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The effect of the nitrogen non-bonding electron pair on the NMR and X-ray in 1,3-diazaheterocycles

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ABSTRACT

The effect of the nitrogen nonbonding electron pair on the $^1J_{C,H}$ values of 1,3-diazaheterocycles was analyzed and compared to 1,5-diazabiciclo[3.2.1]octanes, which have a restricted conformation. The $^1J_{C,H}$ values were measured by observing the ^{13}C satellites in the ^1H NMR spectra and then determining the ^1H-coupled ^{13}C NMR spectra. The $^1J_{C,H}$ values are 10 Hz larger when the α-hydrogen is synperiplanar rather than antiperiplanar to the nonbonding electron pair on the nitrogen, which serves as experimental evidence of the orbital $n_N \rightarrow \sigma^*_{C,Hap}$ interactions. In addition, the homoanomeric effect from the interactions of the nitrogen lone pair with the antibonding orbital of the equatorial hydrogen, which was in the β position, was discussed ($n_N \rightarrow \sigma^*_{C(\beta),Heq}$).

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Introduction

Stereoelectronic effects have attracted the attention of many researchers with an interest in organic chemistry[1] because of the major role that conformation plays in cyclic and alicyclic molecules with X–C–Y and X–C–C–Y composition,[2] where X represent an atom containing a lone pair and Y is an electronegative atom. Two of the best known stereoelectronic effect are sigma conjugation ($\sigma_{C,X} \rightarrow \sigma^*_{C,Y}$)[3] and the hyperconjugation ($n_X \rightarrow \sigma^*_{C,Y}$).[4]

It was determined via ^1H NMR that the hydrogens in cyclohexane have different chemical shifts, and their spin–scalar coupling constants are dependent on their environment, where the spin-scalar coupling constant of the equatorial hydrogen (H*eq*) is 4 Hz higher ($^1J_{C,Heq}$) than the axial one ($^1J_{C,Hax}$).[3] This difference in the $^1J_{C,H}$ values has been explained by the hyperconjugation between the C1–H*ax* sigma bond and the C2–H*ax* antibonding orbital ($\sigma_{C1,Hax} \rightarrow \sigma^*_{C2,Hax}$), which involves the elongation of the C1–H*ax* bond and would, therefore, decrease the magnitude of $^1J_{C,Hax}$.[5]

The effect of the nonbonding electron pair on the $^1J_{C,H}$ value has been analyzed from both theoretical and experimental points of view.[6] The one-bond scalar spin coupling constants $^1J_{C,Hax}$ and $^1J_{C,Heq}$ have different magnitudes for the carbon α to the oxygen in 1,3-dioxanes because of the lone pair orientation. Therefore, the coupling constant for the hydrogen in the equatorial position was 10 Hz less than for the axial hydrogen.[7] This fact has been explained for the normal Perlin effect by the $n_O \rightarrow \sigma^*_{C,Hax}$ interactions elongating the C–H*ax* bond and thereby decreasing the coupling constant. It was observed in the case of 1,3-dithianes, that the $^1J_{C,Hax}$ on the α-sulfur was 10 Hz greater than the $^1J_{C,Heq}$ because of the interaction between σ_{C-S} and $\sigma^*_{C,Heq}$, which is known as an inverse Perlin effect.[8]

There are experimental and theoretical evidence of nonbonding electron pairs affecting the $^1J_{C,H}$ coupling constant in 1,3-dioxanes and 1,3-dithianes. The primary challenge in analyzing the effects of the nonbonding electron pair on the nitrogen of 1,3-hexahydropyrimidine is their rapid inversion on the NMR time-scale and the conformational changes in the six membered ring.[9,10] Anderson and Davies synthesized 1,5-diazabicyclo[3.2.1]octenes[11] with rigid conformation and provided some NMR evidence of the lone-pair effect in the $^1J_{C,H}$ coupling constant. Perillo et al.[12] synthesized imidazolidines with restricted conformation and this effect has been theoretically estimated.[13]

In this Letter, the preparation of imidazolidines, hexahydropyrimidines and 1,5-diazabicyclo[3.2.1]octenes with restricted conformations is described. The energy barrier of the nitrogen lone pair in the imidazolidines is over 83 kJ mol^{-1} (^1H NMR at 270 MHz and 423 K), which means the nitrogen is comported as a stereogenic center at room temperature.[14] The interactions between the nonbonding electron pair on the nitrogen with the $\sigma^*_{C,Hax}$ orbital of the α-carbon ($n_N \rightarrow \sigma^*_{C\alpha,Hax}$) were revealed using NMR to determine the magnitude of $^1J_{C,H}$ and via single-crystal X-ray diffraction. In addition, the homoanomeric effects from the interactions between the nonbonding electron pair on the nitrogen and the $\sigma^*_{C,Heq}$ of the β-carbon ($n_N \rightarrow \sigma^*_{C\beta,Heq}$) were discussed. This effect is known as either the Plough or W-effect depending on the lone pair orientation.[15]

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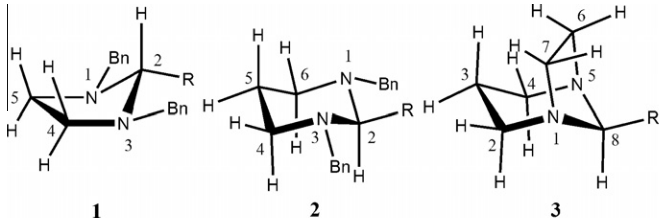
Results and discussion

To analyze the effect the nitrogen nonbonding electron pair has on the $^1J_{C,H}$ value, 12 heterocyclic compounds were synthesized with restricted conformations (Scheme 1). These compounds were characterized by ^1H and ^{13}C NMR as well as mass spectrometry, and their connectivities were established via 2D homo- and heteronuclear correlation spectroscopy (^1H,^1H-COSY and ^{13}C,^1H-HETCOR). The conformations were determined via analysis of the chemical shifts, spin–spin coupling constants, $^3J_{H,H}$, and the *t*-ROESY spectra. The conformations were also observed via single-crystal X-ray diffraction in the solid state.

Table 1 contains the ^1H NMR data for compounds **1a** through **2d**. A typical ^1H NMR spectrum for the aliphatic region of an imidazolidine (**1a–1d**) consisted of one singlet at 3.95 ± 0.08 ppm, an AB system for the diastereotopic benzyl hydrogens at 3.28 ± 0.05 and 3.79 ± 0.05 ppm, which had an average $\triangle\delta_H = 0.49$ and a $^2J_{H,H} = 13$ Hz, and an AA′XX′ system with resonances at 3.25 ± 0.05 and 2.55 ± 0.03 ppm to give a $\triangle\delta_H = 0.68 \pm 0.3$ ppm, these spectra were assigned using a simulation.[16] The 1,3-hexahydropyrimidine spectra possessed a single signal between 3.62 and 3.86 ppm that depended on the substituent at C2, an AB system for both the benzyl group and 4 multiplets for the hydrogens from C4 to C6. The resonances for both C4 and C6 were 2.995 ± 0.015 ppm for H*eq* and 2.065 ± 0.055 ppm for H*ax* and $\triangle\delta$s for the hydrogens on C5 were 0.23–0.39 ppm for the equatorial and axial hydrogens, respectively. The ^1H NMR spectra for 1,5-diazabiciclo[3.2.1] compounds were observed (Table 1) as an addition of the imidazolidine and 1,3-hexahydropyrimidine spectra without the benzyl hydrogen signals. The primary difference in these spectra was that their $^3J_{H2eq,H3ax}$ was less than the line width ($\triangle\nu_{1/2} = 2.4$). A W coupling constant was observed for between H6*endo* and H8 ($^4J_{H,H} = 1.3$ Hz), while H6*exo* demonstrated a W coupling to H2*ax* ($^4J_{H,H} = 1.0$ Hz); these observations supported a restricted conformation.

The difference between the chemical shift for H4*sp* ($\delta = 3.2$) in compound **1a** and H6*endo* ($\delta = 2.87$) in compound **3a** was caused by the orientation of the nitrogen lone-pair. Because the lone-pair was synperiplanar to the α-hydrogens in compound **1a**, the hydrogens were electronically deprotected and shifted to higher frequencies; however, in **3a**, the lone-pair was synclinal to the α-hydrogens.

The conformation for the imidazolidines determined by NMR (**1a**–**1d**) was an envelope with CH_2–CH_2 eclipsed and the *N*-Benzyl group in a pseudoequatorial position *trans* to the aryl group on C2. The six membered rings were in the chair conformation with the nitrogen and C2 substituents in equatorial positions. The bicycle had a six membered ring with an extended angle for C2 in agreement with a $^3J_{H2eq,H3ax}$ value near zero, which is indicative of a 90° torsion angle. The conformations of these compounds in solution were in good agreement with their structures as determined by solid state X-ray diffraction.



Scheme 1. Structure and labelling of the compounds. Imidazolidines **1**, hexahydropyrimidines **2** and 1,5-diazabicyclo[3.2.1]octanes **3**. (**a**) *R* = phenyl, (**b**) *R* = 2-pyridyl, (**c**) *R* = 3-pyridyl, and (**d**) *R* = 4-pyridyl.

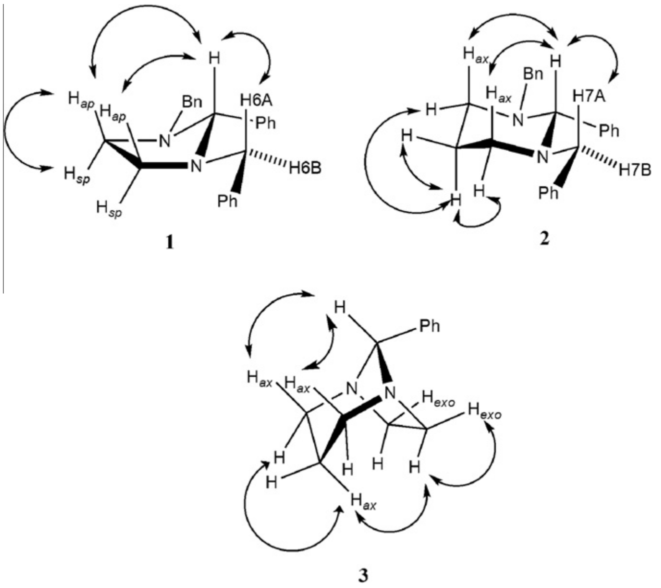
Table 1
Select ^1H NMR data for compounds **1a** through **3d** in $CDCl_3$

δ_H	**1**[a]	**1b**	**1c**	**1d**
H2	3.87	4.12	3.91	3.91
$H4_{sp}$	3.20	3.22	3.20	3.30
$H4_{ap}$	2.52	2.57	2.55	2.58
H6A	3.23	3.39	3.24	3.33
H6B	3.81	3.84	3.74	3.76
δ_H	**2a**	**2b**	**2c**	**2d**
H2	3.62	3.86	3.74	3.73
$H4_{eq}$	2.99	3.00	3.00	2.98
$H4_{ax}$	2.05	2.0	2.10	2.12
$H5_{ax}$	1.85	1.86	1.82	1.77
$H5_{eq}$	1.46	1.50	1.51	1.54
H7A	2.86	3.03	2.97	3.02
H7B	3.62	3.46	3.58	3.58
δ_H	**3a**	**3b**	**3c**	**3d**
$H2_{eq}$	3.06	2.99	2.97	2.95
$H2_{ax}$	3.32	3.26	3.23	3.19
$H3_{ax}$	1.94	1.86	1.86	1.83
$H3_{eq}$	1.17	1.10	1.11	1.08
$H6_{endo}$	2.87	2.86	2.85	2.81
$H6_{exo}$	2.61	2.6	2.5	2.45
H8	5.02	4.95	4.94	4.83
	1a	**1b**	**1c**	**1d**
$^2J_{H4sp,H4ap}$	−9.5	−9.5	−9.3	−9.5
$^3J_{H4sp,H5ap}$	+5.6	+5.3	+5.2	+5.5
$^3J_{H4sp,H5sp}$	+9.8	+9.8	+9.4	+10.0
$^3J_{H4ap,H5ap}$	+7.8	+8.0	+7.4	+9.0
$^2J_{H6A,H6B}$	13.0	13.4	13.1	13.0
	2a	**2b**	**2c**	**2d**
$^2J_{H4ax,H4eq}$	11.5	11.4	12	11.5
$^2J_{H5ax,H5eq}$	13	12.8	12.8	13.1
$^3J_{H4ax,H5ax}$	12.1	12	11.8	11.1
$^3J_{H4eq,H5ax}$	2.7	2.8	2.7	2.8
$^3J_{H4eq,H5eq}$	3.7	3.9	3.7	3.7
$^2J_{H7A,H7B}$	13.1	13.6	13.3	13.2
	3a	**3b**	**3c**	**3d**
$^2J_{Hax,H2eq}$	12.7	12.7	12.7	12.7
$^3J_{H2ax,H3ax}$	13.9	14.2	14.1	13.6
$^3J_{H2ax,H3eq}$	4.7	4.8	4.8	4.8
$^3J_{H2eq,H3eq}$	6.3	6.1	6.3	6.2
$^2J_{H3ax, H3eq}$	14.3	14.4	14.4	14.3
$^2J_{H6endo,H6exo}$	11.65	11.8	11.8	12.0
$^3J_{H6endo,H7endo}$	8.3	8.3	8.3	8.2
$^3J_{H6endo,H7exo}$	4.9	5.3	5.2	4.9
$^3J_{H6exo,H7exo}$	9.3	9.3	9.3	9.2
$^4J_{H6exo,H2ax}$	1.3	1.3	1.3	1.3

The AA′XX′ coupling constants were determined as a second order system by simulation with the software Spin Works.[16a,b] The *sp* and *ap* positions were assigned using the nitrogen non-bonding electron pair effect.

Based on the ^1H NMR, other isomers were present at a ratio of less than 200:1, which means the difference in energy between isomers was over 14 kJ/mol. The energy barrier for nitrogen inversion was greater than 83 kJ/mol (^1H NMR at 270 MHz and 423 K) because it was impossible for us to determine the point of signal coalescence (the AA′XX′ systems in the five membered ring or the AB system in the benzyl group).

Both the spatial disposition of the hydrogens and the primary conformation of the compounds were established using the *t*-ROESY spectra. Compound **1a**–**1d** demonstrated a nOe between H2 and the hydrogens antiperiplanar to the nitrogen lone-pair (H4*ap*, H5*ap*) as well as among the benzyl CH_2 groups; a correlation between H4*sp* and H4*ap* was also observed. *Syn*-axial interactions were observed for compounds **2a**–**2d** between the H2, H4*ax* and H6*ax* hydrogens in addition to the nOe between H2 and H-Bn. These observations were consistent with a chair conformation with an equatorial benzyl group *trans* to the C2 aryl group. An nOe was observed between the H8 and both the H2*ax* and H4*ax* hydro-



Scheme 2. The primary of imidazolidine, hexahydropyrimidines and 1,5-diazabicyclo[3.2.1] octane conformations in solution as determined using the nOe.

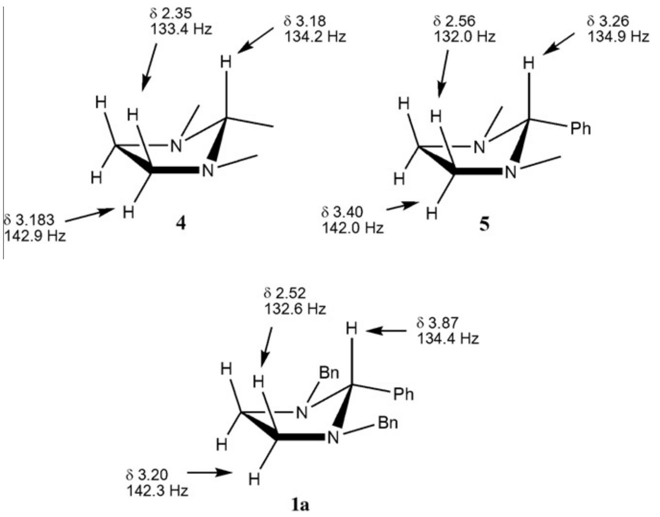
gens in compounds **3a**–**3d**, while H3*ax* experienced a nOe with the H6*endo* and H7*endo* hydrogens. These observations indicated that both the nitrogen lone-pairs and the aryl group were in the equatorial position of the six membered rings (Scheme 2).

A comparison of the chemical shift of H4*sp* (3.35 ± 0.5 ppm) in the five membered imidazolidine rings (**1a**–**1d**) to that of H6*endo* (2.84 ± 0.3 ppm) in the bicycles (**3a**–**3d**) can help explain the difference in the aryl group orientation. This orientation is in the same direction as the C–H bond in the imidazolidines and orthogonal to this bond in the bicycles. To determine the chemical shift effect of the phenyl substituent, we compared compound **1a** to both **4** and **5** (Scheme 3). The AA′XX′ coupling pattern in the heterocycle had a difference for H2 of less than △δ = 0.2 ppm, which was most pronounced for compounds **4** and **1a** (△*δ* 0.69).

Effect of the lone pair electrons on the one-bond coupling constant, $^{1}J_{C,H}$, with the α and β carbons

The coupling constants, $^{1}J_{C,H}$, for the carbons α and β to the nitrogen in compounds **1a** through **3d** were determined using the ^{13}C satellite signals in both the ^{1}H NMR and ^{13}C NMR spectra; these data are presented in Table 2. For compound **1a**, it was observed that the $^{1}J_{C,H}$ coupling constant with H4*ap* and H5*ap* was 132.6 Hz whereas it was 142.3 Hz for the H4*sp* and H5*sp*. A difference of 9.7 Hz was due to the interactions of the nitrogen lone-pair with the sigma antibonding orbital (σ*) of the antiperiplanar C–H bond ($n_N \rightarrow \sigma^*_{C,Hap}$). The decrease in the coupling constant of the synperiplanar hydrogen can be explained by the increased *p* character of the C–N bond when the C–H bond was elongated.

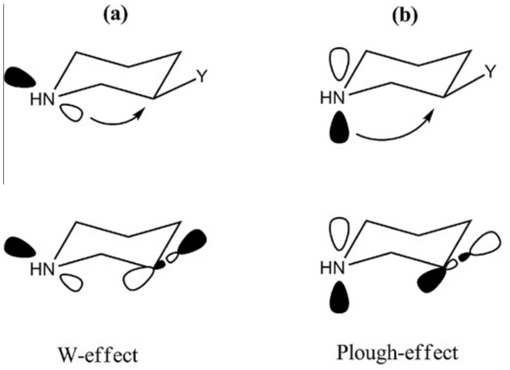
A one-bond C, H coupling between the H4*ax* and H6*ax* carbons with $^{1}J_{C,H}$ = 125.3 Hz was observed for compound **2a** whereas the coupling constant for the equatorial hydrogens was 136.1 Hz. The difference between these coupling constants was caused by the



Scheme 3. ^{1}H NMR data for the imidazolidines substituted at both C2 and the nitrogen.

Table 2
Select ^{13}C NMR data of aliphatic region for compounds **1a** through **3d** in CDCl$_3$

δ_C	**1a**	**1b**	**1c**	**1d**
C2	89.12	89.31	86.62	87.67
C4	57.02	56.92	56.97	57.192
C6	50.76	50.81	50.93	51.06
δ_C	**2a**	**2b**	**2c**	**2d**
C2	89.14	89.17	85.83	86.74
C4	51.88	51.44	51.49	50.93
C5	24.53	24.65	24.07	23.54
C7	58.55	58.32	58.38	58.41
δ_C	**3a**	**3b**	**3c**	**3d**
C2	55.95	56.01	55.83	55.79
C3	18.85	18.63	18.65	18.54
C6	50.13	50.2	49.92	49.91
C8	88.52	89.52	86.82	87.33
$^{1}J_{C,H}$	**1a**	**1b**	**1c**	**1d**
C2–H	134.4	136.7	135.4	135.4
C4–H$_{ap}$	132.6	133.1	133.7	133.6
C4–H$_{sp}$	142.3	145.8	145.33	145.7
$^{1}J_{C,H}$	**2a**	**2b**	**2c**	**2d**
C2–H	137.3	139.4	136.2	138.1
C4–H$_{ax}$	125.3	126.5	126.5	125.9
C4–H$_{eq}$	136.1	135.1	134.3	132.5
C5–H$_{ax}$	126.5	125.7	126.6	126.6
C5–H$_{eq}$	127.7	126.8	128.6	129.5
$^{1}J_{C,H}$	**3a**	**3b**	**3c**	**3d**
C2–H$_{ax}$	137.3	132.5	136.7	137.3
C2–H$_{eq}$	140.5	135.5	137.2	137.9
C3–H$_{ax}$	125.3	126.3	125.2	125.3
C3–H$_{eq}$	127.6	127.7	128.1	127.7
C6–H$_{endo}$	138.1	139.3	139.6	140.1
C6–H$_{exo}$	144.5	143.7	143.9	141.5
C8–H	146.4	146.9	146.8	146.4

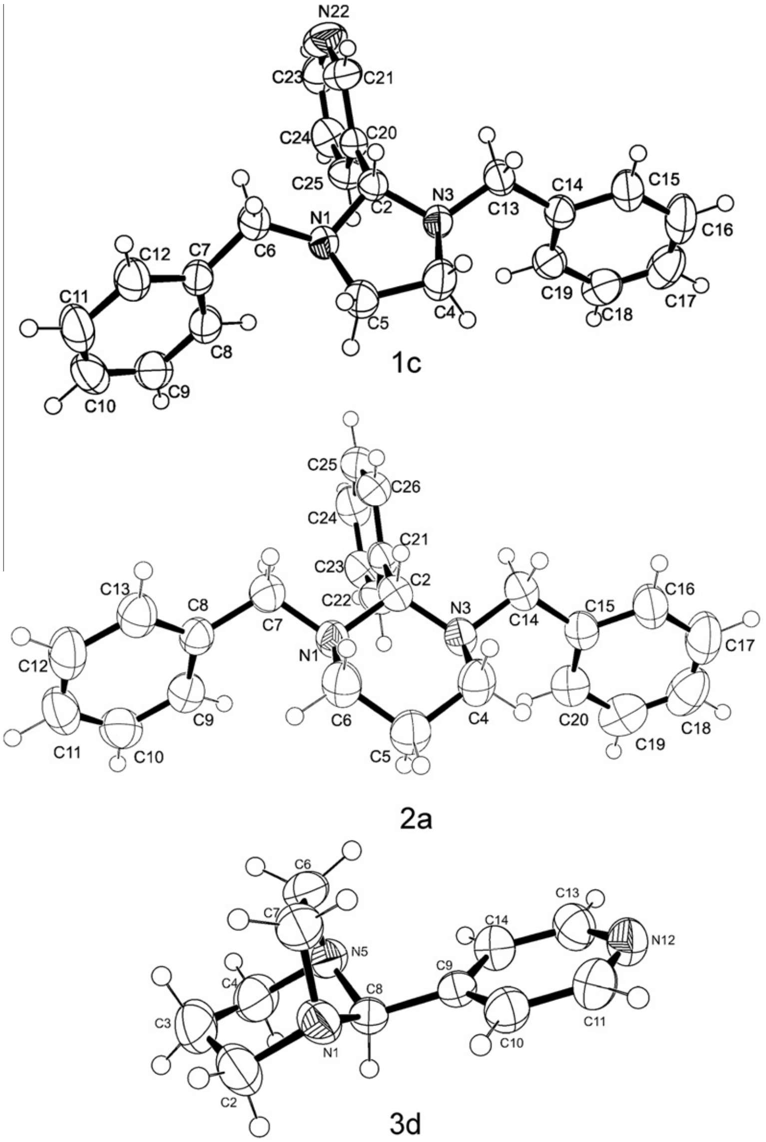


Scheme 4. Homoanomeric interaction of the six membered rings containing nitrogen.

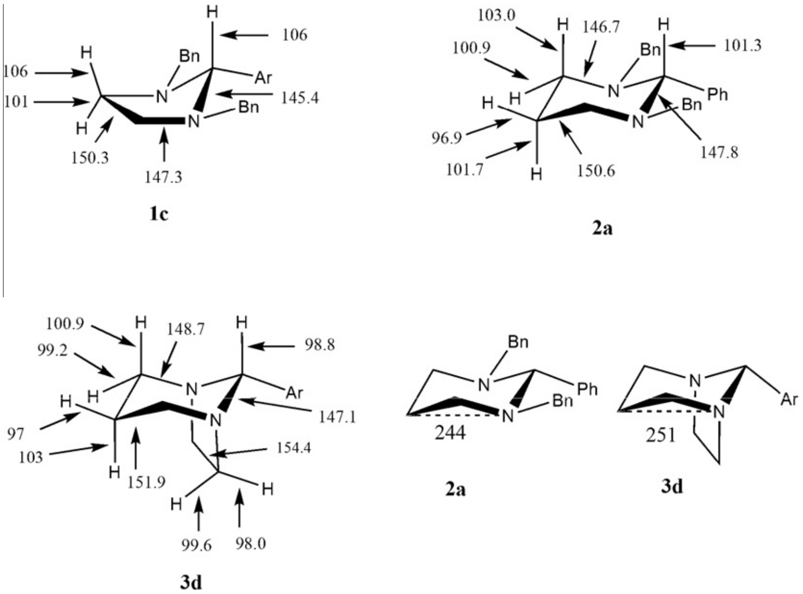
interaction between the nitrogen lone-pair and the anti-bonding sigma C–H*ax* orbital ($n_{N}\rightarrow\sigma^{*}_{C-H}$) on the α carbon in compound **2a–2d**. The elongation of the C–H*ax* bond and consequent reduction in the $^{1}J_{C,H4ax}$ and $^{1}J_{C,H6ax}$ coupling constants can be similarly explained for compounds **1a–1d** because of the lessened Fermi contact contribution.[17]

The hydrogen β to the nitrogen in compound **2a** possesses coupling constants, $^{1}J_{C,H}$, of 126.5 Hz with H5*ax* and 127.7 Hz with H5*eq*. For the cyclohexane moiety, the $\triangle^{1}J_{C,H}$ between H*ax* and H*eq* was approximately 4 Hz, which was explained as hyperconjugation of the C1–H*ax* bond with the antibonding sigma C2–H*ax* orbital ($\sigma_{C1,Hax}\rightarrow\sigma^{*}_{C2,Hax}$). The smallest coupling constant difference for the $^{1}J_{C,H5ax}$ and $^{1}J_{C,H5eq}$ hydrogens in **2a–2d** relative to the cyclohexane was because of the homoanomeric effect.[18] This effect causes the nitrogen lone pair to interact with the sigma antibonding orbital, Cβ,H*eq* ($n_{N}\rightarrow\sigma^{*}_{C(\beta),Heq}$). There are two such interactions; the first is the W-effect, which involves non-bonding electrons in the equatorial position interacting with the $\sigma^{*}_{C,Heq}$ orbital; the second is caused by the decrease in the coupling constant with H5*ax* and H5*eq* in compounds **2a–2d**, which is known as the Plough effect and explained by the interaction between the lone pair in the axial position and the $\sigma^{*}_{C(\beta),Heq}$ orbital (Scheme 4).

The primary difference between compounds **1a** through **2d** and the compounds **3a**–**3d** was the orientation of the nitrogen lone-pair, which was in the equatorial position of these compounds because their conformational rigidity did not allow inversion. Compounds **3a**–**3d** did not demonstrate any $n_{N}\rightarrow\sigma^{*}_{C(\alpha),H}$ interactions because such interactions between orbitals are very sensitive to the lone pair orientation. The hyperconjugation effect, $n_{N}\rightarrow\sigma^{*}_{C,H}$, was observed for H2 in compounds **1a** through **2d** because the antibonding orbital, $\sigma^{*}_{C,H}$, was synperiplanar to both of the nitrogen lone-pairs, which elongated the C–H bond and reduced the coupling constant. For instance, compounds **1a** and **2a** have a $^{1}J_{C2,H}$ value of 134.4 and 137.3 Hz, respectively. However, in compounds **3a**–**3d,** the nitrogen lone-pairs are synclinal to the $\sigma^{*}_{C8,H}$ orbital; therefore, there was no hyperconjugation and the coupling constant, $^{1}J_{C,H}$, was unaffected, for example, $^{1}J_{C,H}$ = 146.4 Hz in compound **3a**. In addition, the observed differences between $^{1}J_{C,Hax}$ and $^{1}J_{C,Heq}$ in compound **3a** was 2.3 Hz for the hydrogens β to the lone pair whereas the $\triangle^{1}J_{C,H}$ for compound **2a** was 1.2 Hz.



Scheme 5. ORTEP drawing of the crystal structure of compounds **1c**, **2a**, and **3d.**



Scheme 6. Bonding and non-bonding distance (in pm) as determined by the single-crystal X-ray diffraction structures for compounds **1c**, **2a** and **3d**.[†]

Table 3
Select bond distance (pm) and angles for compounds **1c**, **2a**, and **3d** as determined by X-ray diffraction[‡]

1c		2a		3d	
N1–C2	145.4(3)	N1–C2	147.82(16)	N1–C8	147.13(14)
N1–C5	147.3(4)	N1–C6	146.71(18)	N1–C2	148.75(16)
C5–C4	150.3(4)			C7–C7#1	154.4(3)
		C5–C4	150.6(2)	C3–C2	151.8(2)
		C5–C6	149.9(2)	C3–C2#1	151.9(2)
C20–C2	149.5(4)	C21–C2	151.97(19)	C8–C9	151.6(2)
N1–C2–N3	101.2(2)	N1–C2–N3	110.74(14)	N1#1–C8–N1	106.29(13)
		C2–N1–C6	111.45(11)	C8–N1–C2	106.65(11)
		C4–C5–C6	109.01(15)	C2–C3–C2#1	111.51(18)
		N1–C6–C5	110.55(12)	N1–C2–C3	113.24(14)
C2–N1–C5	106.4(2)			C8–N1–C7	101.17(10)
N1–C5–C4	105.1(2)			N1–C7–C7#1	105.88(7)

X-ray diffraction

We obtained adequate crystals of compounds **1c**, **2a**, **2d**, **3a** and **3d** for structural analysis by X-ray diffraction (Scheme 5), which indicated compounds **1c** and **2a** had each nitrogen lone-pair oriented on the same side in the axial position, while in the structure of compounds **3a** and **3d,** the lone-pairs were equatorial. The aromatic ring at C2 in the single crystals of monoheterocycles **1c** and **2a** was observed in equatorial position in the symmetry plane that bisected the five or six membered ring, whereas the aryl group in compounds **3a** and **3d** were perpendicular to the C2–H bond (Scheme 5). This implies that the solubility of compound **3** in organic solvents was better than the other materials.

The positions of the hydrogen atoms were determined using a difference Fourier map. The C–C and C–H bond lengths and angles were sensitive to changes in the hybridization of the atoms, which indicates an orientation change for the nitrogen lone-pair in the molecules. A comparison of the C2–N1 bond in compound **2a** (147.8 pm), where both lone-pairs are *sp* to the antibonding σ^*_{C-H} orbital, to the C8-N1 bond in compound **3d** (147.13 pm), which has the lone-pair in the equatorial position and, therefore, *sc* to the σ^*_{C-H} antibonding orbital, neglects the difference in bond lengths (Table 3). However, an increase in the C8–N1 bond length in compound **3d** was expected relative to molecule **2a**, which had an $n_N \rightarrow \sigma^*_{C-H}$ effect. The explanation for this result is that the lone-pair on the nitrogen in **3d** was *sp* to the antibonding σ^*_{C2-N3} orbital, and there was a $n_N \rightarrow \sigma^*_{C-N3}$ type interaction. Therefore, the change in the C8–N1 bond length in **3d** was neglected and the coupling constant magnitude increased because of the enhanced *p* character of C8.

Table 3 shows the bond length and angle data for compounds **1c**, **2a**, and **3d**. It was determined that the C2–H bond lengths for compounds **1c** and **2a** were 106 and 101.3 pm, respectively, but for compound **3d**, the C8-H length was only 98.8 pm, which was a significant reduction due to the $n_N \rightarrow \sigma^*_{C-H}$ effect.

Compounds **2a–2d** display Plough interactions, which explains their different $^1J_{C,H}$ values, and the homoanomeric W-effect was observed in compounds **3a–3d**. Scheme 6 shows the C–N, C–C and C–H distances obtained by crystallography. It was observed that C–H*ax* was longer than C–H*eq* for the six membered rings (compounds **2a** and **3d**), while the distance between the nitrogen with a β-carbon was longer in compound **3d** than for **2a**. These data show that the Plough interaction competes with the homoanomeric W-effect in 1,3-diazacyclehexanes.[†]

Conclusion

The evidence obtained by NMR and single-crystal X-ray diffraction indicated that the nitrogen lone pair electrons in

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[‡] Crystal data: **1c**: Monoclinic, *P*21/*n*, $a = 604.10(2)$ $b = 1592.20(6)$ $c = 1936.60(2)$pm, $\beta = 90.646°(4)$, $Z = 4$, ρCalcd = 1.175, $\theta = 3.31–27.50°$, 4161 independent reflections ($R_{int} = 0.0271$), $R1 = 0.0474$ for 4161 with $I > 2\sigma(I)$, $wR2 = 0.1143$ for all data, 318 parameters, GOF = 1.042. **2a**, monoclinic, *P*21/*n*, $a = 608.70(6)$ $b = 1688.20(3)$ $c = 1961.00(5)$pm, $\beta = 98.330°(3)$, $Z = 4$, ρCalcd = 1.141, $\theta = 4.18–26.00°$, 3732 independent reflections ($R_{int} = 0.0360$), $R1 = 0.0474$ for 3732 with $I > 2\sigma(I)$, $wR2 = 0.0982$ for all data, 339 parameters. GOF = 1.042. **3d**, orthorhombic, *Pbnm*, $a = 696.60(3)$ $b = 1360(4)$ $c = 1102.40(7)$pm, Z=8, ρCalcd = 1.203, $\theta = 2.99–27.44°$, 1231 independent reflections ($R_{int} = 0.0427$), $R1 = 0.0430$ for 1231 with $I > 2\sigma(I)$, $wR2 = 0.1057$ for all data, 103 parameters, GOF = 1.037.

[†] There are additional factors that complicate the comparison as the double hyperconjugation (Alabugin, I. V.; Manoharan, M. *J. Org. Chem.* **2004**, *69*, 9011–9024) and the rehybridization (Alabugin, I.V.; Manoharan, M. *J. Compt. Chem.* **2007**, *28*, 373–390), both were shown to change the properties of C–H bonds in related systems.

imidazolidines **1a–1d** and hexahydropyrimidines **2a–2d** interact with the C–H sigma antibonding orbitals, $n_N \rightarrow \sigma^*_{C-H}$, which causes a 10 Hz difference in the α-hydrogen coupling constants, $\triangle {}^1J_{C,H}$. This difference was less pronounced in 1,5-diazabiciclo[3.2.1]octanes because both hydrogens were in the synclinal position relative to the nitrogen lone pair.

The stereoelectronic effect of homohyperconjugation was most evident when the lone-pairs were in the axial rather than equatorial position because the distance between the nitrogen and the β carbon was longer in the latter case.

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Supplementary data

Supplementary data (the crystallographic data for compounds **1c**, **2a**, **2d**, **3a** and **3d** have been deposited in the Cambridge Crystallographic Data Centre, with the deposition numbers CCDC 848653, 849019, 867286, 848463 and 848654, respectively. These data can be obtained free of charge from www.ccdc.cam.ac.uk/data request/cif) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.04.077.

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