A NOVEL CONFORMATIONAL ENERGY PREFERENCE IN 7-CHLORO-7-CARBOXAMIDO-6b,7,8,8a-TETRAHYDROCYCLOBUT[A]ACENAPHTHYLENE

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Abstract The title compound (*E*-1) exhibits a conformational energy preference in which the carbonyl oxygen lies over the aromatic ring. This preferred conformation is shown to exist in the solid state by X-ray analysis of the crystal structure and in the solution phase by COSY studies of the NMR spectrum. Related compounds show no conformational preference in solution at room temperature on the NMR time scale. The computational program MMX reproduces closely the geometry of the favored conformation of *E*-1 and verifies that it has a unique conformational energy minimum compared to other derivatives of this system.

We are studying the [2+2] cycloadducts of acenaphthylene and 2-chloroacrylonitrile as model systems for potential cycloadducts of cyclopentene-fused polycyclic aromatics.[1-5] We have synthesized by photochemical cycloaddition *E* and *Z* - 7-chloro-7-cyano-6b,7,8,8a-tetrahydrocyclobut[a]-acenaphthylene (**2**)[6] and produced from it both *E*- and *Z*-1 and *E* - and *Z*-7-chloro-7-carboxy-6b,7,8,8a-tetrahydrocyclobut[a]acenaphthylene(**3**).[7] The chemical shift assignments are based upon the 300 MHz NMR spectra.[8] A COSY study of *E*-1 was initiated because an analysis of the chemical shifts and coupling constants for it seemed incompatible with the data from related compounds. In Tables 1 and 2 the shift data and coupling constants are reported and Figures 1 and 2 illustrate the COSY data from *E*-1 and *E*-3. The cyclobutyl proton H_a resonating near δ= 4.7 ppm typically exhibits long range coupling with proton H_d near δ=3.0 and very weak coupling with H_c. The larger value of the coupling constant J_{ad} compared to J_{ac} suggests a more efficient coupling geometry similar to W-coupling while the constant J_{ac} reflects a poor geometry for coupling. In *E*-1 the COSY spectrum shows that H_a is more strongly coupled to the peak at δ= 2.9 than the proton at δ= 3.1. In the acid *E*-3 the spin coupling of H_a to H_c and H_d is reversed and this general pattern is found for other derivatives. The COSY data illustrate that the chemical shift of protons labeled H_c and H_d are inverted for *E*-1 when compared with other similar derivatives. The expected chemical shift of H_c relative to H_d in these compounds is to higher field because the adjacent aromatic nucleus generates a diamagnetic

anisotropic shielding component for H_C. The inversion in chemical shifts for structure E-1 requires that H_C experience on average a deshielding effect to counter the ring current contribution. This result requires that in solution a conformation in which the carbonyl group is on average close to proton H_C is favored. In Figure 3 the X-ray diagram of the crystal structure of E-1 clearly shows that H_C lies in a plane nearly parallel with the carbonyl group and the distance between carbonyl oxygen and H_C is found to be 251(4) pm.[9]
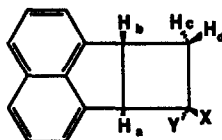

Table 1.   Proton Chemical Shifts for Cyclobutane Derivatives [a]

Compound			Chemical Shift (δ)				
	X	Y	H_a	H_b	H_c	H_d	$-NH_2$
Z-1	$CONH_2$	Cl	4.88	4.23	2.30	3.58	5.57,6.65
E-1	Cl	$CONH_2$	4.67	4.46	3.13	2.93	5.32,6.32
Z-2	CN	Cl	4.95	4.34	2.48	3.64	
E-2	Cl	CN	4.69	4.52	2.84	3.30	
Z-3	COOH	Cl	4.92	4.20	2.39	3.65	
E-3	Cl	COOH	4.67	4.45	2.90	3.02	

(a) Run as < 5% solutions in $CDCl_3$ with internal TMS at 25^0.
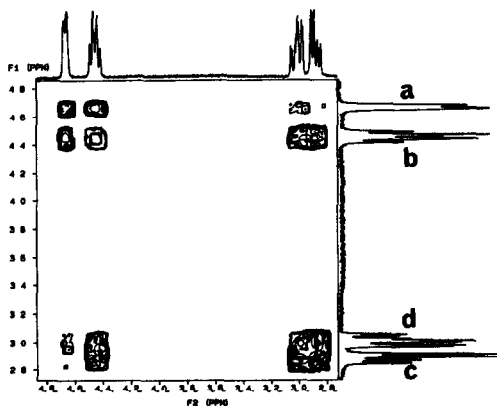

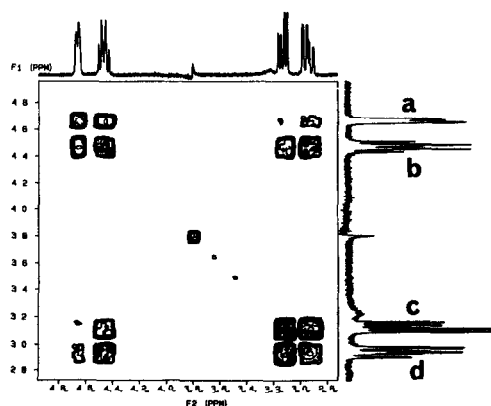Figure 1.   Figure 2.

Figure 1. Standard COSY spectrum of the cyclobutyl region between 2.8-4.8 ppm of 7-chloro-7-carboxyl-6b,7,8,8a-tetrahydrocyclobut[a]acenaphthylene in $CDCl_3$ at 25°:(a) 2D spectral width= 682 Hz (b) acquisition time=0.188 s (c) delay=1.0 s (d) pulse width=90° (e) pseudo-echo shaped (f) 64 repetitions x 64 increments.**Figure 2.** Standard COSY spectrum of the cyclobutyl region of 7-chloro-7-(aminocarbonyl)-6b,7,8,8a-tetrahydrocyclobut[a]acenaphthylene.

This orientation places H_C (on C11 in the X-ray ORTEP) in a position in which the anisotropic diamagnetic deshielding component of the carbonyl group counteracts the shielding effect of the adjacent aromatic ring. This result supports our interpretation of the NMR spectrum in solution.

We have calculated by the use of the molecular modeling program MMX [10] the conformational

Table 2. Coupling Constants (Hz) for Cyclobutane Derivatives

Compound	J_{ab}	J_{ac}	J_{ad}	J_{bc}	J_{bd}	J_{cd}
Z-1	5.29	1.17	2.42	5.98	8.89	13.02
E-1	6.59	1.26	2.64	6.50	9.45	13.82
Z-2	6.47	1.16	2.68	6.40	8.65	13.65
E-2	6.36	1.27	2.51	6.10	9.33	14.05
Z-3	6.26	1.20	2.63	6.18	8.81	13.52
E-3	6.51	1.15	2.59	6.66	9.26	14.09

energy minima of the derivatives listed in Table 3. A computation of the barrier height to rotation for E-1 produces an estimate of 10-12 kcal/mol[11] but this value does not explain why only one conformer is detected in the NMR experiment. The molecular mechanics calculation predicts that conformer **O** is favored by 4 kcal/mol over conformer **N**. To see if the steric effect of the chlorine atom is important we calculated the steric energy for the derivative with chlorine substituted by methyl
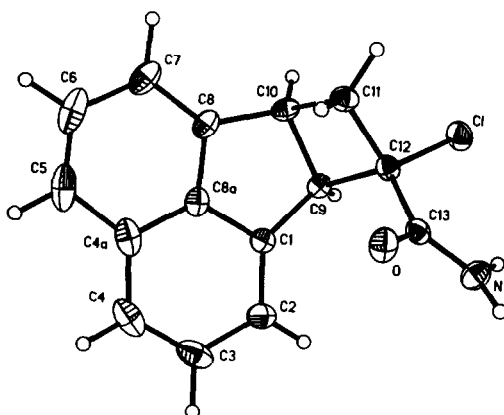

Figure 3. ORTEP drawing of the molecular structure of compound E-1. All non-hydrogen atoms are represented by thermal vibration ellipisoids to encompass 50% of the electron density. Hydrogen atoms are shown as arbitrary spheres of constant size.

whose van der Waals radius is larger than that of chlorine.[13] The calculated difference between

Table 3. Computed Strain Energies of Conformational Minima N and O by MMX

| Compound | Strain Energies (kcal/mol) | | Energy Difference |
R	N	O	between N and O
H	55.4	55.0	0.4
CH3	56.2	55.9	0.3
Cl	64.5	60.6	3.9
Cl(Acid)a	54.0	56.4	-2.4

(a) 7-chloro-7-carboxy-6b,7,8,8a-tetrahydrocyclobut[a]acenaphthylene

conformations **N** and **O** in this compound is less than 0.5 kcal/mol suggesting that the steric size of the chlorine substituent is not the major source of the conformational energy difference in *E-1* . The calculated energy for conformations **N** and **O** for *E-3* showed an interesting reversal in that the
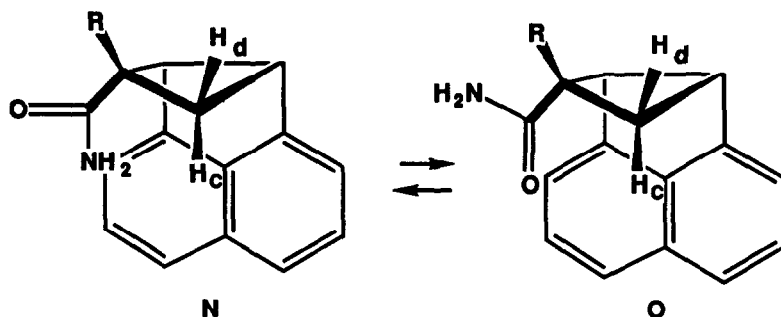
hydroxyl positioned over the ring is favored by an estimated 2 kcal/mol. Because the conformational energy difference between **N** and **O** for most of these derivatives is computed to be less than 1 kcal, the NMR spectra reflect the chemical shift data on a time average basis from all minimum energy populations. However, because of the 4 kcal/mol difference favoring conformation **O** in *E-1* , the NMR measurement reflects the chemical shift associated with that population which constitutes greater than 99% of the equilibrium conformations in solution. Similarly, conformation **O** is preferred in the crystalline state as well. The origin of the conformational preference is attributable to electronic effects which can be separated into three identifiable components; enhanced resonance, dipole, and hydrogen bonding. It is clear from the X-ray data and MMX calculations that the C=O bond dipole is oriented such that it minimizes its vector resultant with that of the C-Cl bond dipole at the α-carbon position. The amide resonance is also enhanced by the inductive effect of the chlorine substituent.

This tends to create a more rigid amide function and also enhances the negative charge of the C-O bond dipole. The β-hydrogen, H_c, located at a distance of 250 pm and an intramolecular angle of about 90° to the carbonyl group seems to fall outside of the statistical limit of 240 pm required for a significant intramolecular hydrogen bond between it and the carbonyl group.[14] Similarly, the existence of an intramolecular N-H······Cl hydrogen bond is questionable because this bond distance is also about 250 pm. The inductive effect of the neighboring electron withdrawing groups creates a weak C-H dipole on the β-carbon mutually supporting the position of the carbonyl dipole in its favored geometry.The NH_2 protons are separated into two distinct resonances for both E-1 and Z-1, supporting the assumption that the amide resonance is enhanced by the α-chloro inductive effect The chemical shift of the amide protons reflect their syn or anti geometry with respect to the naphthalene ring as confirmed by the X-ray data.Variable temperature NMR measurements on E-1 up to 85° have shown no significant change in its spectrum.[15] In Table 4 a comparison is made between the data derived from X-ray analysis and the values computed for selected bond angles and bond lengths in the chloroamide E-1. It is noteworthy that the cyclobutyl moiety in these strained bicyclo[3.2.0] compounds is non-planar as computed by the use of the MMX force field calculation and verified for E-1 by the X-ray crystallographic analysis. The close agreement between the predicted complex geometry of E-1 based upon the use of the MMX computation and that shown by the X-ray data reinforces confidence in the predictive power of molecular mechanics calculations for complex molecules which contain heteroatoms.

Table 4. Selected Bond Angles and Bond Distances for E-1 [a]

	Bond Angles(°)			Bond Lengths (pm)	
	Found	Computed		Found	Computed
C(1)-C(8A)-C(8)	113.0(2)	110.5	C(1)--C(2)	136.4(3)	138
C(8)-C(10)-C(11)	116.1(2)	114.1	C(8)-C(10)	149.7(3)	150
C(1)-C(9)-C(12)	118.1(1)	118.8	C(11)-C(12)	153.4(3)	155
C(10)-C(9)-C(12)	88.9(1)	89.5	C(1)-C(9)	150.6(3)	150
C(10)-C(11)-C(12)	90.3(2)	90.6	C(9)-C(10)	156.3(3)	158
C(9)-C(10)-C(11)	88.8(1)	88.9	C(10)-C(11)	155.7(3)	155
C(9)-C(12)-C(11)	89.5(1)	89.9	C(9)-C(12)	156.7(3)	155
C(11)-C(12)- Cl	109.7(1)	110.6			

(a) Computed values obtained by the MMX force field calculation; atom numbers are taken from the ORTEP diagram and standard deviations are listed in parentheses. X-ray data have been deposited as supplementary material.

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8. All new compounds produce correct elemental analyses and mass spectra consistent with their assigned structures. The syntheses and complete NMR analyses of all derivatives will be reported in a future article.

9. Monoclinic space group $P2_{1}/n$, a=9.523(1), b=9.633(1), c=13.128(1) Å, D_x=1.433 g cm^3. $M_oK_\alpha(\lambda$=0.71069 Å), R=0.0404 for 211 parameters and 1756 reflections.

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11. This estimate is subject to significant error because it was obtained by positioning arbitrarily the NH_2 group over the pi cloud by use of the dihedral driver routine in MMX. As is well known, such force field calculations are designed primarily to detect energy minima rather than energy maxima.[12]

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15. Future NMR experiments using high temperature solvents will be reported. It is possible that very low temperature spectra might detect the small fraction of conformers with the NH_2 group over the ring. But if the population of this conformer is really less than 0.1% as the calculation indicates we doubt that it can be detected in the NMR experiment.