

1.50 M hexane solution, 20 mmol) at -78° . After 15 min, ethyl trimethylsilylacetate (3.20 g, 20 mmol)⁴ was added dropwise over a 10-min period and the mixture was stirred for 10 min at the same low temperature. Cyclododecanone (1.82 g, 10 mmol) in tetrahydrofuran (20 ml) was added dropwise and the resulting pale yellow solution was stirred at -78° for 1 hr, -25° for 1 hr, and 25° for 1 hr. Extractive work-up followed by chromatography (silica gel, 100 g, using hexane as eluent) gave the desired ester as a colorless semisolid (2.36 g, 94%).¹⁰

Acknowledgment. We are indebted to Dr. Keiji Yamamoto for stimulating discussions.

(10) Bp 155° (bath temp, 2 mm); ir (neat) 1720 (conjugated ester), 1644 (C=C), 1150 cm^{-1} ; nmr (CCl_4 , TMS) δ 1.24 (t, $J = 7\text{ Hz}$, $-\text{CH}_3$), 2.21 (br t, $J = 7\text{ Hz}$, $-\text{CH}_2\text{C}=\text{C}$), 2.71 (br t, $J = 7\text{ Hz}$, $-\text{CH}_2\text{C}=\text{C}$), 4.06 (q, $J = 7\text{ Hz}$, CH_2CH_3), 5.63 (br s, olefinic proton); mass m/e 252 (M^+), 128 (base peak); homogeneous by tlc. Anal. Calcd for $\text{C}_{12}\text{H}_{20}\text{O}_2$: C, 76.14; H, 11.18. Found: C, 75.89; H, 11.11.

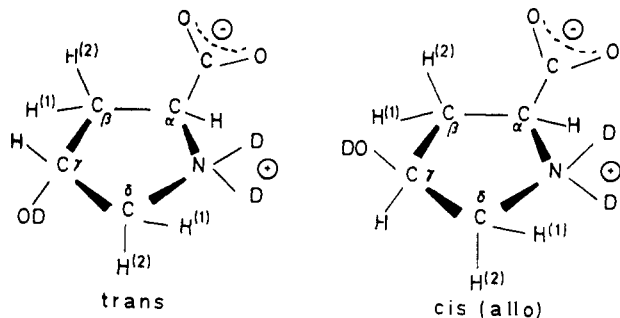
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Anisotropy Effects of the Carboxylic Group in the Proton Magnetic Resonance Spectra of L-Hydroxyproline

Sir:

In the course of a systematic investigation of proline compounds by proton magnetic resonance (pmr),^{1,2} we have paid special attention to the anisotropy effect of the carboxylic plane on the chemical shift of the ring protons. The comparison between the chemical shift titration curves corresponding to each proton provides a qualitative location of the carboxylic group, *i.e.*, gives a rough value of the torsion angle around the $\text{C}^\alpha\text{-C}^\gamma$ axis (ψ angle in the peptides).

Abraham and Thomas³ have analyzed the pmr spectra of *allo*- and *trans*-L-hydroxyproline in strong



acid, neutral, and strong alkaline solutions and deduced the conformation of the molecular ions in these solutions from the observed coupling constants. If we plot their chemical shift data against the pH and examine them in the light of our recent results on proline² and *trans*-hydroxyproline¹ some interesting conclusions about the carboxyl position in the *trans* and *allo* compounds can be reached.

The trend of the curves is the one expected from the titration of the neighboring carboxyl and amino

(1) L. Pogliani and M. Ellenberger, *Spectrosc. Lett.*, **6**, 261 (1973).

(2) M. Ellenberger, L. Pogliani, K. Häuser, and J. Valat, *Chem. Phys. Lett.*, in press.

(3) R. J. Abraham and W. A. Thomas, *J. Chem. Soc.*, 3739 (1964).

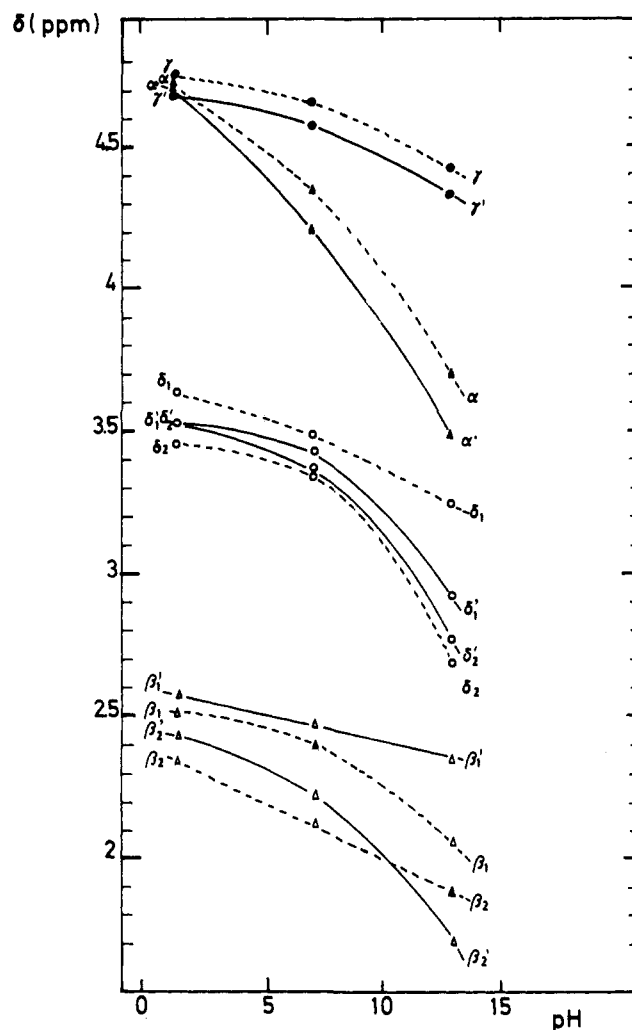


Figure 1. Chemical shift *vs.* pH of the protons of hydroxyproline *cis* (allo) and *trans* in aqueous solution, data from ref 3. Chemical shifts are given in ppm. Internal reference in DSS: (—) *allo* compound, (---) *trans* compound.

functional groups (the hydroxyl titration which occurs at higher pH has not been considered here), but, since the $\text{pK}'\text{s}$ for both functions are the same within 0.1 pH unit in the *trans* and *allo* isomer, the difference between the curves belonging to the same proton in both species and their relative position reflects mainly structural features (Figure 1). Roughly, a high field shift denotes a position above the COO^- π plane and a low field shift denotes a location in this plane.⁴

The curves have to be discussed by keeping in mind the conformation of both species as given by Abraham and Thomas.³ These conformations are briefly summarized here. The *trans*-L-hydroxyproline (THP) is in an *exo* envelope conformation in acid and neutral solution. In alkaline solution a rapid interconversion occurs between the isomers corresponding to the two positions of the nitrogen lone pair, one of which allows an intramolecular hydrogen bonding.

The *allo*-L-hydroxyproline (AHP) is in an *endo* envelope conformation in acid and neutral solution. In alkaline solution two rapidly exchanging half-chair conformations are mixed to this envelope, an intramolecular hydrogen bond occurring also between the

(4) L. M. Jackman and S. Sternhell, "Applications of NMR Spectroscopy in Organic Chemistry," Pergamon Press, Oxford, 1969, p 88.

hydroxyl group and the nitrogen lone pair for the convenient inversion at the nitrogen. (For stereochemical figures see ref 3.)

The chemical shift curves show that in the trans isomer the δ_1 proton is characteristically less high field shifted than δ_2 at basic pH, whereas in the allo isomer both protons are nearly equally shifted as H_{β_2} . In the allo isomer the β_2' proton is more high field shifted than the β_1' one at basic pH.

For the THP we have shown that in neutral solution¹ the carboxyl group is nearly coplanar with the plane defined by C^O , C^α , and N (as it is in the zwitterion crystal⁵). The trend of the curves shows that this is also true at acid pH's, but, in alkaline solution as shown by the consistent low field shift of the δ_1 proton with respect to the δ_2 proton, the carboxylic plane must pass roughly through the δ carbon. The increase of the dihedral angle ($C^O O O^-$, $C^O C^\alpha N$) with the pH would result from a change in the equilibrium between alternative repulsive and attractive interaction of the COO^- with the nitrogen lone pair and the NH proton, respectively. This is consistent with the behavior of the β protons which implies that the carboxyl group is nearly perpendicular to the plane defined by H_{β_1} , C_β , and H_{β_2} ; the β_2 proton is high field shifted with respect to the β_1 proton, whose chemical shift is nearly constant along the whole pH range.

The magnitude of the observed chemical shift anisotropy is greater on the β than on the δ geminal proton pair as expected from its distance dependence.

For AHP the chemical shift data indicate that the carboxylic plane passes roughly through the γ -carbon at acid and neutral pH, whereas at alkaline pH it rotates slightly toward the amino group. After this rotation the carboxylic plane becomes more perpendicular to the β -carbon; the β_2 proton is high field shifted with respect to the β_1 proton. The δ protons remain roughly in the carboxylic plane; the δ_1 is low field shifted with respect to the δ_2 proton, the chemical shift difference between them increasing with the pH. This is again satisfactorily consistent with a hydrogen bond between the hydroxyl and the carboxyl groups in acid and neutral solution, whereas in alkaline solution another intramolecular hydrogen bonding possibility occurs between the hydroxyl group and the nitrogen lone pair for the convenient inversion at the nitrogen.

A further effect of this intramolecular hydrogen bond may appear in the upfield position of the γ' (and perhaps of the α') curve (allo isomer) with respect to the corresponding curve of the trans compound.

Thus, the chemical shift curves contain more information than expressed by their obvious interpretation as titration of the charged groups. They contain finer intramolecular chemical shift data which reflect structural features as the torsion angle of the carboxylic plane. Of course the reported purely qualitative interpretation should be supported by quantitative analysis. This would require data on the charge distribution in the molecule for the different ionization states and the calculation of the carboxyl anisotropy.

(5) J. Donohue and K. N. Trueblood, *Acta Crystallogr.*, **5**, 414 (1952).

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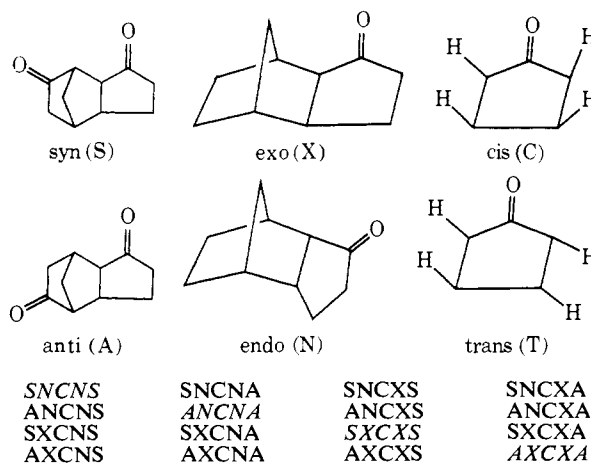
Stereochemistry of the Reaction of Strained Olefins with Iron Carbonyls

Sir:

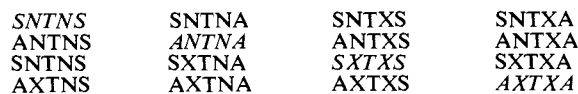
In order to delineate further the stereochemical features of the iron carbonyl-olefin reaction that produces carbonyl-inserted dimers,¹ we have selected norbornen-5-one-2² as a substrate. With alkyl substitution at the 5- and 6-positions of norbornene, exo-trans-exo adducts are obtained,^{1,3} while the presence of methoxy substituents on the 7-position leads to the exclusive formation of an adduct with exo-trans-endo stereochemistry.¹ Norbornenone was chosen for this study because the carbonyl group distinguishes the front from the rear. Furthermore, the homoconjugation present in the molecule, as gauged by the difference in cmr shifts between C-5 and C-6, viz., 12.2 ppm, might help the metal to discriminate between insertion of CO at C-5 or at C-6.

When norbornen-5-one-2 (*R,S*) is treated with $Fe(CO)_5$ in refluxing *n*-heptane for 48 hr, a white crystalline solid (mp 236–237°) is isolated in 15% yield. The formula $C_{15}H_{16}O_3$ is deduced from the molecular peak in the high-resolution mass spectrum (calcd *m/e* 244.1099; obsd *m/e* 244.1113). Carbonyl bands are present in the infrared spectrum at 1725 and 1745 cm^{-1} .

The 36 stereoisomers that can be seriously envisaged are presented below in matrix form, according to whether they belong to the syn (*S*) or anti (*A*) series, with exo (*X*) or endo (*N*) substitution, and with a cis (*C*) or trans (*T*) cyclopentanone central ring



cis series, four *meso* isomers plus six pairs of enantiomers



trans series, four pairs of enantiomers with a C_2 axis plus six pairs of enantiomers.

We were greatly helped in the elucidation of this stereochemical maze by the observation that the 300-MHz pmr spectrum is made of eight multiplets, each corresponding to two protons, and that the cmr spec-

(1) A. Speert, J. Gelan, M. Anteunis, A. P. Marchand, and P. Laszlo, *Tetrahedron Lett.*, 2271 (1973), and references herein cited.

(2) P. K. Freeman, D. M. Balls, and D. J. Brown, *J. Org. Chem.*, **33**, 2211 (1968).

(3) J. Mantzaris and E. Weissberger, *Tetrahedron Lett.*, 2815 (1972).