J. Phys. Chem. A **2009,** *113,* 7769–7773 **7769**

Shape of Biomolecules by Free Jet Microwave Spectroscopy: 2-Amino-1-phenylethanol and 2-Methylamino-1-phenylethanol

Sonia Melandri,* Stefano Ragno, and Assimo Maris

Dipartimento di Chimica "G. Ciamician", via Selmi 2, 40126 Bologna, Italy

Received: March 27, 2009; Revised Manuscript Received: April 24, 2009

We report a free jet microwave absorption study of 2-amino-1-phenylethanol and 2-methylamino-1-phenylethanol, which are analogues of noradrenaline and adrenaline, respectively. The spectra, recorded under different expansion conditions and with different carrier gases, show the presence of several conformational species: two conformers for 2-amino-1-phenylethanol and three for 2-methylamino-1-phenylethanol. The assignment is based on the comparison of the experimental rotational constants and the orientation of the molecular dipole moment with the ones predicted by theoretical methods and allows the univocal identification of all observed conformers while intensity measurements give information on their relative stability. All of the observed conformational species are stabilized by an intramolecular hydrogen bond between the hydroxyl hydrogen atom and the amino nitrogen atom, whereas the alkylamino side chain can be in the extended anti or folded gauche conformation. The presence of the bulky methyl group substituent on the alkylamino side chain of 2-methylamino-1-phenylethanol influences the relative stability of the conformers.

Introduction

Intra- and intermolecular weak forces govern the shape and function of active molecules, and the hydrogen bond, in particular, assumes a central role in essential biological processes such as molecular recognition, neurotransmission, intracellular transport, and drug−receptor interaction.[1] The shape of flexible molecules, such as the neurotrasmitters, which present a number of low-energy conformations, is generally the result of a delicate balance between intra- and intermolecular nonbonding interactions, and it is therefore very important to understand the different roles and the importance of each of them.

In the last 10 years, a variety of powerful experimental and theoretical techniques have been used to explore the conformational behavior of biomolecules, biomimetic molecules, or small molecular complexes under the isolated conditions of supersonic expansions, and the experimental data coupled to high-level ab initio calculations have proved to be essential for the understanding of the factors that govern the shape of the isolated molecules or their weakly bound complexes.[2] Among the possible experimental techniques, rotational spectroscopy gives the most detailed structural picture of the conformational space.[3]

Experiments on active molecules performed on isolated molecules or on simple molecular complexes constitute a starting point in evaluating the behavior of the species in the actual biological environment that cannot be studied yet at this level of precision.

Noradrenaline and adrenaline are two important biogenic cathecolamines formed from tyrosine that are involved in almost all vital processes and apparatuses of the living organisms, including the cardiovascular, respiratory, excretory, and digestive systems.[4]

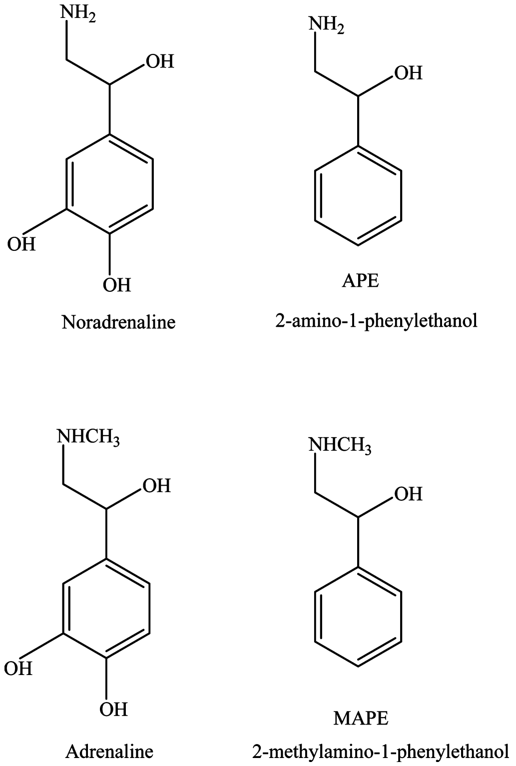


Figure 1. Sketch of the relevant biomolecules and their analogues.

2-Amino-1-phenylethanol (APE) and 2-methylamino-1-phenylethanol (MAPE) are, respectively, a noradrenaline and adrenaline analogue, and, as shown in Figure 1, they differ from the real cathecolamines by the absence of the two hydroxyl groups in the phenyl ring. Whereas this difference lowers the melting point, facilitating the spectroscopic analysis, it maintains the main molecular characteristics, at least in the gas phase, making these molecules an optimal model in studying adrenergic neurotransmitters. The structure of these neurotransmitter analogues is characterized by the presence of a highly flexible amino-hydroxyl side chain, and this accounts for the existence of several energy minima in the conformational potential energy hypersurface.

---

* Corresponding author.

10.1021/jp902784h CCC: $40.75

Conformational studies utilizing different experimental and theoretical tools have been carried out on molecules containing a phenyl ring and an amino side chain such as the prototypical molecule phenylethylamine,[5,3c,d] histamine,[6] *p*-methoxyphenethylamine,[7] tryptamine,[8,3b] serotonin,[9] and tyramine.[10,3a]

The group of Prof. J. P. Simons published an investigation on APE[11] and MAPE.[12] In these studies, the authors utilize UV band contour, UV−UV hole-burning, and IR−UV ion dip spectroscopy methods coupled to quantum mechanical calculations to highlight the possible conformations of the molecules and show that intramolecular hydrogen bonds have a key role in determining the conformations of the two molecules. Five stable configurations were predicted for APE, and two of these were detected experimentally, whereas for MAPE, among the seven predicted conformers, four of them were observed.

Although the previous work on these molecules is extensive and convincing, we think that the precise structural data, the information on the orientation of the permanent dipole moment within the molecule, and the estimation of relative conformer population that can be obtained using the free jet absorption millimeter wave technique (FJAMMW) should lead to the unambiguous and conclusive identification of the different conformers and their relative energy scale.

Methods

The design of the Stark and pulse modulated free jet absorption millimeter-wave spectrometer used in this study working in the frequency range of (60 to 78) GHz has previously been described.[13]

Solid APE and solid MAPE (purchased from Aldrich, racemic mixture and used without further purification) were, respectively, heated to about (125 and 85) °C ahead of the nozzle, whereas a stream of the carrier gas (He or Ar) at P_0 ca. 240 mbar was flown over it. The mixture was then expanded to about 5×10^{-3} mbar through a continuous nozzle with a diameter of 0.35 mm. The accuracy of the frequency measurements is estimated to be better than 0.05 MHz.

Ab initio calculations of molecular structure, conformational energies, electric dipole moments, and nuclear quadrupole constants at the MP2/6-311+G** level of theory and performed using the Gaussian 03[14] suite of programs were carried out on the plausible conformers to assist the rotational assignment and to guide the identification of the conformers present in the jet expansion. Calculation of the vibrational frequencies in the harmonic approximation for all of the optimized structures allowed us to check that the stationary points were actual minima and let us estimate the zero point correction to the electronic energy and the values of the quartic centrifugal distortion constants. The analysis of the conformational energy was extended to include thermal Gibbs energies at the temperature and pressure prior to the expansion.

Results and Discussion

1-Amino-2-phenylethanol. For this molecule, extensive molecular orbital calculations, performed as an aid to experimental interpretation, are reported in ref 11. The calculations are repeated here at a higher level of theory (MP2/6-311+G**) to predict the spectroscopic parameters useful for the assignment of the rotational spectrum, that is, the rotational and centrifugal distortion constants, the components of the electric dipole moment in the principal inertia axis system of the molecule, and the nuclear quadrupole coupling constants.

APE is a chiral molecule that exists in the R and S forms, which are spectroscopically identical. There are five low-energy conformations that are depicted in Table 1. The five conformations are classified according to the arrangement anti (A) or gauche (G) of their CCCN and OCCN chains. Two conformations, AG_1 and GG_1, where the OH group acts as the proton donor to the NH_2 group, are by far the lowest in energy conformers and should be easily observed in the jet expansion given that the population ratio established at the temperature prior to the expansion (125 °C) does not change. The detection of the other higher energy conformers depends on the overall intensity of the spectrum, and it is limited by the sensitivity of our instrument and by relaxation processes.

The initial search for the rotational transitions, based on the predicted rotational constants reported in Table 1, was performed using Ar as the carrier gas. Under these conditions, we observed a group of rotational lines that were assigned and interpreted with a set of rotational constants (conformer I). A second scan was performed using He as the carrier gas, and a second set of transitions was observed (conformer II). The rotational transitions' frequencies are given as Supporting Information, whereas the spectroscopic parameters fitted with Watson's semirigid Hamiltonian in the "S" reduction and I^r representation[15] are reported in Table 2.

We observe only μ_b, and μ_c R-type transitions: first, the high K_a lines where the two components coalesce because of near prolate degeneracy and then a few low K_a transitions where we could distinguish between μ_b and μ_c component lines. This is in agreement with the calculated rotational spectra where only the μ_b and μ_c R-type transitions for both conformers should be observable because the μ_a transition are supposed to be too weak because of the high rotational quantum numbers involved. Moreover, in the scanned frequency range, the hyperfine structure due to the coupling of the nuclear quadrupole moment of the nitrogen atom is not resolvable.

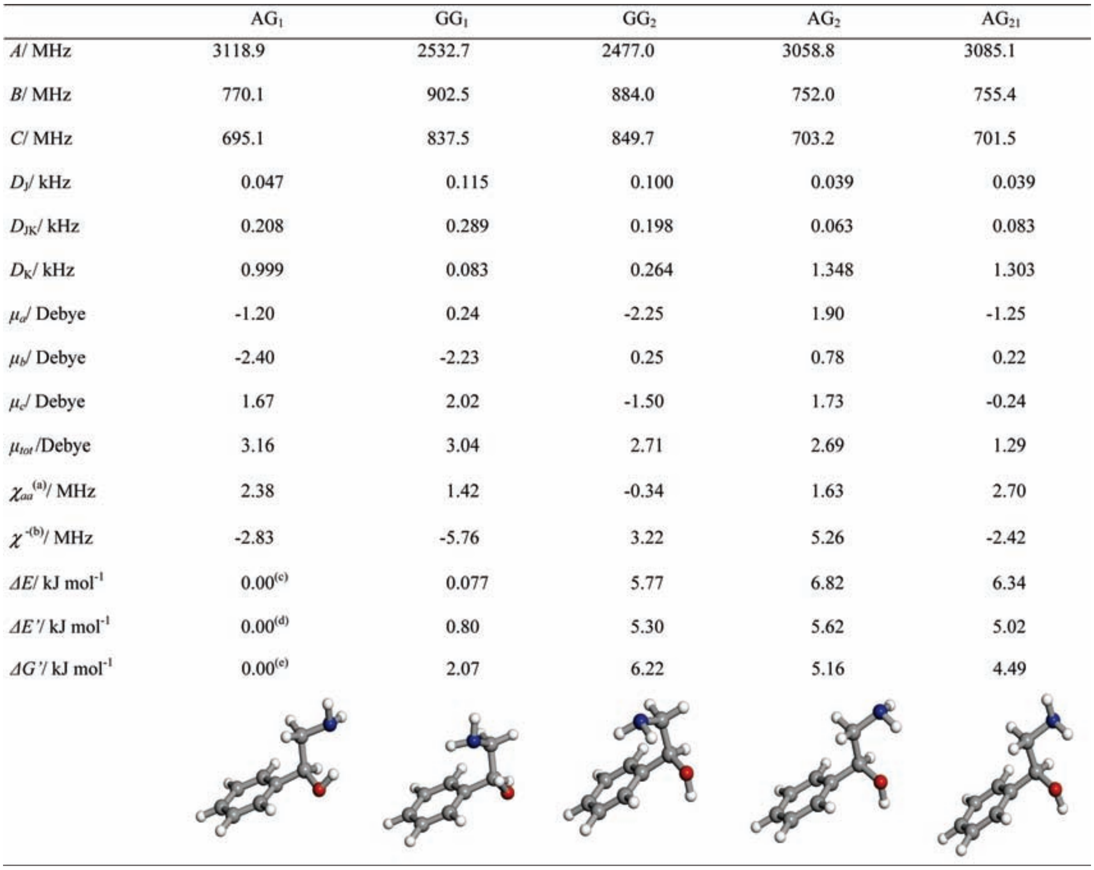
The relative intensities of the rotational transitions directly depend on the transition moment, the square of the dipole moment component involved, and the population fraction of the initial level; therefore, relative intensities measurements can be used to extract information on the orientation of the dipole moment within the molecular frame and on the conformer population.

When the degeneracy due to near-prolate behavior is lost (at lower K_a values), we see a multiplet of lines due to the separation of the μ_b and μ_c component transitions, which have different intensity. Such difference in intensity in the rotational transition of each conformer is mainly due to the different values of the μ_b and μ_c dipole moment components because all of the other factors that contribute to the intensity are very similar. The measurements performed on different sets of transitions that show μ_b and μ_c component lines give the ratio between the dipole moment components for the two different conformers, which are reported at the bottom of Table 2.

Comparing the experimental results of Table 2 and the ab initio results of Table 1, we can easily identify conformer I with AG_1 and conformer II with GG_1. The evidence comes, first of all, from the comparison of the rotational constants and the centrifugal distortion constants (quite different for the two conformers), which are in agreement by less than 1%. Second, considering the different ratios between the μ_b and μ_c dipole moment components for the two conformers (calculated $|\mu_b/\mu_c|_{AG1} = 1.44$ and $|\mu_b/\mu_c|_{GG1} = 1.10$), we again reach the same conclusion, and this represents an independent piece of evidence for the conformational assignment.

From intensities ratios, we can also estimate the population fraction between the two observed conformers. If we consider

TABLE 1: Ab Initio Spectroscopic Parameters of APE (MP2/6-311+G)**



	AG_1	GG_1	GG_2	AG_2	AG_{21}
A/ MHz	3118.9	2532.7	2477.0	3058.8	3085.1
B/ MHz	770.1	902.5	884.0	752.0	755.4
C/ MHz	695.1	837.5	849.7	703.2	701.5
D_J/ kHz	0.047	0.115	0.100	0.039	0.039
D_{JK}/ kHz	0.208	0.289	0.198	0.063	0.083
D_K/ kHz	0.999	0.083	0.264	1.348	1.303
μ_a/ Debye	-1.20	0.24	-2.25	1.90	-1.25
μ_b/ Debye	-2.40	-2.23	0.25	0.78	0.22
μ_c/ Debye	1.67	2.02	-1.50	1.73	-0.24
μ_{tot} /Debye	3.16	3.04	2.71	2.69	1.29
$\chi_{aa}^{(a)}$/ MHz	2.38	1.42	-0.34	1.63	2.70
$\chi^{-(b)}$/ MHz	-2.83	-5.76	3.22	5.26	-2.42
ΔE/ kJ mol^{-1}	0.00$^{(c)}$	0.077	5.77	6.82	6.34
$\Delta E'$/ kJ mol^{-1}	0.00$^{(d)}$	0.80	5.30	5.62	5.02
$\Delta G'$/ kJ mol^{-1}	0.00$^{(e)}$	2.07	6.22	5.16	4.49

[a] Electric quadrupole moment value $Q(^{14}N) = 0.0193(8)$ barns was used.[19] [b] $\chi^- = \chi_{bb} - \chi_{cc}$. [c] Relative electronic energy. Absolute energy: −440.286826 hartree. [d] Relative electronic energy including zero point correction. Absolute energy: −440.107087 hartree. [e] Relative free energy at 358 K, 0.247 atm. Absolute energy: −440.160313 hartree.

TABLE 2: Spectroscopic Constants of APE

	I (AG_1)	II (GG_1)
A/MHz	3131.822(6)[a]	2546.452(5)
B/MHz	773.951(8)	894.954(5)
C/MHz	688.753(8)	827.197(5)
D_J/kHz	0.043(4)	0.107(2)
D_{JK}/kHz	0.23(5)	0.258(7)
D_K/kHz	0.94(3)	0.17(1)
N[b]	65	67
σ/MHz[c]	0.08	0.07
N_{II}/N_I	0.4	
$\lvert\mu_b/\mu_c\rvert$	1.55(23)	1.00(65)

[a] Error in parentheses in units of the last digit. [b] Number of transitions in the fit. [c] Standard deviation of the fit.

rotational transitions originating from the two different conformers and normalize them by taking into consideration the different values of the dipole moment components, the rotational line strength, and the transition frequencies, then the values of the intensity depend only on the population of the initial level of the rotational transitions.[16] Taking into consideration 10 different transitions, we estimate the population ratio between conformer GG_1 and AG_1 in the jet expansion to be $N_{GG1}/N_{AG1} = 0.4$.

Previous studies have shown[17] that when a barrier between two different conformations is present, relaxation is prevented if He is used as the carrier gas; therefore, under these conditions, the population ratio measured in the expansion equals the one that is established at the stagnation temperature and should therefore depend on the relative energy of the conformers and on the temperature prior to the expansion.

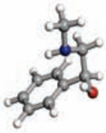
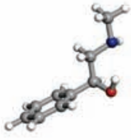
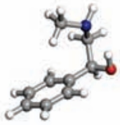
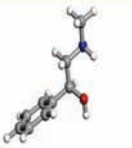
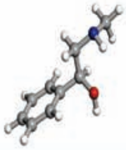
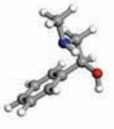
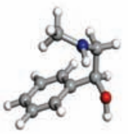
The measured conformational ratio between GG_1 and AG_1 is very close to the 1:3 measured in ref 11, but it is inconsistent with the population fraction that can be calculated from the electronic energy difference corrected for zero point vibrations, which is 0.76. The apparent inconsistency of the results is explained by Miller and Clary,[18] who, applying the torsional path integral Monte Carlo method, show that the population fraction of conformer GG_1 over AG_1 established at the temperature prior to the expansion is close to the observed one.

Using the data of Table 1, we show that the agreement between observed and calculated conformer fraction can be improved by considering the thermal Gibbs energies contribution predicted from the Gaussian 03 harmonic force field. The population ratio between GG_1 and AG_1 calculated from the theoretical relative Gibbs energies at the temperature and pressure prior to the expansion is 0.54, to be compared with the experimental value 0.42.

2-Methylamino-1-phenylethanol. The conformations of MAPE can be generated from the conformers of APE by replacing a hydrogen atom of the amino group with the methyl residue. Obviously, because there are now two different groups linked to the nitrogen atom, in some cases, we generate two different conformations from each of the ones of APE. In the work of Butz et al.,[12] seven geometries were optimized at the MP2/6-31G* level, and the four most stable configurations were then further optimized at a higher level of theory (MP2/6-311+G**).

We repeat the calculations at the higher level (MP2/6-311+G**) for all eight stable conformers to obtain the rotational spectroscopic parameters and a more accurate estimation of the

TABLE 3: Ab Initio Spectroscopic Parameters of MAPE (MP2/6-311+G)**

	GG_{1a}	AG_{1b}	AG_{1a}	GG_{1b}	AG_{2a}	AG_{2b}	GG_{2a}	GG_{2b}
A/ MHz	1855.8	2677.2	2544.9	1766.2	2495.5	2642.6	1887.4	1692.5
B/ MHz	684.3	577.6	544.1	803.0	535.6	572.4	673.8	828.4
C/ MHz	645.3	520.4	517.0	738.7	519.6	529.5	619.3	745.8
D_J/ kHz	0.120	0.023	0.032	0.149	0.028	0.023	0.132	0.119
D_{JK}/ kHz	-0.371	0.044	0.055	0.040	-0.122	-0.065	-0.698	0.202
D_K/ kHz	1.493	1.883	2.252	0.283	2.697	2.724	2.800	-0.066
μ_a/ Debye	0.24	1.68	-1.58	-0.50	1.22	1.49	0.36	2.43
μ_b/ Debye	-2.84	2.04	-2.46	2.85	0.03	0.76	0.41	-0.63
μ_c/ Debye	0.34	1.69	0.77	0.61	0.11	1.54	-0.44	0.54
μ_{tot}/ Debye	2.87	3.13	3.02	2.96	1.23	2.27	0.70	2.57
$\chi_{aa}^{(a)}$/ MHz	1.91	2.53	2.54	-0.51	-2.08	1.86	-2.45	-3.75
$\chi^{-(b)}$/ MHz	-1.84	-2.95	-6.31	-0.93	-1..38	6.06	-1.54	-0.74
ΔE/ kJ mol^{-1}	0.00$^{(c)}$	0.69	1.15	2.81	6.05	9.51	10.48	14.78
$\Delta E'$/ kJ mol^{-1}	0.00$^{(d)}$	0.02	0.26	2.85	3.75	7.65	8.43	13.26
$\Delta G'$/ kJ mol^{-1}	1.29	0.00$^{(e)}$	0.13	5.29	3.46	7.27	8.25	15.60
								

[a] Electric quadrupole moment value $Q(^{14}N) = 0.0193(8)$ barns was used.[19] [b] $\chi^- = \chi_{bb} - \chi_{cc}$. [c] Relative electronic energy. Absolute energy: −479.471818 hartree. [d] Relative electronic energy including zero point correction. Absolute energy: −479.263245 hartree. [e] Relative free energy at 358 K, 0.247 atm. Absolute energy: −479.312420 hartree.

relative energies, reporting the results in Table 3. Again as for APE, the lowest-lying group of conformers ($AG_{1a,b}$ and $GG_{1a,b}$) presents an interaction between the hydroxyl group and the nitrogen atom, whereas the higher energy group ($AG_{2a,b}$ and $GG_{2a,b}$) sees the amino group as the donor to the hydroxyl oxygen atom. The energy scale between conformers varies if we take into consideration the purely electronic energy, the zero point vibrational correction, or the thermal Gibbs energies at the temperature and pressure prior to the expansion. The folded gauche conformation that presents a secondary N−H → π interaction (GG_{1a}) has the lowest electronic energy, whereas the extended anti conformation (AG_{1b}) presents the lowest Gibbs energy contribution. Moreover, the conformer that is fourth in the relative electronic energy scale (GG_{1b}) becomes less stable when we consider the thermal contribution, whereas the AG_{2a} conformer's Gibbs energy is lowered to the point that this configuration is now the fourth in the energy scale.

On the basis of the predicted values of the rotational constants and dipole moment components, we expect to observe μ_b and μ_c R-type lines for at least the three lowest-energy conformers and eventually for the fourth.

The first spectrum was ran using Ar as carrier gas, and under these conditions, we observed two groups of μ_b and μ_c R-type lines named I and II. A second experiment was ran using He, and in this spectrum, we observed a third group of μ_b and μ_c R-type lines assigned to conformer III. Even after an extensive search, it was not possible to observe other lines that could have been assigned to a fourth conformer. No splitting due to internal rotation of the methyl group was observed, which is in agreement with a high barrier to the methyl group rotation. Indeed, for MAPE, the barrier to the internal rotation of the methyl group is very high: 3.1 kJ·mol^{-1} calculated at the MP2/6-311+G** level for the AG_{1b} conformer and probably very similar for the other conformers.

TABLE 4: Spectroscopic Parameters of MAPE

	II (AG_{1a})	I (AG_{1b})	III (GG_{1a})
A/MHz	2565.063(3)^a	2693.86(1)	1877.483(3)
B/MHz	546.230(3)	576.743(6)	674.904(7)
C/MHz	510.014(4)	517.505(6)	633.737(7)
D_J/kHz	0.0297(6)	0.024(2)	0.120(1)
D_{JK}/kHz	0.113(5)	0.050(7)	−0.371(4)
D_K/kHz	2.06(1)	1.96(3)	1.623(6)
N^b	104	70	76
σ/MHz^c	0.06	0.08	0.08

[a] Error in parentheses in units of the last digit. [b] Number of transitions in the fit. [c] Standard deviation of the fit.

All rotational transitions frequencies are given as Supporting Information, whereas the spectroscopic parameters of all three spectra fitted with Watson's semirigid Hamiltonian in the "S" reduction and I^r representation[15] are reported in Table 4.

The agreement between the observed and calculated rotational constants, centrifugal distortion constants, and the ratio of dipole moment components allow us to establish that the identification of conformers for MAPE is the following: AG_{1a} = (II), AG_{1b} = (I), and GG_{1a} = (III). The ratio between dipole moment components was determined only for conformer I, and this resulted to be $|\mu_b/\mu_c| = (1.1 \pm 0.1)$ compared with the theoretical value of 1.18 calculated for conformer AG_{1b}.

In the same way as we did for the APE molecule, we measured the intensity ratio between rotational transitions originating from different conformers, from which we estimate the ratio between conformational populations in the jet expansion using the calculated values of the dipole moment components.

The first observation is that when He is used as the carrier gas, we do not observe any lines originating from the GG_{1a} conformation, and second, the population fraction that can be calculated from the transitions intensities is very similar for all three conformers such that the measured differences are smaller than the estimated error on the measurements.

The relative energy picture that can be extrapolated from these observations is close to the one represented by the thermal Gibbs energy contributions calculated at the stagnation temperature and pressure. From these data reported in Table 3, we see that the GG_{1a} conformer is not the global minimum of the conformational space we can calculate the population fraction: ($N_X/N_{AG1b} = 1$, 0.95, and 0.64 for X = AG_{1b}, AG_{1a}, and GG_{1a}, respectively).

Given the overall intensity of the spectrum, the relative stability of the conformers, and the values of the dipole moment components, the observation of a fourth conformer is beyond the sensitivity of our instrument.

The presence of a fourth conformer was reported in ref 11, and it was assigned to GG_{1b}. On the basis of the data reported in Table 3, we believe that this assignment warrants reconsideration as the thermal energy contribution stabilizes the AG_{2a} conformer with respect to GG_{1b}.

Conclusions

We analyzed the pure rotational spectra of APE and MAPE recorded in the gas phase under the isolated condition of a supersonic expansion. These flexible molecules, which are analogues of noradrenaline and adrenaline, respectively, possess a rich conformational space, and we could observe two conformers for APE and three for MAPE.

The conformational assignment is initially based on the comparison of the experimental and calculated spectroscopic parameters (rotational and centrifugal distortion constants), which are better than 1% for values calculated at the MP2/6-311+G** level of theory.

An independent piece of evidence for the conformational assignment comes from the orientation of the electric molecular dipole moment that can be estimated experimentally from intensity measurements and compared with the ab initio values of the dipole moment components in the principal axis system.

All of the observed conformers present an intramolecular hydrogen bond between the hydroxyl hydrogen atom and the nitrogen atom, whereas the akylamino side chain is either in the extended (anti) or in the folded (gauche) arrangement.

The population fraction in the jet expansion that is estimated from relative intensity measurements is in agreement with the one calculated using the ab initio Gibbs thermal energies at the temperature and pressure prior to the expansion. On the basis of these observations, we believe that the assignment of the fourth conformer reported for MAPE in ref 12 should be reconsidered.

For both molecules the extended (anti) form is stabilized with respect to the folded (gauche) form, and the effect of the presence of the bulky methyl group, which is present in MAPE and not in APE, is the destabilization of the gauche conformer, where the methyl group is over the π cloud (GG_{1b}). This result is different from what was observed for the prototype molecule phenylethylamine[5,3c,d] or *p*-methoxyphenylethylamine,[7] where the gauche forms are by far the lowest in energy and are stabilized by a $N-H \rightarrow \pi$ interaction. In our case, the presence of the hydroxyl group in the alkylamino side chain leads to a different situation in which the extended form is more stable, meaning that the conformational preferences are a delicate balance between competing interactions.

Supporting Information Available: Rotational transition frequencies of conformer I of APE (1-amino-2-phenyl ethanol) and rotational transitions of conformer II of APE (1-amino,2-phenyl ethanol) and conformers I, II, and III of MAPE (2-methylamino-1-phenyl ethanol). This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Rhoades R. A. Brooks, P. *Human Physiology*, 4th ed.; Cole Publishing Company: Pacific Grove, CA, 2002.

(2) (a) Robertson, E. G.; Simons, J. P. *Phys. Chem. Chem. Phys.* **2001**, *3*, 1. (b) Zwier, T. S. *J. Phys. Chem. A* **2001**, *105*, 8827.

(3) (a) Melandri, S.; Maris, A. *Phys. Chem. Chem. Phys.* **2004**, *6*, 2863. (b) Caminati, W. *Phys. Chem. Chem. Phys.* **2004**, *6*, 2806. (c) Godfrey, P. D.; Hatherley, L. D.; Brown, R. D. *J. Am. Chem. Soc.* **1995**, *117*, 8204. (d) Lopez, J. C.; Cortijo, V.; Blanco, S.; Alonso, J. *Phys. Chem. Chem. Phys.* **2007**, *9*, 4521.

(4) Snyder, S. H. *Drugs and the Brain*; Scientific American Library: New York, 1999.

(5) (a) Martinez, S. J.; Alfano, J. C.; Levy, D. H. *J. Mol. Struct.* **1993**, *158*, 82. (b) Sun, S.; Bernstein, E. R. *J. Am. Chem. Soc.* **1996**, *118*, 5086. (c) Dickinson, J. A.; Hockridge, M. R.; Kroemer, R. T.; Robertson, E. G.; Simons, J. P.; McCombie, J.; Walker, M. *J. Am. Chem. Soc.* **1998**, *120*, 2622.

(6) (a) Vogelsanger, B.; Godfrey, P. D.; Brown, R. D. *J. Am. Chem. Soc.* **1991**, *113*, 7864. (b) Godfrey, P. D.; Brown, R. D. *J. Am. Chem. Soc.* **1998**, *120*, 10724.

(7) Yi, J. T.; Robertson, E. G.; Pratt, D. W. *Phys. Chem. Chem. Phys.* **2002**, *4*, 5244.

(8) (a) Carney, J. R.; Zwier, T. S. *J. Phys. Chem.* **2000**, *104*, 8677. (b) Dian, B. C.; Clarkson, J. R.; Zwier, T. S. *Science* **2004**, *303*, 1169.

(9) LeGreve, T. A.; Baquero, E. E.; Zwier, T. S. *J. Am. Chem. Soc.* **2007**, *129*, 4028–4038.

(10) Martinez, S. J.; Alfano, J. C.; Levy, D. H. *J. Mol. Struct.* **1993**, *158*, 82.

(11) Graham, R. J.; Kroemer, R. T.; Mons, M.; Robertson, E. G.; Snoek, L. C.; Simons, J. P. *J. Phys. Chem. A* **1999**, *103*, 9706.

(12) Butz, P.; Kroemer, R. T.; McLeod, N. A.; Robertson, E. G.; Simons, J. P. *J. Phys. Chem. A* **2001**, *105*, 1050.

(13) (a) Melandri, S.; Caminati, W.; Favero, L. B.; Millemaggi, A.; Favero, P. G. *J. Mol. Struct.* **1995**, *352/353*, 253. (b) Melandri, S.; Maccaferri, G.; Maris, A.; Millemaggi, A.; Caminati, W.; Favero, P. G. *Chem. Phys. Lett.* **1996**, *261*, 267.

(14) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C. Pople, J. A. *Gaussian 03*, revision B.01; Gaussian, Inc.: Pittsburgh, PA, 2003.

(15) Watson, J. K. G. In *Vibrational Spectra and Structure*, Durig, J. R., Ed.; Elsevier: New York, 1977; Vol. 6, pp 1−8.

(16) Gordy, W.; Cook, R. L. *Microwave Molecular Spectra*; Wiley: New York, 1984.

(17) Ruoff, R. S.; Klots, T. D.; Emilsson, T.; Gutowsky, H. S. *J. Chem. Phys.* **1990**, *93*, 3142.

(18) Miller, T. F.; Clary, D. C. *J. Phys. Chem. B* **2004**, *108*, 2484.

(19) (a) Winter, H.; Andrä, J. *Phys. Rev. A* **1980**, *21*, 581–587. (b) Raghavan, P. *At. Data Nucl. Data Tables* **1989**, *42*, 189–291.

JP902784H