Tetrahedron Letters No.46, pp. 4625-4628, 1967. Pergamon Press Ltd. Printed in Great Britain.

SPIN COUPLING IN N-ACYLDIHYDROISOINDOLES

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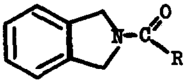
(Received in USA 22 May 1967)

Spin coupling between protons separated by more than three saturated bonds is not often detected(1). The available evidence suggests that long-range coupling over four bonds is observable only when the nuclei lie in a favorable geometrical arrangement ("M" or "W" pattern), usually enforced by a rigid, bicyclic carbon skeleton or when an sp^2 hybridized carbon atom intervenes between the remote protons(2).

We have now found large long-range spin-spin interactions between nuclei separated by four bonds in several N-acyl derivatives of dihydroisoindole (Ia-d)(3). In this system, the benzylic protons are separated by an sp^2 hybridized nitrogen atom; molecular models suggest that



Ia R = CH_3

b R = OCH_3

c R = CF_3

d R = C_6H_5

these molecules are planar and relatively rigid.* These nuclei can be made magnetically non-equivalent by sufficiently slow rotation of the acyl portion of the molecule and it, thus, should be possible to detect spin-spin interactions between the two non-identical sets of protons. As can be seen from the projection drawing below, there are two distinct long-range couplings, J_{13} and J_{14}, under these conditions.

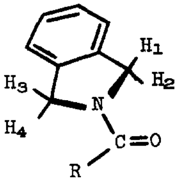


Table I records our results. Both of the expected spin-spin interactions are appreciable when the N-acyl group is carbomethoxy or acetyl (Ia,b) and, for these compounds, are similar in magnitude to equivalent couplings found in various bicyclic hydrocarbon derivatives.(1,5) At higher temperatures the magnetic non-equivalence disappears as rotation of the acyl group becomes rapid and the spectra of both materials evolve into a single sharp line. The spin couplings observed at lower temperature are thus not the result of interaction with distant aromatic protons in the isoindoline system; this conclusion is substantiated by the observation that strong irradiation of Ib at the aromatic proton frequency does not alter the low-temperature spectrum. The analyses of the spectra of Ia and Ib showed that J_{13} and J_{14} must both be positive or both negative in sign but did not allow a clear-cut choice between these two alternatives. Since the coupling in indene oxide analogous to J_{14} is positive(5), both couplings are presumed to be positive. The larger of the two observed couplings in the dihydroisoindole system is tentatively assigned to the H_1 - H_4 interaction, primarily because these nuclei appear to be in a somewhat better arrangement for W-plan couplings.

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*We have found no evidence for detectable inversion of the amide nitrogen(4).

TABLE I

Spin Coupling Constants in N-Acyl Dihydroisoindoles[a]

R	T, deg. C.	δ,Hz	J_{12},Hz	J_{34},Hz	J_{13},Hz	J_{14},Hz
CH_3O-	-25	7.6	-12.2	-12.1	0.9	2.6
CH_3-	36	8.4	-12.7	-12.7	1.1	1.7
C_6H_5-	38	25.5	--	--	< 1.2	< 1.2
CF_3-	36	11.4	--	--	< 0.8	< 0.8

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[a] Spectra were recorded with a Varian Associates HA-100 spectrometer utilizing 10% solutions of the materials in $CDCl_3$. Although the resonances were broadened by N^{14} quadrapolar effects, it was possible to make an analysis for the spin coupling data by the Swalen-Reilly(6) method. It is believed that the coupling constants for the first two compounds are accurate to at least 0.2 Hz.

[b] The solvent was 10% benzene in $CDCl_3$.

Regrettably when the N-acyl group is trifluoroacetyl or benzoyl, the benzylic methylene resonances appear only as two broad singlets with no resolvable fine structure. The crude estimates of the long-range spin-coupling constants in these materials as quoted in the Table were obtained by considering the width of these signals at high and low temperatures.

An interesting feature of the data in Table I is the marked dependence of J_{14} on the nature of the substituent, R. This indicates that the molecular orbitals by which spin information is transmitted from H_1 to H_4 encompass the amide nitrogen atom. If these orbitals have to a considerable degree characteristics of the nitrogen p-π orbital(7), one might anticipate a correlation between the magnitude of the energy barrier to rotation, E_a, and the variation in J_{14}.

Preliminary rate data were obtained by approximate analysis of the spectral line shapes at various temperatures. These data lead to the activation parameters listed in Table II. The free energy barriers to rotation of the acyl groups appear to be determined by both enthalpic and entropic factors and, at this stage, it does not appear to be profitable to attempt correlation of these kinetic parameters with the spin coupling constants.

TABLE II

Preliminary Activation Parameters for Rotation in N-Acyl Isoindolines

R	ΔF*, kcal./mole	ΔH*, kcal./mole	ΔS*, e.u.
CH_3O-	17	19	7
CH_3-	20	20	1
C_6H_5-	17	19	7
CF_3	20	33	33

We are currently investigating the factors which determine the magnitude of these long-range couplings and the energy barriers to rotation with the hope of elucidating the electronic mechanism by which this coupling occurs.

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Acknowledgement. This work was supported in part by grant 868-G1 from the Petroleum Research Fund of the American Chemical Society.