

STRUCTURAL STUDIES BY NUCLEAR MAGNETIC RESONANCE. VII. THE  
STEREOSPECIFICITY OF COUPLING BETWEEN PROTONS SEPARATED BY SIX BONDS.

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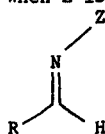
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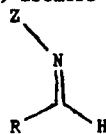
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The stereospecificity of coupling between protons separated by three (1), four (2), and five (3) bonds, and its application to conformational studies has been extensively demonstrated. We wish to present an example of stereospecific coupling between protons separated by six bonds.

When Z is NHY, both syn (I) and anti (II) isomers of aldehyde



I (syn)



II (anti)

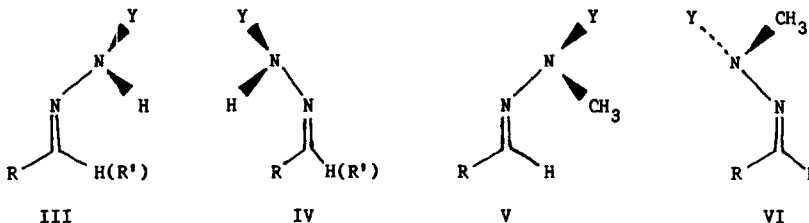
derivatives are present in solution, the isomer ratios being functions of the size and nature of R. When Z is  $N(CH_3)_2$  or  $N(CH_3)C_6H_5$  however, a single isomer is present that does not isomerize on heat or acid treatment.

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Regardless of the nature of Z, both syn and anti isomers of ketone derivatives are present.

Steric considerations offer a rational explanation of these differences. When Z is NHY, syn (III) and anti (IV) isomers should have similar conformations, the unshared pair of electrons in both isomers being parallel to and overlapping with the  $\pi$ -orbitals. When

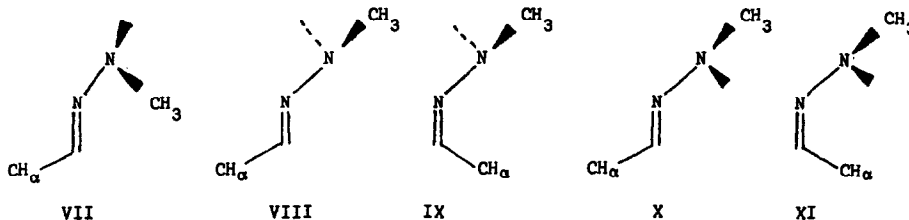


Z is  $N(\text{CH}_3)_2$  or  $N(\text{CH}_3)\text{C}_6\text{H}_5$ , only the syn (V) isomers could assume such conformations; in the anti, because of strong nonbonded interactions between R and methyl or phenyl, the unshared electrons would become nonparallel with the  $\pi$ -orbital (VI) (4). This explanation can be tested, because it implies that when Z is  $N(\text{CH}_3)_2$  or  $N(\text{CH}_3)\text{C}_6\text{H}_5$  ketone derivatives will have conformation VI and aldehyde derivatives conformation V. We shall show that such is the case.

Ultraviolet spectra. Aldehyde N,N-dimethylhydrazones have  $\lambda_{\text{max}}$  (95% EtOH cyclohex.) = 240  $\mu$  ( $\epsilon = 5.5 \times 10^3$ ); ketone derivatives have  $\lambda_{\text{max}}$  (cyclohex.) = 274  $\mu$  ( $\epsilon = 8 \times 10^2$ );  $\lambda_{\text{max}}^{95\% \text{ EtOH}} = 266 \mu$  ( $\epsilon = 8 \times 10^2$ );  $\lambda_{\text{max}}^{\text{H}_2\text{O}} = 253 \mu$  ( $\epsilon = 8 \times 10^2$ ). These values are consonant with conformations V and VI. The ketone band, although unusually intense, is probably the imide  $n \rightarrow \pi^*$  transition (5). Derivatives of N-methylphenylhydrazones behave similarly. Aldehyde derivatives have  $\lambda_{\text{max}}$  (95% EtOH, cyclohex.) = 278  $\mu$  ( $\epsilon = 1.8 \times 10^4$ ). For ketone

derivatives  $\lambda_{\max}^{95\% \text{ EtOH}} = 250 \text{ m}\mu$  ( $\epsilon = 1.0 \times 10^4$ ),  $280 \text{ m}\mu$  ( $\epsilon = 3.5 \times 10^3$ );  
 $\lambda_{\max}^{\text{cyclohex.}} = 250 \text{ m}\mu$  ( $\epsilon = 5.0 \times 10^3$ ),  $280 \text{ m}\mu$  ( $\epsilon = 2.5 \times 10^3$ ). These values are again in accord with conformations V and VI. The  $250 \text{ m}\mu$  band compares favorably with the  $247 \text{ m}\mu$  ( $\epsilon = 1.0 \times 10^4$ ) band of *N*-methylphenylhydrazine and the  $251 \text{ m}\mu$  ( $\epsilon = 1.5 \times 10^4$ ) band of *N,N*-dimethylaniline. In contrast to these differences, the ultraviolet spectra of aldehyde and ketone derivatives are similar when Z is NHX; e.g. both aldehyde and ketone *N*-methylhydrazones have  $\lambda_{\max}^{95\% \text{ EtOH}} = 228 \text{ m}\mu$  ( $\epsilon = 4.7 \times 10^3$ ).

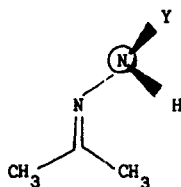
Nuclear magnetic resonance spectra. The *N*-methyl and  $\alpha$ -methyl hydrogens of acetaldehyde *N*-methylphenylhydrazone couple with  $J = 0.40$  c.p.s. (conformation VII). The coupling is about 0.3-0.4 c.p.s. in the propionaldehyde derivative and about 0.2 c.p.s. in the isobutyraldehyde and cyclohexylcarboxaldehyde derivatives. All ketone derivatives (syn and anti) on the other hand show zero coupling (VIII, IX), as judged from signal half-widths of 0.50 c.p.s. (tetramethylsilane half-width of about 0.5 c.p.s.). Similarly, while ketone *N,N*-dimethylhydrazones show zero coupling (VIII, IX), the aldehyde derivatives



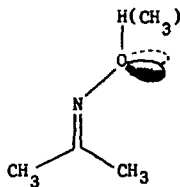
show the *N*-methyls (equivalent because of rapid rotation about the *N-N* bond) coupled to  $\alpha$ -hydrogens with  $J \approx 0.2$  c.p.s. Since this coupling should be the average of those in conformations VII and X we suggest that the coupling in conformation X is also zero. The absence of such coupling in aldehyde and ketone *N*-methylhydrazones (both syn and anti), support the suggestion that

the coupling in X is zero, and indicates further that conformation XI has zero coupling (6).

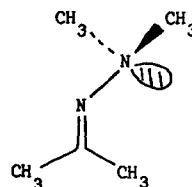
The above observations are also consonant with the finding that, when Z is NHY,  $\alpha$ -methyl hydrogens cis to Z resonate at higher fields than trans; when OH or OCH<sub>3</sub>, the difference is about zero; and when N(CH<sub>3</sub>)<sub>2</sub>, cis resonate at lower fields than trans. An obvious difference in these compounds is the stereochemical relationship of the methyl groups to the lone pairs of electron and to the directions of the N-H, N-Y, O-H(CH<sub>3</sub>) and N-CH<sub>3</sub> bonds (XII, XIII, XIV). To what extent the anisotropies of the bonds and those of the lone pair of electrons contribute to these differences cannot be ascertained from the



XII



XIII



XIV

present data.

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- (5) For the solvent dependence of  $n \rightarrow \pi^*$  transitions see H. H. Jaffe and M. Orchin, "Theory and Application of Ultraviolet Spectroscopy", John Wiley and Sons, Inc., New York, 1962, pp. 187-195.
- (6) The conclusions that the couplings in X and XI are zero are based on the assumption that a hydrogen, methyl, or phenyl attached to the nitrogen does not significantly alter the coupling in VII.