coupling in a  $\beta$ -carboline ring system encountered during our studies on indole alkaloids. These results, incidental to the main object of the research program, are reported at this time because of their current interest and because the long range coupling observed appears to be characteristic of the structural grouping  $\text{CH}_3\text{-C=N-CH}_2\text{-}$  when present in a ring system (3).

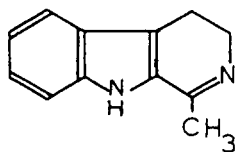
The n.m.r. spectrum of 1-methyl-3,4-dihydro-9H-pyrido[3,4-b]indole (I) showed an unexpected splitting pattern in the absorption peak of the 1-methyl protons (7.61  $\tau$ ) and the 3-methylene protons (6.09  $\tau$ ). The 1-methyl peak was resolvable into a triplet with coupling constant,  $J(\text{CH}_3, \text{CH}_2) = 1.2$  cps. The two sets of methylene protons (an  $A_2B_2$  system) have triplet absorption patterns ( $J = 8.2$  cps) at 6.09  $\tau$  and 7.10  $\tau$ . The low field triplet was assigned to the 3-methylene protons in view of their position  $\alpha$  to the ring nitrogen atom. The intensity of the 6.09  $\tau$  triplet was noticeably less than that at 7.10  $\tau$  but was not resolvable into any well-defined, hyperfine splitting pattern. This broadening effect on the 3-methylene protons' absorption, the triplet character of this absorption, as well as the triplet character of the 1-methyl protons' absorption, suggest a long range, spin coupling interaction between these two groups over a separation of five bonds (Fig. 1).

It has been suggested that increased conjugation in a system could facilitate a larger coupling constant (4). However, in the unsaturated analog of (I), 1-methyl-9H-pyrido[3,4-b]indole (II), ring C behaved as a typical heteroaromatic system. The 1-methyl proton absorption appeared as a sharp singlet with no indication of the doublet character which would be present had the 1-methyl and the 3-proton been spin coupled. The spectrum was similar to those reported recently (5) for these types of aromatic systems.

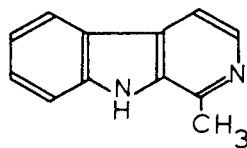
Verification of the spin coupling between the 1-methyl protons and the 3-methylene protons was accomplished by the double irradiation technique (6). The method of observing side bands in this technique did not make possible the high resolution of the 1-methyl proton absorption with three well-defined peaks. However, irradiating the peak at 6.09  $\tau$  while scanning the peak at 7.61  $\tau$  caused a marked increase in the intensity of the peak (Fig. 2). A similar increase in intensity of the triplet at 6.09  $\tau$  was obtained when the peak at 7.61  $\tau$  was irradiated. The intensities of both triplets were the same under these conditions and these intensity changes confirm the spin coupling between the 1-methyl and the 3-methylene protons. Only partial deuteration of the methyl group (60.9%  $\text{CD}_3$ , 25.6%  $\text{CH}_2\text{D}$  or  $\text{CHD}_2$ , and 13.5%  $\text{CH}_3$ ) could be achieved under mild conditions; more vigorous reaction conditions resulted in partial decomposition of this cyclic Schiff base. However, the broadening of the peaks of the 3-methylene triplet absorption was reduced in the partially deuterated product and, with the increase in peak height, the 3-methylene protons were resolved almost to the extent of the 4-methylene protons.

The long range coupling shown in this dihydro- $\beta$ -carboline system is very similar to that present in 2-methyl-4-oxazoline (III) and the corresponding thiazoline (3). Here the long range coupling between the 2-methyl protons (8.029  $\tau$ ) and the 4-methylene protons (6.225  $\tau$ ) resulted in a coupling constant  $J(\text{CH}_3, \text{CH}_2) = 1.38$  cps and for the adjacent methylene protons,  $J(\text{CH}_2, \text{CH}_2) = 9.5$  cps in the oxygen ring system; in the sulfur containing ring system,  $J(\text{CH}_3, \text{CH}_2) = 1.61$  cps and  $J(\text{CH}_2, \text{CH}_2) = 8.22$  cps are of the same order.

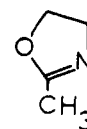
In these ring systems the geometrical restrictions require co-planarity of the atoms involved and the coupling effect is transmitted through the  $\pi$ -electron system. It is most likely that similar long-range spin-spin coupling will be detected in other heterocyclic systems with this common structural feature.



I



II



III

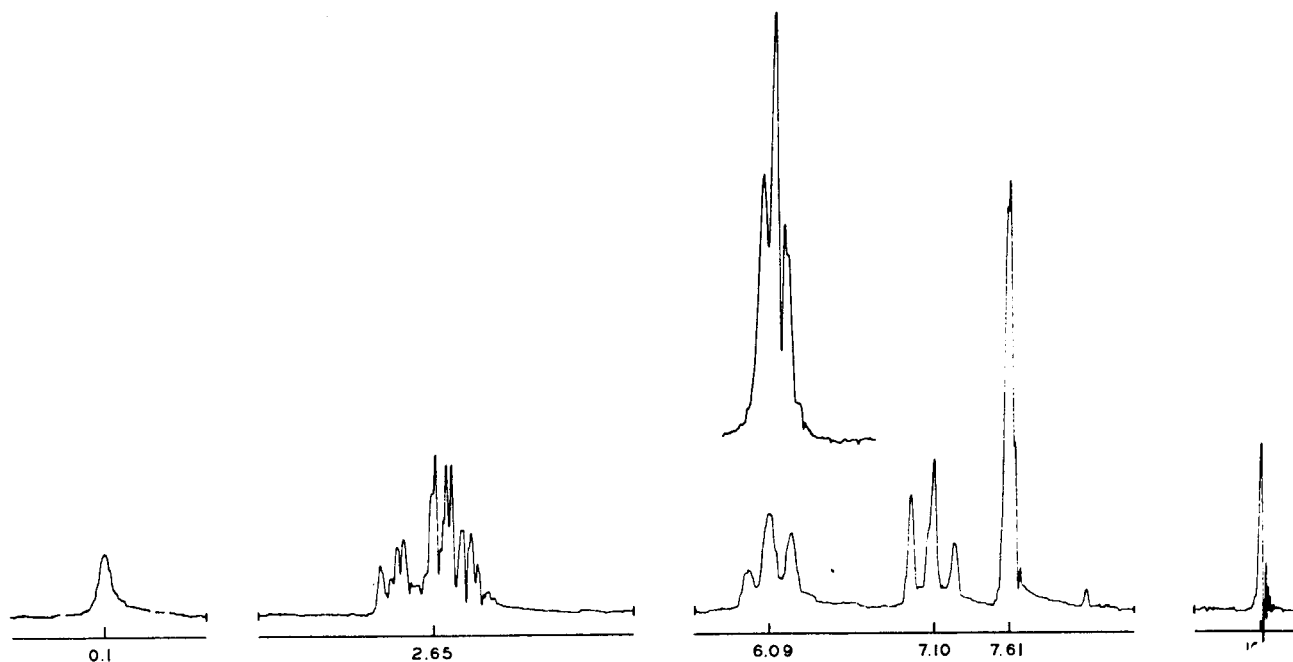


Fig. 1

Nmr spectrum of (I). Insert shows triplet splitting of the 1-methyl protons. All chemical shifts are reported in  $\tau$  units.

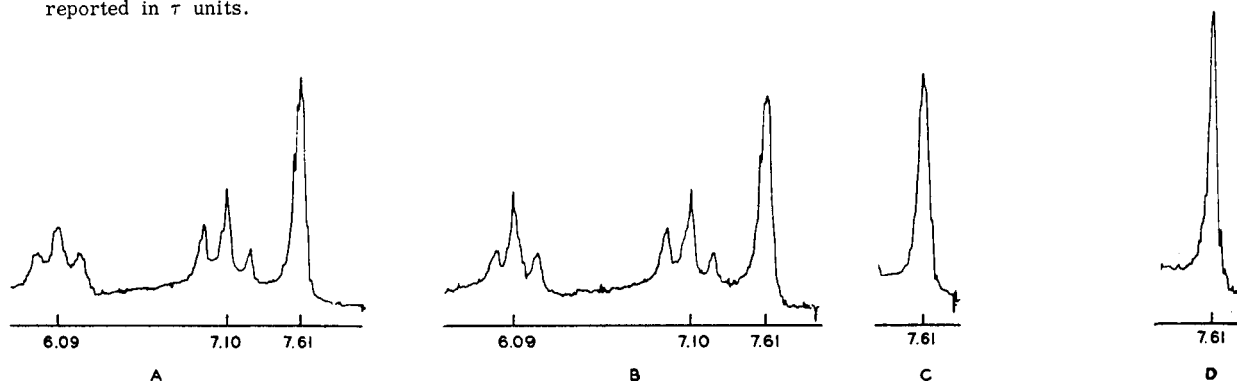


Fig. 2

(A) Normal spectrum with 3-methylene triplet broadened through spin coupling with 1-methyl protons. (B) Double irradiated spectrum; 3-methylene protons spin-decoupled from the 1-methyl protons, broadening removed. (C) Normal spectrum of 1-methyl protons, broadened through spin coupling with 3-methylene protons. (D) Double irradiated spectrum; 1-methyl protons spin-decoupled from the 3-methylene protons, broadening removed. All chemical shifts are reported in  $\tau$  units.

## EXPERIMENTAL

Spectra were determined in deuteriochloroform solution, using a Varian V-4302 Dual Purpose nmr spectrometer operating at 60 mc/s, and were calibrated with TMS as internal reference using the side band technique and a Hewlett Packard 521 C Electronic Counter. The compounds investigated were prepared by standard procedures (7) and were of analytical purity (8).

## REFERENCES

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