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Density functional and spectroscopic studies of nitrogen inversion in substituted dizocilpines

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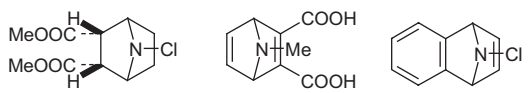
While developing a synthesis towards tagged dizocilpine (MK-801) analogues, we observed highly restricted inversion of a nitrogen centre in a number hydroxylamines obtained as key intermediates. These compounds are shown to possess some of the structural elements which are expected to significantly hinder the nitrogen inversion, potentially leading to hydroxylamines with a chiral nitrogen centre. Free energy barriers ($\Delta G^{\neq}$) of the nitrogen inversion were estimated to be *ca.* 22 kcal mol^{-1} at temperatures near 420 K using variable temperature NMR measurements in DMSO-d_6. Further density functional studies of a number model systems were undertaken in order to better rationalize the measured inversion barriers and follow the role of various structural factors in raising the barrier height of the nitrogen inversion process. Copyright © 2008 John Wiley & Sons, Ltd.

Keywords: dizocilpine; hydroxylamines; nitrogen inversion; chiral nitrogen; energy barrier; transition state; NMR spectroscopy; DFT calculations

INTRODUCTION

Various aspects of pyramidal nitrogen inversion have been a subject of detailed studies in the past.[1] While a simple NH_3 molecule shows a low barrier of inversion (*ca.* 6 kcal mol^{-1}), the introduction of electronegative atoms (such as oxygen) directly bonded to nitrogen is known to lead to a significant increase of the nitrogen inversion barrier. The increase of the number of oxygen atoms directly attached to nitrogen leads to further increase of the inversion barrier. Inclusion of the nitrogen atom into a three-membered ring is also known to significantly slow down the nitrogen inversion. A classic example combining both structural elements, electronegative substituent and ring angle strain, is an oxaziridine ring with a chiral nitrogen atom. In particular, the nitrogen inversion barrier was determined to be 25–32 kcal mol^{-1} in *N*-alkyl oxaziridines.[2] Such a high value of the inversion barrier was attributed to the fact that the transition state (TS) for thermal epimerization significantly increases the ring strain.[3] Note that when the inversion barriers are greater than *ca.* 23 kcal mol^{-1} the isolation of *N*-invertomers or optically active substances becomes feasible.[1]

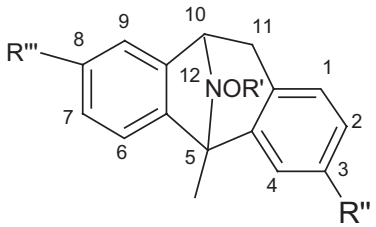
There are various other structural arrangements in which the nitrogen inversion may be significantly altered. In the case of rigid bicyclic systems, the nitrogen inversion barrier can be significantly hindered. For example, the energy barriers for the nitrogen inversion in 7-aza-bicyclo[2.2.1]heptanes are comparable to those in aziridines[1,4]



$\Delta G^{\neq}$(kcal mol^{-1}): 21[1] 19.5[1] 23.5[4]

The origin of this 'bicyclic' effect is not clear. However, it has been suggested that the destabilization of the TS by repulsions between nitrogen lone pair and the bonding electrons in both two carbon bridges of the bicyclic system may be responsible for high nitrogen inversion barriers.[1] Further detailed studies of N-bridged bicyclic amines have been reported.[5–7] From the natural bond orbital (NBO) analysis for azabicycles, it was concluded that the relatively high barrier (13.8 kcal mol^{-1}) in 7-azabicyclo[2.2.1]heptanes is mostly determined by the energy of the σ-orbitals of the C_α—C_β bonds as well as the nitrogen lone pair.[6]

Here we report new examples of hindered nitrogen inversion in bicylic hydroxylamines **1**-**5** studied by NMR spectroscopy and DFT calculations



1 R′=R″=R‴=H

2 R′=Me, R″=R‴=H

3 R′=Me, R″=NO_2, R‴=H

4 R′=Me, R″=R‴= NO_2

5 R′=Me, R″=NH_2, R‴=H

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The set of hydroxylamines **1**-**5** were prepared for the synthesis of tagged analogues of dizocilpine (MK-801) used as *N*-methyl-D-aspartate (NMDA)-receptor antagonist.[8–13] They possess some of the structural elements which are expected to significantly hinder the nitrogen inversion, potentially leading to hydroxylamines with a chiral nitrogen centre. In particular:

(i) the nitrogen atom is a part of both five- and six-membered rings;
(ii) both five- and six-membered rings are rigid, that is no ring interconversions are possible due to the specific structural arrangement;
(iii) there is an electronegative oxygen atom with unshared electrons attached to nitrogen.

COMPUTATIONAL AND NMR DETAILS

DFT calculations were carried out using Gaussian 03.[14] Geometry optimizations and nitrogen inversion barriers were calculated using the B3LYP/6-31G(d) level of theory. Solution state calculations used IEFPCM model,[15] as implemented in Gaussian 03. ^{1}H and ^{13}C NMR chemical shifts were computed at the B3LYP/6-311+G(2d,p) level using the GIAO method[16] and are given relative to that of TMS calculated at the same level of theory (B3LYP/6-311+G(2d,p)//B3LYP/6-31G(d)).

Solution ^{1}H and ^{13}C NMR spectra were recorded on Bruker NMR spectrometers AMX300, AVANCE III 400 and AVANCE 500 with ^{1}H Larmor frequencies of 300, 400 and 500 MHz, respectively. ^{1}H and ^{13}C chemical shifts are given relative to TMS. Unless otherwise specified, spectra were recorded at 296 K. Selective NOE and 2D experiments were measured using AVANCE III 400 and AVANCE 500, equipped with *z*-gradient facilities. Variable temperature spectra were measured using the AVANCE III 400 instrument. The high temperature calibration was carried out using a standard sample of 80% 1,2-ethanediol in DMSO-d_6.[17]

RESULTS AND DISCUSSION

Two sets of peaks with unequal intensities were observed in ^{1}H and ^{13}C NMR spectra of **1**-**5** in $CDCl_3$ and DMSO-d_6 solutions recorded at room temperature. The sets of peaks with the 5-Me peak resonating at lower and higher frequencies in ^{1}H NMR spectra are denoted as **A** and **B**, respectively (Fig. 1 and Table 1). Note that this order of appearance of the 5-Me peaks is reversed in the ^{13}C spectra (Table 1). In all the compounds studied, except **5**, the preferred form with higher intensity of peaks was **A**. Similar sets of two peaks were also observed previously in ^{1}H NMR spectra of 3-bromo, 7-bromo, 7-methoxy and 7-amino derivatives of **1**.[18]

There is no direct evidence available from experimental NMR spectra measured in $CDCl_3$ or DMSO-d_6, which can be used to establish whether the *cis*- or *trans*-configuration of the N—OH and 11-CH_2 is preferred. However, both the ^{1}H and ^{13}C chemical shifts show some significant differences for the major and minor forms and we used GIAO B3LYP 6-311G(2d,p) IEFPCM(DMSO) chemical shift calculations for **2** (Table 1) in order to relate these differences to the structural changes. All the significant relative changes in ^{1}H ($|\Delta\delta| = |\delta(\mathbf{2A})\text{-}\delta(\mathbf{2B})| > 0.04$ ppm) and ^{13}C ($|\Delta\delta| > 0.4$ ppm) aliphatic chemical shifts were reproduced. These DFT GIAO calculations, allowed to unambiguously assign

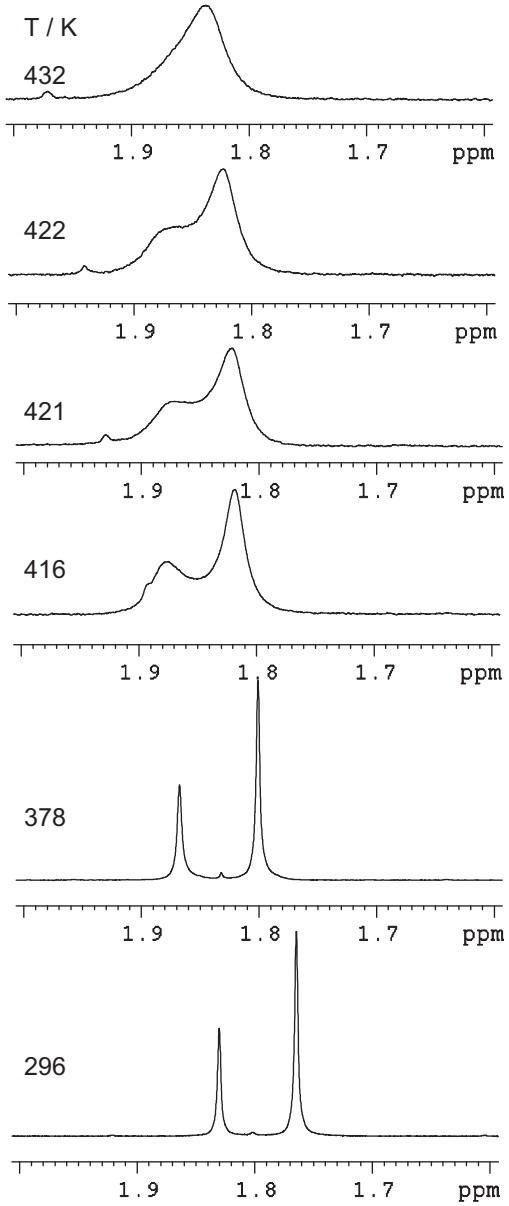

Figure 1. The temperature dependence of the C-Me ^{1}H NMR line shape in **1** (DMSO-d_6, 400 MHz)

the major form **A** to the *cis*(O,CH_2)-configuration and the minor form **B** to the *trans*(O,CH_2)-configuration (Fig. 2).

In the case of **1** in DMSO-d_6, sharp lines due to the hydroxyl protons were observed in the ^{1}H NMR spectra recorded at room temperature: 7.97 ppm (**A**) and 8.20 ppm (**B**). These were selectively excited in DPFGSE-NOE (Double Pulsed Field Gradient Spin Echo-NOE)[20] experiments (Fig. 3). A significant enhancement for one of the methylene protons was found in the case of **A**, whereas no such NOE was observed for **B**. Considering the relative orientations of the OH and CH_2 protons, such observation is in favour of the *cis*(O,CH_2)-configuration in **A** and the *trans*(O,CH_2)-configuration in **B**, in agreement with the results of the chemical shift calculations above.

The preference of the structure **A** can be rationalized in terms of non-covalent interactions between oxygen lone pairs and

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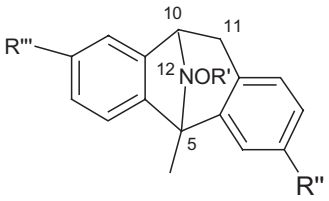
Table 1. ^{1}H and ^{13}C NMR chemical shifts (δ, ppm) of 1-5 (DMSO-d_6, 296K). The relative chemical shift changes are calculated as $\Delta\delta = \delta(A) - \delta(B)$



Proton	1A	1B	2A	2B	3A	3B	4A	4B	5A	5B	Calc.,[a] 2A	Calc.,[a] 2B	$\Delta\delta^{exp}$	$\Delta\delta^{calc}$
5-Me	1.77	1.83	1.85	1.90	1.97	2.01	2.05	2.10	1.76	1.80	1.92	2.02	−0.05	−0.10
N-OMe	7.97[b]	8.20[b]	3.55	3.49	3.61	3.56	3.58	3.53	3.47	3.53	3.72	3.67	0.06	0.05
10-H	4.44	4.54	4.74	4.75	4.83	4.83	4.99	4.99	4.66	4.67	5.15	5.10	−0.01	0.05
11-CH_2	2.40	2.71	2.44	2.77	2.63	2.94	2.69	3.00	2.26	2.58	2.73	3.05	−0.33	−0.32
	3.47	3.48	3.36	3.49	3.50	3.63	3.51	3.68	3.20	3.32	3.73	3.85	−0.13	−0.12
Carbon	1A	1B	2A	2B	3A	3B	4A	4B	5A	5B	Calc.,[a] 2A	Calc.,[a] 2B	$\Delta\delta^{exp}$	$\Delta\delta^{calc}$
5-Me	17.92	15.26	18.00	14.59	17.90	14.48	17.80	14.43	18.10	14.66	19.47	15.73	3.41	3.74
5-C_q	67.74	73.46	67.74	73.39	67.85	73.21	67.86	73.29	67.72	73.41	75.43	81.57	−5.64	−6.14
N-OMe	—	—	60.94	60.58	61.15	60.80	61.42	60.96	60.94	60.53	63.23	63.52	0.36	−0.2
10-H	62.75	69.30	59.73	66.98	59.30	66.41	59.25	66.42	60.05	67.39	66.32	74.54	−7.25	−8.22
11-CH_2	27.97	34.51	28.17	34.84	28.60	35.19	27.97	34.56	29.23	34.10	32.76	40.86	−6.67	−8.10

[a] DFT GIAO B3LYP/6-311+G(2d,p)/IEFPCM(DMSO), geometries from B3LYP/6-31G(d)/IEFPCM(DMSO).
[b] Proton N–OH.

aromatic electrons. For example, almost equal populations of **A** and **B** in **5** can be attributed to increased electron density of the aromatic ring with the amino substituent which leads to increased repulsion with the oxygen lone pairs in **5A** which in turn leads to a decreased relative population of **5A**. Similarly, the increase of the population of **A** relative **B** in **3** compared to **2** can be attributed to decreased electron density of the aromatic ring with the nitro substituent in **3A** compared to **2A**.

High temperature ^{1}H NMR measurements were undertaken in order to verify whether the observed two species are in dynamic exchange. On increasing the temperature above 373 K, line shape changes characteristic for dynamic systems were observed (Fig. 1). The coalescence temperatures measured were very high (~400 K) suggesting that the chemical exchange between the two species observed at room temperature must be very slow in the NMR chemical shift timescale. Since the C-Me fragment is common in **1-5**, the corresponding peaks at *ca.* 2 ppm were chosen for quantitative estimates of the energy barriers and for their accurate comparisons. Free energy barriers ($\Delta G^{\neq}$) were estimated using the method described by Shanan-Atidi and Bar-Eli, which is suitable for the case of unequal populations ($p_A \neq p_B$).[21] The results of variable temperature NMR measurements together with the $\Delta G^{\neq}$ values are summarized in Table 2. As apparent from Table 2, the replacement of OH in **1** by OMe in **2** does not cause any significant changes in the measured $\Delta G^{\neq}$ values. In principle, the inequivalence of the peaks due to **A** and **B** species observed in NMR spectra can also be associated with a hindered N—O rotation in **1-5**. However, the almost equal $\Delta G^{\neq}$ values for **1** and **2** are in favour of the hindered nitrogen inversion process. This conclusion was further supported by the DFT calculations of the energy barriers described below.

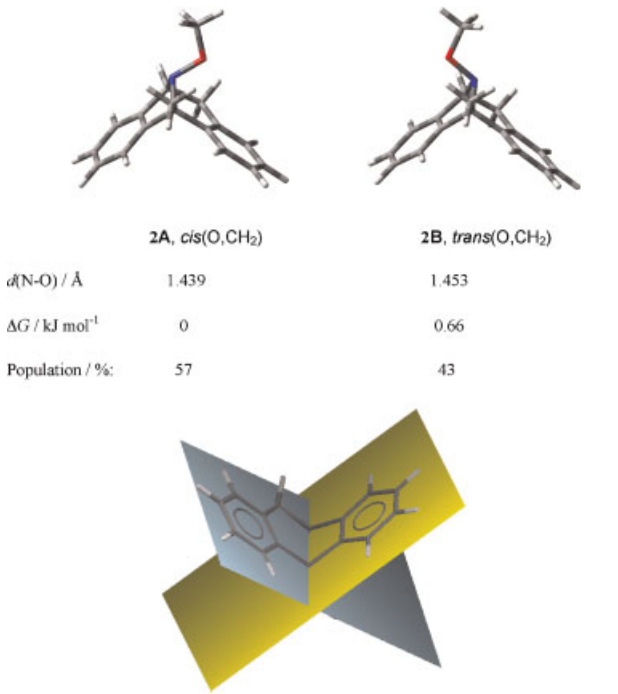


Figure 2. The results of the DFT B3LYP 6-31G(d) IEFPCM(DMSO) geometry optimizations with frequency calculations. The relative free energy difference is calculated as the difference between the values of the sum of electronic and thermal free energies for **2A** and **2B**. The experimentally measured populations of **2A** and **2B** were 57 and 43% in DMSO-d_6 solution. The V-angle between the two aromatic ring planes is 105° in both **2A** and **2B** (*ca.* 93–97° in Tröger's bases)[19]

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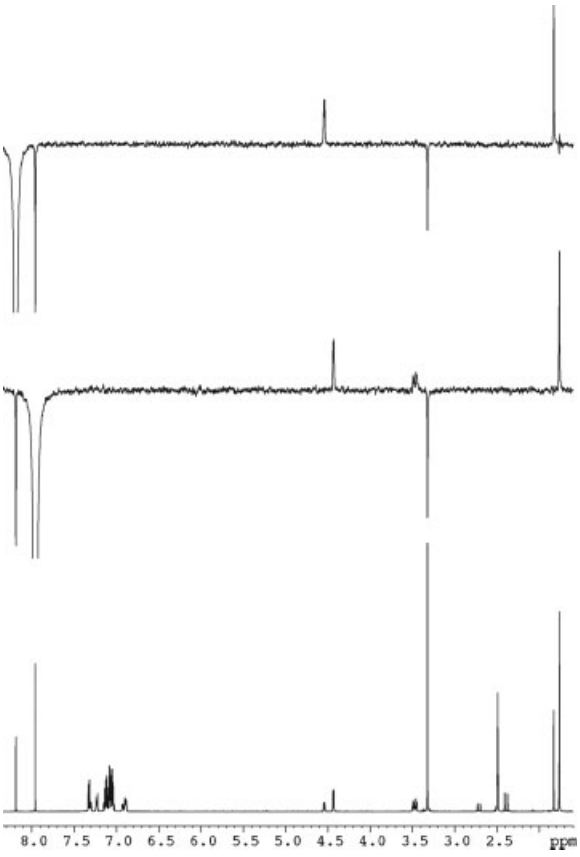
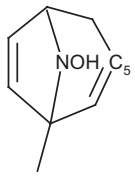


Figure 3. Top: selective NOE spectrum of **1B** ({OH}, with 2 Hz line broadening). Middle: selective NOE spectrum of **1A** ({OH}, with 2 Hz line broadening). Bottom: ^{1}H NMR spectrum of **1** (no line broadening). Spectra were recorded in DMSO-d_6 at 296 K (500 MHz)

Further DFT calculations were carried out in order to better rationalize the measured inversion barriers. Initially, a model compound **6** was used for the gas phase B3LYP 6-31G(d) calculation of the nitrogen inversion barrier.



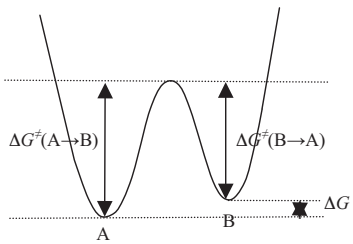
6

The bond angle O—N—C_5 was 79.9° in the starting structure (form **A** with the *cis*(O,CH_2)-configuration). This bond angle was increased in 10° increments. From Fig. 4, the estimated barrier is 22.2 kcal mol^{-1}. The structure with the highest energy (at the bond angle of O—N—C_5 *ca.* 130°) shows a nearly planar nitrogen. The N—O rotation was also simulated starting from structure **A** with the H—O—N—C_5 dihedral angle of 180°. The estimated barrier for the N—O rotation is less than 7.6 kcal mol^{-1}.

Similar calculations for the starting structures **1A** and **2A** led to an estimate of 20.5 and 20.1 kcal mol^{-1}, respectively, for the nitrogen inversion barrier. The structures with the highest energies for **1** and **2** show a nearly planar nitrogen atom with the dihedral angle of C_5—O—C_{10}—N equal to *ca.* 3°.

Encouraged by the success of the DFT calculations in predicting the inversion barriers of hydroxyl amines, we undertook further calculations of model molecules in order to follow the role of various structural factors in hindering the nitrogen inversion. The results are summarized in Table 3. The barrier predicted for the dimethyl hydroxylamine **7** is of the order of values previously measured for acyclic molecules, such as

Table 2. Free energy barriers ($\Delta G^{\neq}$) measured from variable temperature ^{1}H NMR spectra in DMSO-d_6 at 9.4 *T*. The values of chemical shift differences ($\Delta\nu$) at 296 K and coalescence temperatures (T_c) used in the calculations $\Delta G^{\neq}$ are also shown



	Ratio,[a] p_A/p_B	$\Delta G^{\neq}_{A\to B} = (T_c)$ (kcal mol^{-1})	$\Delta G^{\neq}_{B\to A} = (T_c)$ (kcal mol^{-1})	$\Delta G\ (T_c)$[b] (kcal mol^{-1})	ΔG (296 K)[c] (kcal mol^{-1})	T_c (K)	$\Delta\nu$ (Hz)
1	1.94	22.2	21.6	0.6	0.4	422	26
2	1.31	22.0	21.8	0.2	0.2	420	20
3	2.20	21.9	21.2	0.7	0.5	408	17
4	1.36	21.2	20.9	0.3	0.2	403	18
5	0.99	22.0	22.0	0	0	424	18

[a] Measured at 296 K.

[b] $\Delta G\ (T_c) = \Delta G^{\neq}_{A\to B}(T_c) - \Delta G^{\neq}_{B\to A}(T_c)$

[c] $\Delta G(296\ \mathrm{K}) = RT\ \ln(p_A/p_B)$.

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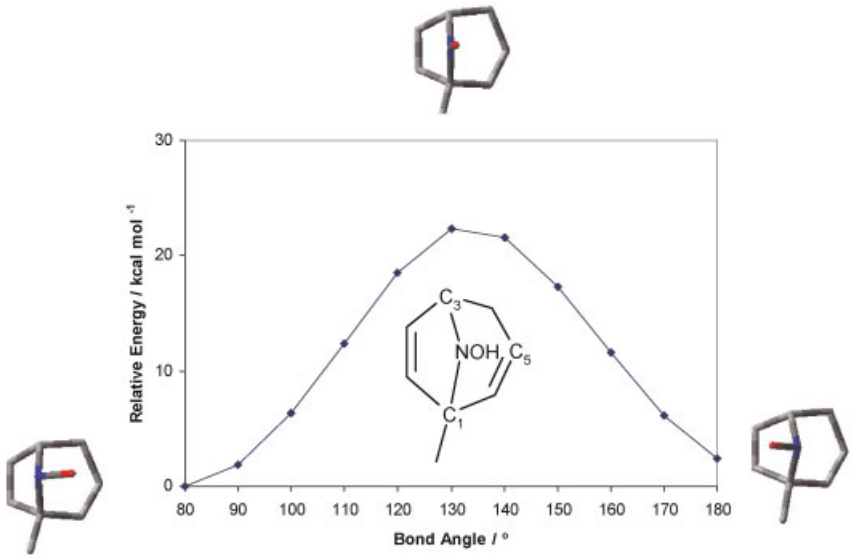


Figure 4. The relative energy changes as a function of bond angle O—N—C_5 in **6**.The maximum corresponds to a nearly planar nitrogen with the dihedral angle of C_1O—C_3—N equal to 3.2°

Table 3. The gas phase DFT B3LYP 6-31G(d) predicted nitrogen inversion barriers in model molecules. The barrier values were calculated as the Hartree-Fock (HF) energy difference (E_{HF}^{total}(TS) − E_{HF}^{total}(GS), where TS denotes the transition state with a planar nitrogen and GS denotes the lowest energy invertomer in its ground state with a pyramidal nitrogen)

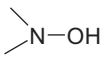
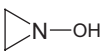
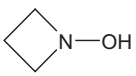
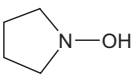
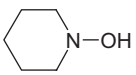
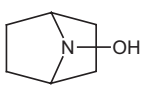
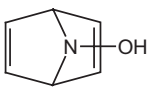
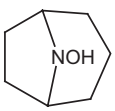
Number	Molecule	Calculated Barrier,(kcal mol^{-1})
7		12.8
8		31.8
9		14.6
10		11.3
11		15.8
12		25.0
13		30.2
14		21.3

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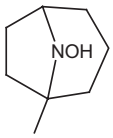
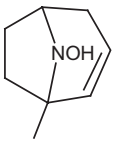
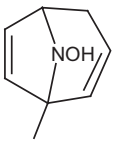
Table 3. (Continued)

Number	Molecule	Calculated Barrier,(kcal mol^{-1})
15		20.4
16		21.1
6		22.2

N,N′-dibenzyl-*N,N′*-diarylhydrazines.[22] As expected, the introduction of the three-membered ring led to a significant increase of the inversion barrier by about 19 kcal mol^{-1} in **8** compared to **7**. The decrease of the inversion barriers in four, five and six-membered rings compared to aziridine **7** agrees qualitatively with the fact that the strain in the TS can be relaxed by the ring inversion. A similar TS relaxation model can be used in the case of **12** and **13**, where the introduction of double bonds eliminates any possible ring flexibility in **13** compared to **12**, leading to *ca*. 5 kcal mol^{-1} increase of the nitrogen inversion barrier. The predicted high value of *ca*. 30 kcal mol^{-1} in **13** also suggests that hydroxyl amine derivatives of 9,10-dihydroanthracen-9,10-imines may serve as a source of chiral nitrogen. Further examples of **14** and **15** show that despite its pharmacological importance,[18] the introduction of the bridgehead methyl group does not have a significant effect on the nitrogen inversion. In addition, comparison of **13** and **6** suggests that the attenuation of the ring strain via introduction of additional methylene group is exploited efficiently in the TS in order to lower its energy, hence leading to significantly decreased nitrogen inversion barriers. Finally, the results of DFT calculations suggest that structural analogues of **12** and **13** may serve as a source of bicyclic hydxylamines with a chiral nitrogen centre.

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REFERENCES

[1] J.-M. Lehn, *Top. Curr. Chem.* **1970**, *15*, 311.
[2] J. Bjorgo, D. R. Boyd, *J. Chem. Soc. Perkin Trans.* **1973**, 1575.
[3] A. Forni, G. Garuti, I. Moretti, G. Torre, G. D. Andreetti, G. Bocelli, P. Sagarabotto, *J. Chem. Soc. Perkin Trans.* **1978**, 401.
[4] V. Rautenstrauch, *Chem. Commun.* **1969**, 1122.
[5] S. F. Nelsen, J. T. Ippoliti, T. B. Frigo, P. A. Petillo, *J. Am. Chem. Soc.* **1989**, *111*, 1776.
[6] A. M. Belostotskii, H. E. Gottlieb, M. Shokhen, *J. Org. Chem.* **2002**, *67*, 9257.
[7] A. M. Belostotskii, Z. Goren, H. E. Gottlieb, *J. Nat. Prod.* **2004**, *67*, 1842.
[8] K. A. Trujillo, H. Akil, *Drug Alcohol Depend.* **1995**, *38*, 139.
[9] M. Elhallaoui, M. Laguerre, A. Carpy, F. Ouazzani, *J. Mol. Model.* **2002**, *8*, 65.
[10] E. H. Wong, J. A. Kemp, T. Priestley, A. R. Knight, G. N. Woodruff, L. L. Iversen, *Proc. Natl. Acad. Sci. USA* **1986**, *83*, 7104.
[11] M. Benveniste, M. L. Mayer, *J. Physiol.* **1995**, *483*, 367.
[12] G. P. Hess, A. Gameiro, R. C. Schoenfeld, Y. Chen, H. Ulrich, J. A. Nye, B. Sit, F. I. Carroll, B. Ganem, *Biochemistry* **2003**, *42*, 6106.
[13] T. R. Lamanec, D. R. Bender, A. M. DeMarco, S. Karady, R. A. Reamer, L. M. Weinstock, *J. Org. Chem.* **1988**, *53*, 1768.
[14] *Gaussian 03*, Revision D.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr, T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, J. A. Pople, Gaussian Inc., Wallingford, CT, **2004**.
[15] E. Cances, B. Mennucci, *J. Math. Chem* **1998**, *23*, 309.
[16] R. Ditchfield, *J. Chem. Phys.* **1972**, *56*, 5688.
[17] S. Braun, H.-O. Kalinowski, S. Berger, *150 and More Basic NMR Experiments*, (2nd edn). Wiley-VCH, Weinheim, **1998**.
[18] W. J. Thompson, P. S. Anderson, S. F. Britcher, T. A. Lyle, J. E. Thies, C. A. Magill, S. L. Varga, J. E. Schwering, P. A. Lyle, M. E. Christy, B. E. Evans, C. D. Colton, M. K. Holloway, J. P. Springer, J. M. Hirshfield, R. G. Ball, J. S. Amato, R. D. Larsen, E. H. F. Wong, J. A. Kemp, M. D. Tricklebank, L. Singh, R. Oles, T. Priestly, G. R. Marshall, A. R. Knight, D. N. Middlemiss, G. N. Woodruff, L. L. Iversen, *J. Med. Chem.* **1990**, *33*, 789.
[19] L. Cerrada, J. Cudero, J. Elguero, C. Pardo, *J. Chem. Soc. Chem. Commun.* **1993**, 1713.
[20] K. Scott, J. Stonehouse, J. Keeler, A. J. Shaka, *J. Am. Chem. Soc.* **1995**, *117*, 4199.
[21] H. Shanan-Atidi, K. H. Bar-Eli, *J. Phys. Chem.* **1970**, *74*, 961.
[22] J. R. Fletcher, I. O. Sutherland, *Chem. Commun.* **1979**, 687.

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