Tetrahedron Letters No. 25, pp. 2255-2258, 1971. Pergamon Press. Printed in Great Britain.

STEREOSPECIFIC $^5J_{H-H}$ AND $^6J_{H-H}$ COUPLINGS IN 3-METHYL-3-AZABICYCLO[3.1.0.] HEXAN-2,4-DIONE[1]

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(Received in USA 30 March 1971; received in UK for publication 18 May 1971)

The magnitudes of long-range interproton couplings through σ bonds or a combination of σ and π bonds are known in most cases to be geometrically dependent.[2] Although in some instances the correlation between long-range coupling constants and molecular geometry has not been precisely mapped,[2e] there is growing evidence that allylic (^4J) and homoallylic (^5J) interactions through carbon-carbon double bonds can be reliable stereochemical probes.[2c] It has been proposed that ^4J and ^5J couplings across amide bonds are mechanistically related to allylic and homoallylic couplings in which the carbon-carbon double bond has been replaced with a carbon-nitrogen "partial" double bond.[2c,3] On this basis, one would expect ^4J and ^5J couplings to show a similar dihedral angle dependence for protons attached to an sp^3 carbon and the adjacent π system for both olefins and amides. At the present time, data concerning this aspect of long-range coupling in amides and related systems are scarce.[2c,3b] The ^{1}H nmr spectrum of 3-methyl-3-azabicyclo [3.1.0] hexan-2,4-dione (**1**)[4] provides new stereochemical information about homoallylic (^5J) coupling through an amide linkage and clearly demonstrates a novel, stereospecific $^6J_{H-H}$ coupling.

The ^{1}H 100 MHz nmr spectrum[6] of **1** had a two-proton pattern centered at 1.38 ppm which was initially assigned to H_A and H_B, and a two proton pattern at 2.38 ppm, assigned to H_M, on the basis of chemical shifts.[3b,7] A distinct wiggle-beat pattern for the apparent three-proton "singlet" at 2.79 ppm gave a preliminary indication of long-range coupling to the methyl protons.[2c,8,9] Double resonance experiments demonstrated that only peaks at 1.32, 1.365, 1.44, 1.475 and 1.52 ppm sharpened noticably upon irradiation of the methyl signal at 2.79 ppm, and final confirmation of the long-range interaction was obtained from the expanded spectrum shown in Figure 1a. The coupling between H_X and either H_A and H_B is clearly visible as partially resolved four and six[10] line patterns. In addition, the methyl resonance appeared as a partially resolved doublet. Refined values for chemical shifts and coupling constants (Table 1) were obtained by computer calculation,[11] assuming an ABM_2X_3 spin system. The experimental (Figure 1a) and computed (Figure 1b) spectra are in excellent agreement.

Figure 1. Experimental and Computer Simulated NMR Spectra of 3-Methyl-3-azabicyclo [3.1.0] hexan-2,4-dione.

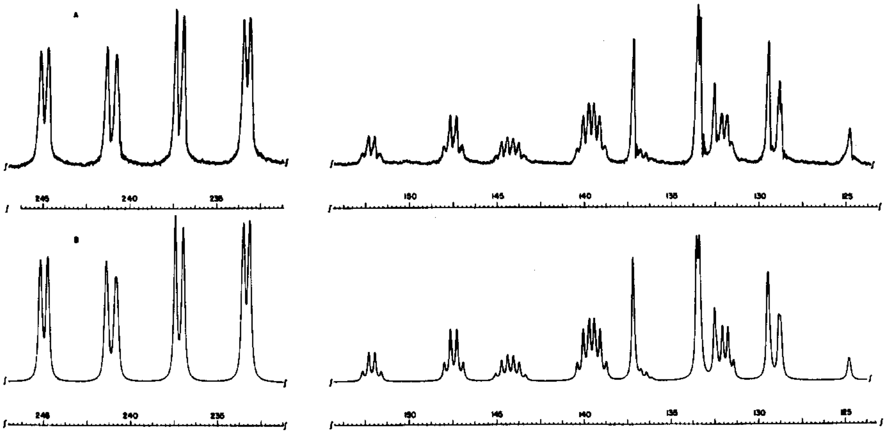
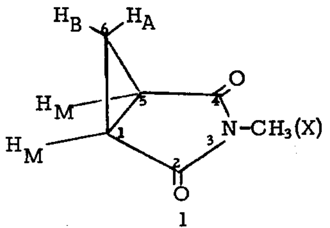


Table 1. ^1H NMR Parameters for 3-Methyl-3-azabicyclo [3.1.0] hexan-2,4-dione (1).[a,b,c]

δ_A = 1.3170	$^2J_{AB}$ = - 4.69
δ_B = 1.4167	$^3J_{AM}$ = 3.54
δ_M = 2.3897	$\lvert ^6J_{AX} \rvert <$ 0.05[d]
δ_X = 2.7944	$^3J_{BM}$ = 8.12
	$\lvert ^6J_{BX} \rvert$ = 0.37[e]
	$\lvert ^5J_{MX} \rvert$ = 0.06

[a] Chemical shifts are reported in δ , ppm, downfield from tetramethylsilane. [b] Coupling constants are reported in Hz. [c] The probable errors of all calculated parameter sets (δ and J) were $\leq$ 0.01 Hz. [d] No broadening due to long-range coupling was observed. [e] Obtained by the wiggle-beat procedure.

Assignment of stereochemistry at C_6 is based on the relative magnitudes of J_{AM} and J_{BM}. Although the ranges of *cis* and *trans* vicinal coupling constants in cyclopropanes overlap, J_{cis} is always larger than J_{trans} for a given pair.[12] A value $^6J_{BX}$ = 0.36 Hz obtained by measuring peak separation[13] of the methyl resonance compared favorably with $^6J_{BX}$ = 0.37 Hz obtained by the wiggle-beat procedure.[2c,8,14] No broadening due to long-range coupling between H_X and H_A was observed, and an estimated upper limit of J_{AX} is 0.05 Hz.[15] Careful examination of the peaks centered at 2.38 ppm revealed a small, but



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noticeable, coupling between H_M and H_X. Widths at half height for each of the eight peaks were considerably larger than the measured resolution of 0.16 Hz. Calculated widths and relative intensities of the peaks between 2.30 and 2.50 ppm were very sensitive to J_{MX}. The excellent agreement between experimental and computer simulated spectra for $J_{MX} = 0.06$ Hz was used to assign an absolute value for the magnitude of the ^5J coupling.

The ^6J coupling between H_B and the methyl protons (H_X) represents a new, stereospecific long-range interproton interaction. It may be suggested that $^6J_{BX}$ involves π contributions since the σ framework between H_B and H_X does not have a rigid, planar W-conformation necessary for maximum long-range coupling through σ bonds.[2a,b,c,e,f] In addition, models of **1** indicate that "through space" contributions to $^6J_{BX}$ are highly unlikely.[2c,f;16] The dependence of the six-bond coupling on the relative orientation of H_X with the nitrogen p orbital should parallel that found for long-range couplings to proton which are α to carbon-carbon double bonds.[2d] Since the experimental value is an average over all populated conformations of the methyl group, the maximum possible coupling should be considerably larger than the observed value.[17] Also, the orientation of H_B with respect to the amide π system is obviously critical since J_{BX} is at least six times larger than J_{AX}.[18]

The small homoallylic coupling between H_M and H_X is of interest in view of several reports of sizable couplings between N-alkyl protons and protons α to an amide carbonyl group.[2c] Since previous studies were concerned with acyclic amides or cases where the dihedral angle (θ) between a C-H bond and the adjacent p orbital of the carbonyl carbon was small, the small observed coupling between H_M and H_X in **1**, where θ is *ca.* 60 , is an indication that the stereochemical dependence of interproton homoallylic interactions across an amide bond may well parallel that found in olefinic systems. However, determination of the exact angular dependence for ^5J coupling awaits additional studies with suitable model systems. Similar measurements of ^4J, and ^6J couplings should also be useful in making stereochemical assignments for amides and imides.

REFERENCES

1. Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society and to the University of Utah Research Fund for support of this research.

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3. (a) E. W. Randall and J. D. Baldeschwieler, *J. Mol. Spec.*, **8**, 365 (1962); (b) W. E. Stewart and T.H. Siddall, III, *Chem. Revs.*, **70**, 517 (1970).

4. Imide **1** was prepared from the corresponding acid anhydride and methyl amine[5] and gave a satisfactory combustion analysis. We wish to thank Dr. W. W. Epstein for a generous gift of starting anhydride.

5. A standard route was employed, *Org. Syn.*, Coll. Vol. I, p. 457.

6. Spectra were taken on a Varian XL-100-15 NMR Spectrometer and were obtained with degassed 10% solutions of **1** in deuteriochloroform which contained 2% tetramethylsilane and 4% benzene by volume. Field homogenity was checked by scanning tetramethylsilane while locking on benzene. Resolution of the spectrum shown in Figure 1 is 0.16 Hz. Chemical shifts reported in Table 1 are sensitive to benzene concentrations.[3b]

7. L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, 1969, p. 228.

8. J. W. Elmsley, J. Feeney and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. 1, Pergamon Press, New York, 1965, pp. 40-44 and 276-277.

9. Field homogenity was checked by scanning tetramethylsilane before and after scanning the N-methyl resonance.

10. Two closely spaced transitions, each split into a quartet.

11. LAOCN3 was used to compute coupling constants and chemical shifts.

12. (a) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance in Organic Chemistry," Pergamon Press, New York, 1969, pp. 286-287; (b) W. G. Dauben and W. T. Wipke, *J. Org. Chem.*, **32**, 2976 (1967).

13. A correction for partial resolution was applied.[2c]

14. Wiggle-beat patterns were recorded in the HR operating mode. The methyl resonance was simultaneously monitored with the console oscilloscope and a Tekronix Type 544 Oscilloscope equipped with a polaroid camera. $^6J_{BX}$ was determined from photographs of the wiggle-beat trace.

15. Computer simulated spectra with $J_{AX} = 0.05$ Hz gave noticeable broadening of transitions involving H_A.

16. (a) A. Padwa, E. Shefter, and E. Alexander, *J. Amer. Chem. Soc.*, **90**, 3717 (1968); (b) K. B. Wiberg and B. A. Hess, Jr., *J. Org. Chem.*, **31**, 2250 (1966).

17. The assumption is made that pure σ contributions to $^6J_{BX}$ are small.

18. Preliminary experiments in this laboratory indicate that the ^{1}H NMR spectrum of 2,4-dimethyl-2,4-diazabicyclo[4.1.0] heptan-3,5-dione also shows a stereospecific ^6J coupling between the N_4-methyl protons and the *exo* proton at C_7. In this molecule, dual coupling pathways are not possible.