GIAO-SCF calculation of the chemical shifts in simple enamines. A comparison of theory with experiment

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Methyl-substituted enamines assume overwhelmingly a gauche–out conformation in the absence of steric hinderance. A change of global minimum to the orthogonal–out structure occurs in the presence of steric interactions (*Z*-substitution pattern). Calculation of the ^{13}C NMR shift at the β-carbon atom as a function of the torsional angle about the C–N bond axis reveals that the experimentally observed differential shielding is directly dependent upon the conformation asssumed by the enamine. The GIAO-SCF method reproduces the observed shift difference at C_β quite satisfactorily. Furthermore, we show that, at least in the case of methyl-substituted enamines, conformational assignments *in solution* can be made upon comparison of theoretical with experimental ^{13}C NMR spectra.

Introduction

Variation of the substitution pattern present at the double bond in simple enamines results in characteristic and highly differentiable ^{13}C NMR shifts at the β-carbon with (*Z*)-enamines absorbing uniformly at lower fields than their *E* counterparts.[1–3] This shift difference can be employed as a means of experimentally ascertaining the substitution pattern in substituted enamines.[2a] Indeed, it has even been possible in the case of substituted *N*-morpholinoenamines to derive an increment system for the prediction of the olefinic ^{13}C NMR shifts.[4] The differential shielding in simple enamines has long been interpreted on a mesomeric basis.[1] In the case of a *Z*-substituted enamine, steric hindrance strongly disfavours the coplanar conformation and the nitrogen lone pair then assumes an orthogonal orientation, thus resulting in the loss of mesomeric interaction and a corresponding downfield shift at C_β. An experimental study of the sterically fixed orthogonal enamine, 1-azabicyclo[3.2.2]non-2-ene showed that an orthogonal conformation does indeed result in an unusually low (128.6 ppm) shift at C_β.[7]

Theoretical studies show, however, that the mesomeric picture is much too simple, as it proves impossible to separate the π-system from the σ-skeleton due to the approximate sp^3 hybridization present at the nitrogen in enamines.[5,6] Electron donation due to π-conjugation is accompanied by a simultaneous withdrawal of electron density due to the inductive capability of the nitrogen.[5,6]

Assuming that a change in the preferred conformation is the reason for the observed differential ^{13}C NMR shifts at the β-carbon in enamines, one would expect the magnitude of the chemical shift to depend directly upon the C=C–N–lpr (lone pair) torsional angle. We therefore decided to investigate this phenomenon theoretically with a view towards answering the following questions: (*i*) Can the observed shift difference at C_β be theoretically reproduced? (*ii*) Can conformational assignments for enamines *in solution* be made upon comparison of theoretical with experimental ^{13}C NMR spectra?

Results and discussion

Under consideration of calculational and experimental feasibility, we chose a series of three small methyl substituted enamines for study, **1**–**3**.

Structure of aliphatic enamines

The structure of simple enamines is dominated by the hybridization on the nitrogen and by the position of the lone electron pair with respect to the double bond. This conformational flexibility is confirmed by X-ray structural studies on enamines,[8–12] which indicate that practically the whole spectrum of possible conformations on nitrogen can and do exist. Early PRDDO calculations on enamines predicted the existence of five stationary points on the rotational and inversional potential energy surface[13] (Fig. 1). Extensive higher level *ab initio* calculations have also been carried out on the simplest enamine, vinylamine,[5,6,14] confirming the existence of these five stationary points.

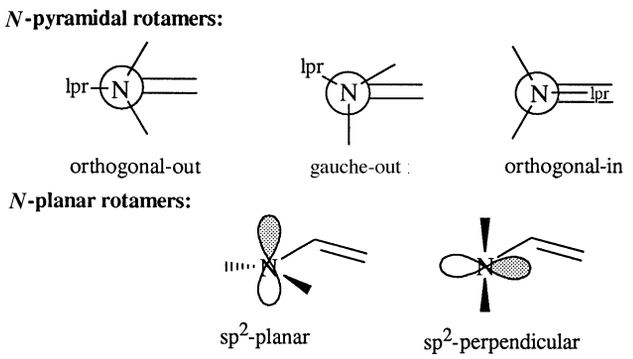
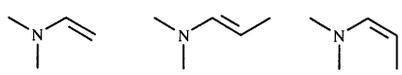


Fig. 1 Stationary points on the rotational and inversional potential energy surface of simple enamines



1 **2** **3**

At the HF and MP2 levels, we find that the structures of the enamines **1** and **2** are completely analogous to vinylamine, even down to their relative energy order and the nature of their stationary points. The global minimum for compounds **1** and **2** is the gauche–out conformer. A further minimum is the orthogonal–in structure. All other conformations represent transition structures for rotation about the C–N bond (orthogonal–out) and inversion at nitrogen (sp^2-planar). The perpendicular sp^2-hybridized structure is a second-order stationary point with the two unbounded modes representing inversion on nitrogen and rotation about the C–N bond axis.

The *Z*-substituted enamine **3** departs from this picture; steric factors now play an important role as clearly seen in a shift of the global minimum from the gauche–out to the orthogonal–in conformer at the HF and MP2 levels of calculation. An add-

Table 1 Energetics, zero-point energies and internal barriers in *N*,*N*-dimethylaminoalkenes

Structure	E_{HF}[a]	φ	ZPE[b]	E_{MP2}[c]	φ	Barrier[d] MP2	(HF)
N,*N*-Dimethylvinylamine, **1**							
gauche–out	−211.125 683	+13.5	0.125 910	−211.837 626	+13.2	0.00	(0.00)
orthogonal–in	−211.118 294	−90.0	0.125 416	−211.829 194	−90.0	4.98	(4.33)
orthogonal–out	−211.112 760	+90.0	0.124 634	−211.823 350	+90.0	8.16	(7.31)
sp^2-planar	−211.122 812	0.0	0.124 811	−211.833 323	0.0	2.01	(1.11)
sp^2-perp.	−211.106 011	90.0	0.123 265	−211.813 872	90.0	13.24	(10.68)
(*E*)-1-(Dimethylamino)propene, **2**							
gauche–out	−250.161 573	+16.6	0.154 117	−251.011 844	+15.2	0.00	(0.00)
orthogonal–in	−250.157 251	−90.0	0.153 543	−251.005 993	−90.0	3.31	(2.35)
orthogonal–out	−250.151 484	+90.0	0.152 762	−251.000 153	+90.0	6.49	(5.48)
sp^2-planar	−250.157 523	0.0	0.152 970	−251.006 357	0.0	2.72	(1.82)
sp^2-perp.	−250.145 076	90.0	0.151 360	−250.990 893	90.0	11.42	(8.62)
(*Z*)-1-(Dimethylamino)propene, **3**							
gauche–out	−250.153 594	+18.5	0.154 436	−251.004 045	+11.3	0.89	(2.54)
orthogonal–in	−250.156 904	−90.0	0.153 703	−250.999 052	−90.0	0.00	(0.00)
orthogonal–out	−250.148 436	+90.0	0.152 906	−250.991 835	+90.0	4.71	(4.35)
sp^2-planar	−250.149 912	0.0	0.152 619	−250.999 052	0.0	4.99	(3.71)
sp^2-perp.	−250.145 058	90.0	0.151 504	−250.991 835	90.0	7.63	(6.05)

[a] HF/6-31+G(d) optimized geometry; values in hartree. [b] Zero point energies calculated at the HF/6-31+G(d) level, corrected to 298 K and scaled by 0.894. Values in hartree. [c] MP2-full/6-31+G(d) optimized geometries; values in hartree. [d] Rotational and inversion barriers in kcal mol^{-1}; all barriers are corrected for ZPE contributions (calculated at HF/6-31+G(d) level). Values in parentheses are the barriers at the HF/6-3+G(d) level.

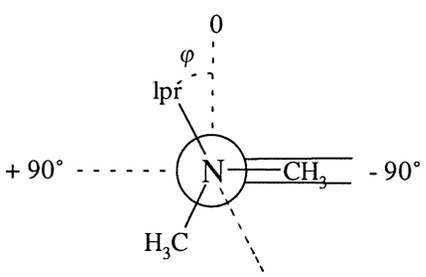


Fig. 2 The dihedral angle that the bisector of the CNC bond angle makes with the reference axis located on C_α is defined to be the C=C−N−lpr torsional angle, φ

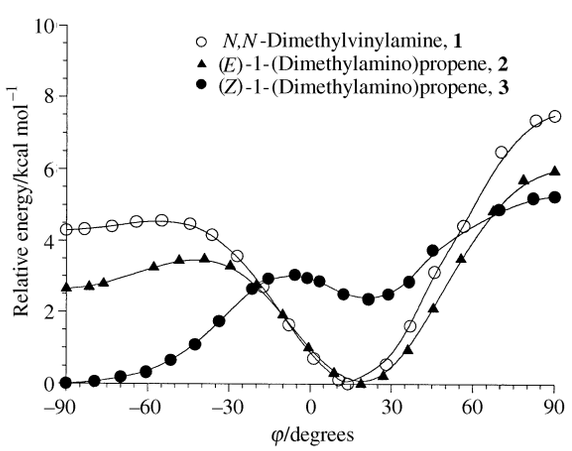


Fig. 3 HF/6-31G(d) torsional barrier to rotation about the C−N bond axis in *N*,*N*-dimethylaminoalkenes

itional difference occurs in the case of the sp^2-planar conformer. This stationary state has now become second order; *i.e.* an unbound rotational mode is now present in addition to inversion. The gauche–out structure remains a minimum.

Barriers to inversion and internal rotation

We then calculated the torsional barrier for rotation about the C−N bond at the HF/6-31G(d) level. (See Fig. 2 for a definition of the torsional angle, φ. The torsional barriers in Fig. 3 are referenced to their respective global minimum for ease of comparison. No zero point energy corrections were performed.) As expected from their structural similarity, the torsional barriers of compounds **1** and **2** closely resemble one another. β-Methyl substitution lowers the calculated barrier, as would be expected due to the inductive effect of the methyl group. The torsional barrier for the (*Z*)-enamine **3** differs fundamentally from that obtained for **1** and **2**, reflecting the change in the global minimum due to sterical interaction.

As determined from geometrical considerations, the hybridization on nitrogen changes considerably upon rotation with the orthogonal conformers being purely sp^3-hybridized. Rotation into the gauche–out position is accompanied by a simultaneous rehybridization, reaching approximately $sp^{2.5}$ for the gauche–out stationary point. This corresponds to an increase in the sum of the bond angles on nitrogen of *ca.* 13° at the HF/6-31G(d) level for all three enamines. This rotational rehybridization has direct consequences for the quality of the torsional barrier determined here. It is well known that the proper description of such phenomena requires methods that include electron correlation.[14a] As such, the picture obtained here at the HF/6-31G(d) level without inclusion of the zero point energy is only qualitatively correct.

Determination of the energy barriers for all three enamines at the HF and MP2 levels with inclusion of zero point contributions using the larger 6-31+G(d) basis set (Table 1) indicates that the process of inversion dominates, as also observed for vinylamine.[13,14]

For compounds **1** and **2**, only the gauche–out conformation is significantly populated at thermal equilibrium. The energy difference between the two minima (gauche–out and orthogonal–in) is seen to *rise* with inclusion of electron correlation effects. On the other hand, the (*Z*)-enamine **3** exists as a mixture of the orthogonal–in and gauche–out rotamers. Inclusion of electron correlation *decreases* the observed energy difference between the two conformers quite dramatically, thus resulting in a double-well potential that is not accurately represented at the HF/6-31G(d) level.

The need for inclusion of electron correlation effects in order to describe accurately these enamines is not only limited to the

Table 2 Theoretical [GIAO-SCF/6-31G(d)] and experimental ^{13}C NMR shifts of *N*,*N*-dimethylaminoalkenes

	gauche–out		orthogonal–in		
	HF[a]	MP2[b]	HF[a]	MP2[b]	Exp.[c]
Dimethylvinylamine, **1**					
C_α	143.3	146.6	143.3	147.1	145.0
C_β	84.7	88.1	112.5	114.6	80.7
C_{m1}[d]	33.9	35.3	40.5	42.1	40.6
C_{m2}[d]	39.2	40.1	40.4	42.1	—
$\Sigma/\delta_{calc} - \delta_{exp}/n_c$[e]	2.0	4.5	16.7	18.0	
(*E*)-1-(Dimethylamino)propene, **2**					
C_α	138.7	142.5	137.3	141.5	141.3
C_β	94.9	98.1	121.9	124.3	93.7
C_γ	16.3	16.6	15.4	15.5	15.6
C_{m1}[d]	39.3	40.5	40.8	42.4	40.9
C_{m2}[d]	34.8	36.3	40.8	42.4	—
$\Sigma/\delta_{calc} - \delta_{exp}/n_c$[e]	1.5	1.9	10.8	10.3	
(*Z*)-1-(Dimethylamino)propene, **3**					
C_α	136.0	140.1	136.1	140.1	140.9
C_β	93.7	95.2	121.7	124.4	102.3
C_γ	12.8	13.1	12.6	12.8	12.4
C_{m1}[d]	36.9	37.9	40.4	42.0	43.9
C_{m2}[d]	39.5	41.2	40.4	42.0	—
$\Sigma/\delta_{calc} - \delta_{exp}/n_c$[e]	4.7	2.9	8.1	7.8	

[a] HF/6-31+G(d) optimal geometries employed. All values in ppm relative to $SiMe_4$. [b] Optimal MP2-full/6-31+G(d) geometries used. [c] Experimental ^{13}C NMR shifts relative to $SiMe_4$ in C_6D_6 at 25 °C. [d] C_m = *N*-methyl group. [e] Average difference between exp. and theory per C atom. *N*-Methyl shifts not included.

energetics; the optimal geometries obtained at the correlated MP2 level show small but significant deviations, especially at the nitrogen, as compared to the HF results. Most noteworthy is a decrease of *ca.* 5° in the sum of the bond angles on nitrogen upon inclusion of correlation effects for all conformers with *N*-pyramidal geometry. Correlation effects are most important (especially for the energetics) in the case of the sterically hindered (*Z*)-enamine **3**.

^{13}C NMR chemical shifts in enamines

Using the HF/6-31G(d) geometries obtained upon calculation of the torsional barriers in Fig. 3, we determined the GIAO-SCF ^{15}/6-31G(d) ^{13}C NMR chemical shifts as a function of the C=C−N−lpr dihedral angle, φ. Rotation of the amino group about the C−N bond has a very large effect on the magnitude of the chemical shift for the β-carbon. Fig. 4 clearly demonstrates that the presence of n–π interaction results in a considerable upfield shift as compared to conformations where such interactions are impossible ($\varphi = \pm 90°$). These findings, along with the experimental fact that (*Z*)-enamines almost always resonate downfield of their *E* counterparts lends weight to the validity of the assumption that (*Z*)-enamines overwhelmingly prefer an orthogonal conformation. Also notable in Fig. 4 is the fact that methyl substitution at the β-carbon results in a downfield shift of *ca.* 10 ppm, regardless of the position of the lone electron pair, reflecting the known α-effect of an alkyl group on the chemical shift in alkenes.[2b] The magnitude of this effect is rather insensitive to whether or not the methyl group occupies the *E* or *Z* position, at least for the enamines considered here.

Table 2 compares experimental ^{13}C NMR chemical shifts with the results of GIAO-SCF/6-31G(d) calculations on the HF and MP2 gauche–out and orthogonal–in minima reported in Table 1. As seen from the experimental magnetic equivalence of the two *N*-methyl groups, rotation about the C−N axis is fast on the NMR timescale at 25 °C. Nevertheless, comparison of calculated chemical shifts with experiment confirms the predomination of the gauche–out conformation for the enamines **1** and **2**. If the orthogonal–in rotamer was present to any great extent, the experimental shift for the β-carbon would lie between the calculated shifts for the gauche–out and orthogonal–in rotamers, as observed for the (*Z*)-enamine **3**. The fact that the experimental C_β shifts for compounds **1** and **2** lie upfield of the theoretical results for the gauche–out isomer indicates that the theoretical methods probably *underestimate* the n–π interaction in **1** and **2**. This conclusion is supported by the fact that the deviation between experiment and theory is smaller for compound **2**, reflecting decreased n–π interaction due to the inductive effect of methyl substitution on C_β.

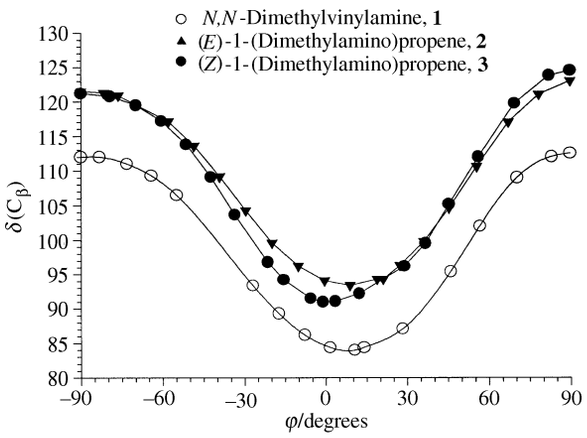


Fig. 4 Dependence of the ^{13}C NMR chemical shift, $\delta(C_\beta)$ at the β carbon as a function of the C=C−N−lpr torsional angle, φ

The fact that a worse agreement between experiment and theory is observed in the case of the (*Z*)-enamine, **3** indicates that both conformers (gauche–out and orthogonal–in) are present to a significant amount in solution. The match between theory and experiment for the orthogonal–in rotamer has become somewhat better (as compared to **1** and **2**) at the expense of the gauche–out structure. Since the system is in rapid equilibrium, the relative populations of the two conformers can be determined by using either the chemical shifts or the calculated energy difference between the two conformations. Employment of the calculated energy difference [0.89 kcal mol^{-1} (1 cal = 4.184 J) at the MP2 level] and use of the relationship $\Delta G = \Delta H(\Delta E) - T\Delta S = -RT \ln K$ under the assumption that the entropy effect cancels, indicates that approximately 80% of enamine **3** is present in the orthogonal–in conformation.

Calculation of the relative population from the chemical shift can be performed by setting up a simple system of two equations (1) and (2) with two unknowns. The value *x* corresponds to the fraction of the gauche–out conformation present and *y* gives the amount of the orthogonal–in isomer.

Substitution of the appropriate values from Table 2 into eqns. (1) and (2) [we used the values calculated with the HF/6-31+G(d) geometries] and solution for *x* and *y* indicates that the gauche–out structure is the preferred conformation and is present in *ca.* 70%. Calculation of the energy difference using this estimate of the relative population indicates that the gauche–out structure lies *ca.* 0.5 kcal mol^{-1} *lower* in energy than the orthogonal–in. This is in direct contrast to the results obtained at the MP2 level.

$$x + y = 1 \quad (1)$$

$$\delta_{C\beta,theor.}x + \delta_{C\beta,\ theor.}y = \delta C_{\beta(exp.)} \quad (2)$$

It should be noted that the introduction of electron correlation effects drastically decreased the energy difference between the gauche–out and orthogonal–in conformations of enamine **3**. It could very well be possible that an even higher computational level would reverse the relative stabilities of the gauche–out and orthogonal–in conformations for this compound.

These results indicate that the use of highly correlated methods is necessary to obtain trustworthy energetics for enamines in general. On the other hand, calculation of the chemical shielding in enamines at the noncorrelated GIAO-SCF level yields results that are quite comparable to experiment. The fact that the HF optimal geometries yield values closer to experiment than the correlated MP2 geometries deserves comment. We believe that the better match of experiment with theory at the SCF level is due to a fortuitous cancellation of error, and use of a *correlated* GIAO-method with the MP2 optimal geometries should considerably improve the match between experiment and theory.

To summarize, simple enamines assume overwhelmingly a gauche–out conformation in the absence of steric hindrance. As soon as steric hindrance comes into play, the orthogonal–in rotamer is present to a greater extent, as has been postulated.[1] For compound **3**, the steric effects are not all that large; one could easily imagine that the substitution of the methyl group with a bulkier substituent would result in a considerably increased preference for the orthogonal–in conformation.

Computational details

All *ab initio* calculations were performed using either the IBM RS/6000 or Fijitsu VP version of GAUSSIAN94.[16] All geometries employed were fully optimized in the necessary symmetry at the HF and MP2-full level of theory using the 6-31+G(d) basis set. All stationary points found at the HF level were characterized as energy maxima or minima by calculating their vibrational frequencies at the HF/6-31+G(d) level. The optimal structures were then used to calculate the absolute chemical shielding using the GIAO-SCF[15] method as implemented in GAUSSIAN94. The calculated ^{13}C NMR shielding values were referenced to $SiMe_4$. Torsional barriers at the HF/6-31G(d) level were obtained by fixing *one* C=C−N−C dihedral angle in steps of *ca*. 10°. All other geometry parameters were allowed to freely optimize in C_1 symmetry.

Experimental

All ^{13}C NMR spectra were recorded using an AM 400 Brüker apparatus at 25 °C. *N*,*N*-Dimethylvinylamine **1** was prepared as previously described by Hall[17] and Dittmer[18] and its ^{13}C NMR spectrum in C_6D_6 recorded. We found it necessary to employ C_6D_6 that had been stored for 24 h over basic aluminium oxide, as traces of acid found in the C_6D_6 were found to catalyse the self condensation of **1**. In addition, a side product which could not be identified was observed upon preparation of the *N*,*N*-dimethylvinylamine. Experimental shifts for **1** in ppm relative to $SiMe_4$ are given in Table 2. (*E*)- **2** and (*Z*)-1-(dimethylamino)-propene **3** were synthesized according to Sauer *et al.*[19] Table 2 contains their experimental shifts which were also recorded in C_6D_6.

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