

Unfortunately, a reference value for purely axial N-Me in the *N*-methylpiperidine series is not available, but it seems likely that this signal, because of the usual van der Waals (γ_a) shift^{10,11} should be at least 6 ppm upfield from the equatorial N-Me signal (note in Table I that the difference is 10 ppm in the *N*-methyl-*trans*-decahydroquinolines so 6 ppm is a very conservative estimate).¹⁶ With this premise, *N*-methylpiperidine would have at least 90% equatorial *N*-methyl, *i.e.*, at best slightly less than *N*-methyl-*trans*-decahydroquinoline.^{17,18}

(16) The difference between the N-Me signals in *N,N*,3-trimethylpiperidinium iodide is 9.0 ppm.¹⁵

(17) The *N*-methyl signal of 4-*p*-chlorophenyl-*N*-methylpiperidine (sample kindly supplied by Dr. Allinger) is at 46.41 ppm, *i.e.*, nearly at the same place as that of 4-phenyl-*N*-methylpiperidine, 46.39 ppm;¹⁸ we conclude that, contrary to the calculation based on dipole measurements,^{3,4} the *p*-chlorophenyl compound also exists with largely equatorial *N*-methyl. Since it seems unlikely that the several experimental dipole measurements^{3,4} are all subject to the same error, the only plausible suggestion we can make is that there is a systematic problem in the calculation of the dipoles for the 4-arylpiperidine models with equatorial and axial N-Me.

(18) A. J. Jones, A. F. Casy, and K. M. J. McLarnan, *Can. J. Chem.*, **51**, 1782 (1973).

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Reinvestigation of *E/Z* Diastereomerism in Imidates

Sir:

In a recent publication Moriarty, *et al.*,¹ reported that open chained O-methyl imidates and large-membered cyclic lactime ethers were configurationally homogeneous existing in the *Z* ("anti") configuration.^{2,3} The configurational instability of the *E* isomers was attributed to interorbital electron repulsion between the nonbonding electrons on oxygen and the lone pair on nitrogen of the imino group in the ground state. The same destabilizing interaction in the transition state should cause a high barrier to inversion at nitrogen ($\Delta G^\ddagger > 23$ kcal mol⁻¹). No long-range homoallylic coupling was observed in the nmr spectra of these compounds.

The large long-range spin-spin coupling in imines is a useful tool for the determination of the *E/Z* configuration.⁴ Thus the five-bond coupling of the *C*-methyl protons to the *N*-methyl protons directly attached to the carbon-nitrogen double bond is much greater when the configuration of the coupling nuclei is "trans" than "cis"⁵⁻⁷ (*e.g.*, $^5J_{trans} = 1.3$ Hz and $^5J_{cis} = 0.7$ Hz in *N*-isopropylidenemethylamine).⁷ Analogously, coupling constants of $^5J_{trans} = 1.4$ Hz and $^5J_{cis} = 0.6$ Hz are also observed in *N*-methyl thioacetimidate-*S*-methyl

(1) R. M. Moriarty, C. L. Yeh, K. C. Ramey, and P. W. Whitehurst, *J. Amer. Chem. Soc.*, **92**, 6360 (1970).

(2) For a review see (a) C. G. McCarty in "The Chemistry of the Carbon Nitrogen Double Bond," S. Patai, Ed., Interscience, London, 1969, p 363; (b) H. Kessler, *Angew. Chem.*, **82**, 237 (1970).

(3) Concerning the *E/Z* nomenclature see J. E. Blackwood, C. L. Gladys, K. L. Loening, A. E. Petrarca, and J. E. Rush, *J. Amer. Chem. Soc.*, **90**, 509 (1968).

(4) S. Sternhell, *Rev. Pure Appl. Chem.*, **14**, 15 (1964).

(5) D. Wurmb-Gerlich, F. Vögtle, A. Mannschreck, and H. A. Staab, *Justus Liebigs Ann. Chem.*, **708**, 36 (1967).

(6) K. Tori, M. Ohtsuru and T. Kubota, *Bull. Chem. Soc. Jap.*, **39**, 1089 (1966).

(7) D. A. Nelson and R. L. Atkins, *Tetrahedron Lett.*, 5197 (1967).

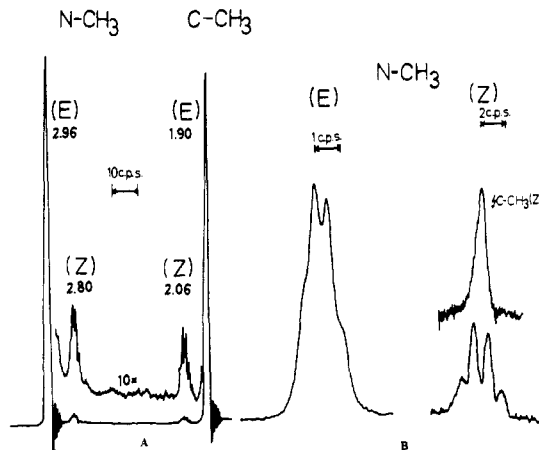
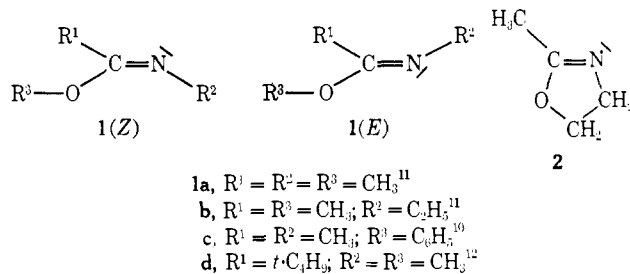


Figure 1. Nmr spectra of the N-CH₃ and C-CH₃ resonances of **1a** in CD₃OD (A) and decoupling of the N-CH₃ (*Z*) quadruplet (B).

ester and -*S*-phenyl ester,⁸ in agreement with a $^5J_{trans}$ value of 1.61 Hz in 2-methylthiazoline.⁹

We now report the homoallylic coupling between the hydrogens in R¹ and R² separated by five bonds in the open-chain acetimidates **1a**, **1b**, **1c**, and 2-methyl-oxazoline (**2**),⁹ leading to the opposite signal assignment than that reported by Moriarty, *et al.*¹ It is known that **1c** exists in the *E* and *Z* isomers.¹⁰ We



have found that **1d** exhibits the same isomerism and that also **1a** and **1b** show a small amount of *Z* isomers in methanol (Table I, Figure 1).

Each of the *C*-methyl resonances of R¹ of **1a**, **1b**, **1c**, and C-CH₃ of **2** showed the expected long-range coupling to the corresponding *N*-alkyl protons and *vice versa* (*e.g.*, N-CH₃ signals of **1a**, Figure 1B). Thus irradiation of the *C*-methyl resonances resulted in the collapse of the coupling *N*-alkyl resonances.

Further support for the signal assignment derived from the long-range coupling is obtained by using Lanthanide shift reagents.¹³ Both signals R² and R³ are strongly shifted when Eu(DPM)₃ or Pr(DPM)₃ is added to carbon tetrachloride solutions of **1a** and **1d**, while proton signals of R¹ are less affected (imidate **1a**: upfield shift, ratio Pr(DPM)₃/**1a** = 0.048, C-CH₃ (0.40 ppm), N-CH₃ (1.00 ppm), O-CH₃ (1.10 ppm); downfield shift, ratio Eu(DPM)₃/**1a** = 0.048,

(8) W. Walter and C. O. Meese, more results will be given in a later communication.

(9) M. A. Weinberger and R. Greenmalgh, *Can. J. Chem.*, **41**, 1038 (1963).

(10) M. Kandel and E. H. Kordes, *J. Org. Chem.*, **32**, 3061 (1967).

(11) H. Bredereck, F. Effenberger, and E. Henseleit, *Chem. Ber.*, **98**, 2754 (1965).

(12) The new compound **1d** was prepared from *N*-methyl pivaloimidochloride and sodium methanolate: $K_p = 123^\circ$; $n_D^{20} 1.4290$; $\nu_{\text{C-N}}$ 1674 cm⁻¹. Satisfactory analytical data have been obtained for all imidates **1a-d** and **2**.

(13) J. P. Bégué, *Bull. Soc. Chim. Fr.*, **5**, 2073 (1972); (b) R. v. Ammon and R. D. Fischer, *Angew. Chem.*, **84**, 737 (1972).

Table I. Coupling Constants and *E/Z* Diastereomer Ratios in the Nmr Spectra of the Imidates **1a-d** and **2**^a

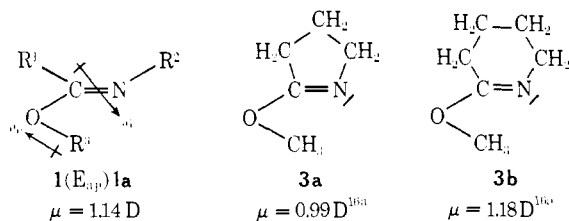
| Compd | Solvent | ⁵ J _{trans} , Hz ^b | ⁵ J _{cis} , Hz ^b | <i>E:Z</i> |
|------------------------|--|---|---|------------|
| 1a | CCl ₄ | | 0.4 q | 100:0 |
| | CD ₃ OD, ^c CH ₃ OH | 1.2 q | 0.4 q | 95:5 |
| 1b | CCl ₄ | | 0.3 (R ¹ t) | 100:0 |
| | CD ₃ OD | 1.0 (R ¹ t) | 0.3 (R ¹ t) | 95:5 |
| 1c | CCl ₄ | 1.3 q | 0.5 q | 69:31 |
| | CD ₃ OD | 1.3 q | 0.5 q | 56:44 |
| 1d ^d | CCl ₄ | | | 87:13 |
| | CD ₃ OD | | | 71:29 |
| 2 | CCl ₄ | 1.4 (CH ₃ t) | | |

^a All spectra were recorded on a Varian A-60 and HA-100 nmr spectrometer at +36° unless otherwise noted. The internal standard was TMS, the concentration was 0.1–0.5 mol/l. ^b The "trans" homoallylic coupling constant belongs to the signals R¹ and R² of the *Z* diastereomer of **1**, ⁵J_{cis} coupling occurs in **1** (*E*); determined from spectra taken at a sweep width of 50 Hz. ^c We found that slow exchange of CH₃O with CD₃O takes place in CD₃OD solutions of **1a** at room temperature. Furthermore, after some days the spectra show a decrease of R¹ signal intensity and an increase of CH₃OH. When methanol was used as a solvent, no spectral changes were observed. Obviously slow imine-enamine tautomerism had occurred with predominating imine concentration. Similar effects have been described before in the cyclic *O*-ethylvalerolactams: V. G. Granik, B. M. Pyatin, J. V. Persianova, E. M. Peregleni, N. P. Kostyuchenko, R. G. Glushkov, and Y. N. Sheinker, *Tetrahedron*, **26**, 4367 (1970). ^d Measured at -14°.

C-CH₃ (0.16 ppm), N-CH₃ (0.23 ppm), O-CH₃ (0.45 ppm)).

This shift pattern indicates that **1a** exists in the *E* form, since complexation takes place on nitrogen rather than on the ether oxygen due to the more basic character of the imine nitrogen in intramolecular competition.¹⁴

The preference for the *E* configuration may be attributed to the conformation at the R³-O bond in imidates.^{15,16} The lowest dipole moments found for imino esters (**1**, R² = H, R³ = C₂H₅)¹⁵ and for various *N*-alkyl imidates¹⁶ favor a (*E*_{app}) (antiperiplanar)¹⁷ form. In fact the dipole moment measurement of **1a** turned out to be an appropriate independent method in support of the configurational assignment taken from the nmr spectra. For the acetimidate, **1a**, we measured a dipole moment of $\mu = 1.14 (\pm 0.08)$ D¹⁸ at 20° in carbon tetrachloride (calcd $\mu = 1.04$ D), which is in good agreement with the values obtained for imidates, e.g., **3a** and **3b**,^{16a} having the same configuration at



(14) (a) H. Hart and G. M. Love, *Tetrahedron Lett.*, 625 (1971); (b) J. K. M. Sanders and D. H. Williams, *J. Amer. Chem. Soc.*, **93**, 641 (1971).

(15) H. Lumbroso, D. M. Bertin, and P. Reynaud, *C. R. Acad. Sci.*, **261**, 399 (1965); H. Lumbroso and P. J. W. Schuijff, *C. R. Acad. Sci., Ser. C*, **264**, 925 (1967); H. Lumbroso and D. M. Bertin, *Bull. Soc. Chim. Fr.*, 1728 (1970).

(16) (a) O. Exner and O. Schindler, *Helv. Chim. Acta*, **55**, 1921 (1972). (b) H. Lumbroso, and G. Pappalardo, personal communication.

(17) Using the nomenclature of analogous carbonic acid esters: W. Klyne and V. Prelog, *Experientia*, **16**, 521 (1960).

(18) Measurement on a dipolmeter DM 01, WTW, Weilheim/Germany; cell DR L2, frequency 2 MHz.

the C=N bond and a similar conformation at the O-R³ bond.

The amount of diastereomer (*Z*_{sp}) with the higher dipole moment (calcd $\mu = 2.40$ D) can increase when the partial compensation of the group dipole moment μ_1 (-O-C=N-C) is diminished by the bond dipole moment μ_e (R³-O). This is the case when the imidate is dissolved in the protic solvent methanol (**1a-d**) or if R³ is a bulky substituent with a more electronegative carbon atom (**1c**). For steric reasons the *E* configuration is less favored in **1d** than in **1a** or **1b** (Table I). Similar effects have recently been observed in thioimides.⁸

In contrast to the above mentioned publication,¹ we measured barriers to inversion on nitrogen of $\Delta G^\ddagger < 23$ kcal mol⁻¹ as predicted for this type of imine derivatives.¹⁹ Using the relationship $k_e = \pi \cdot \Delta\nu / \sqrt{2}$ and the Eyring equation²⁰ we obtained a free enthalpy of activation $\Delta G_e^\ddagger = 19.8$ kcal mol⁻¹ for **1c** ($\Delta\nu_{C-CH_3} = 17$ Hz, coalescence temperature $T_c = +110^\circ$, solvent *o*-dichlorobenzene) and $\Delta G_e^\ddagger = 15.9$ kcal mol⁻¹ for **1d** ($\Delta\nu_{O-CH_3} = 18.5$ Hz, $T_c = +37.5^\circ$, solvent CCl₄). The lower value of **1d** results from steric interactions in the favored ground state (*E*) and is in accordance with the data derived from thioimides.⁸

The governing factors determining the *E/Z* diastereomer ratios of imidates **1a-d** are dipole interactions and steric influences. Contrary to the results of Moriarty, *et al.*,¹ no hints of interorbital effects in imidates could be detected.

(19) H. Kessler, personal communication.

(20) J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. 1, Pergamon Press, New York, N. Y., 1965, Chapter 9.

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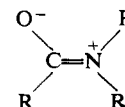
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Electronic and Steric Effects of Substitution at Nitrogen on Hindered Rotation in Formanilides

Sir:

In contrast to the well-documented effects of nitrogen substituents on the inversion process in amines,^{1,2} the electronic and steric effects of substitution at nitrogen on the rotational barrier in amides have received little systematic attention.^{2,3} An increase in electron density at the amide nitrogen should theoretically result in an increase in the activation energy because of an increase in the contribution of the resonance structure



and the resulting stabilization of the ground state. An increase in size of the substituent at nitrogen should result in greater destabilization of the ground state than that of the transition state and consequently a decrease in activation energy. The *N*-alkylformanilide molecule is an ideal system in which to test these expectations;

(1) J. B. Lambert, *Top. Stereochem.*, **6**, 19 (1971).

(2) H. Kessler, *Angew. Chem., Int. Ed. Engl.*, **9**, 219 (1970).

(3) W. E. Stewart and T. H. Siddall, III, *Chem. Rev.*, **70**, 517 (1970).