Registry No. **1a**, 3352-93-0; **1b**, 103437-97-4; **1c**, 103437-98-5; **1d**, 38313-01-8; **2a**, 103438-00-2; **2b**, 103438-01-3; **2c**, 103438-02-4; **2d**, 103530-08-1; **3a**, 103530-05-8; **3b**, 103530-06-9; **3c**, 103530-07-0; **3d**, 53119-31-6; **4a**, 108393-08-4; **4b**, 108393-09-5; **4c**, 108393-10-8; **4d**, 53119-31-6; **5a**, 108345-18-2; **5b**, 108345-19-3; **5c**, 108345-20-6; **5d**, 56391-38-9; **6**, 56391-35-6; **7**, 56421-03-5; **8**, 56421-04-6; **9**, 56391-36-7; **10c**, 108345-22-8; **10c** (X^-=Br^-), 108345-23-9; **11c**, 108345-24-0; 3-bromocyclohexene, 1521-51-3; *trans*-3-bromo-7,2-epoxycyclohexane, 56421-06-8; *cis*-3-bromo-7,2-epoxycyclohexane, 56421-05-7.

Transannular Interactions in Difunctional Medium Rings. 2.[1] Molecular Structure and Conformational Properties of 1-Alkylhexahydroazocin-5-ones

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Conformational properties of 1-alkylhexahydroazocin-5-ones 1–4 with a methyl, ethyl, isopropyl, or *tert*-butyl group as a substituent have been studied by He I photoelectron, ^{13}C NMR, and IR spectroscopy as well as by MM2 and MNDO calculations. The molecular structure of the *tert*-butyl derivative 4 was determined by X-ray crystallography. Transannular interactions of the two functional groups in 1–4 have been determined from the first two ionization potentials with reference to the corresponding data of the respective monofunctional compounds. Since the $\Delta IP(n_O)$ values of 1–4 are nearly identical, these molecules must have rather similar conformations. $\delta_{^{13}C}$ values of the carbonyl group in 1–4 show a systematic variation with substituent size, but this is probably caused by different solvation. From the IR spectra of 1 and 4 in the solid and liquid state and in solution it is concluded that phase transition is not accompanied by conformational changes. The eight-membered ring in 1–4 has a boat–chair conformation with the functional groups occupying positions with the shortest possible transannular distance (approximately 270 pm). It has been found difficult to determine the most stable conformation by theoretical methods, since transannular amide resonance is not treated correctly. For this interaction an energy of approximately 12 kJ/mol is estimated for 4 by comparison of experimental and calculated molecular structures.

Introduction

Transannular interactions in difunctional medium-sized cyclic compounds can be studied by photoelectron spectroscopy.[1,2] As has been shown for cyclic amino ketones[1] and for aminoalkenes,[1,3] the interactions can be determined from the n and π ionization potentials by comparison with the respective data of the analogous monofunctional compounds. Since the size of transannular interaction (homoconjugation[2]) is determined by the intramolecular distance between the two functional groups, the PE data can be used for conformational analysis.

In order to achieve a quantitative basis for the relation between molecular structure and orbital interaction, we have investigated the hexahydroazocin-5-one system in detail by different methods. To establish that changes in spectroscopic findings caused by substituents are realized correctly, the N substituent was varied from methyl over ethyl and isopropyl to *tert*-butyl. The conformational properties have been studied by molecular mechanics (MM2)[4] and quantum theoretical (MNDO)[5] methods. In addition to PE spectroscopy, ^{13}C NMR and IR spectroscopic measurements were performed. The *tert*-butyl derivative, which is solid at ambient conditions, was analyzed by X-ray crystallography.

Results and Discussion

MM2 and MNDO Calculations. Conformational properties of eight-membered rings like cyclooctane and its derivatives have been studied extensively by various experimental[6] and theoretical methods.[7] Several conformations have to be considered. Besides the most symmetrical one, the crown, there are the boat–chair (BC), the chair–chair (CC), and the boat–boat (BB) forms and others. The most stable conformation of cyclooctane and simple derivatives is the BC form. In most cases the positions of the individual ring atoms are not equivalent.

Table I. Heats of Formation (kJ/mol) for Various Conformations of Cyclooctanone, 1-Methylhexahydroazocin-5-one (1), and 1-Methyloctahydroazocine (5) Calculated by the MM2 Method

conformatn	ketone	5	1
crown	−239.9	−43.4	−155.9 (−169.4[a])
(+ +)BB	−236.6	−51.6	−172.8 (−154.4[a])
(00)BB	−225.7	−36.0	−151.2
(+ +)BC	−246.7	−51.2	−171.3 (−163.9[a])
(+ −)BC	−239.8	−46.7	−162.7
(− +)BC	−235.9	−56.2	−169.5
(00)BC	−241.2	−46.4	−162.3

[a] MNDO value.

[†] Institute of Organic Chemistry.

[‡] Institute of Inorganic Chemistry.

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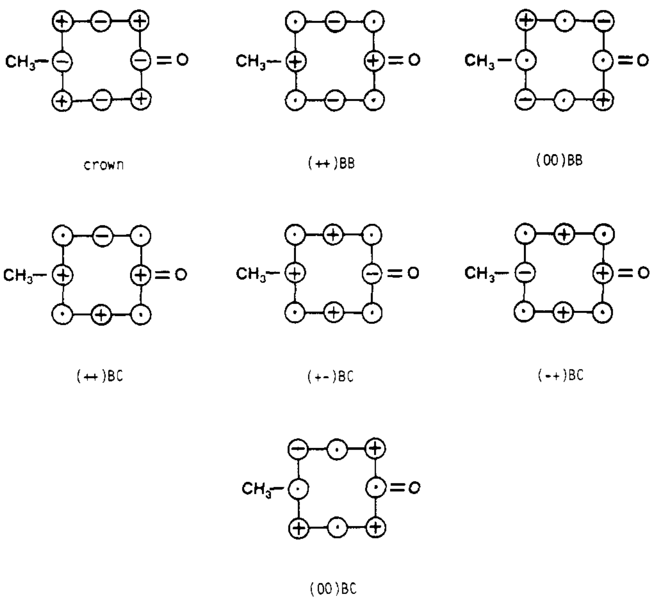

Figure 1. Graphic representation of possible conformations of 1-methylhexahydroazocin-5-one (1).

Therefore, additional conformations have to be taken into account for the molecules studied here. Moreover, twisted forms of the above-mentioned conformations might be more stable than the basic forms.

MM2 calculations were performed on 1-methylhexahydroazocin-5-one (1), cyclooctanone, and 1-methyloctahydroazocine (5) for the crown, four boat–chair, and two boat–boat conformations. The BC forms are distinguished as (++)BC, (+-)BC, (-+)BC, and (00)BC and the BB forms as (++)BB and (00)BB. Graphical representations of these conformations, following a proposal of Dunitz and Prelog,[8] are depicted in Figure 1. All structure parameters were refined without any symmetry restrictions. The minimum energy conformations have been reached from several starting points on the potential hypersurface. The calculated heats of formation, ΔH_f, are summarized in Table I.

The results for cyclooctanone and the amine **5** are in good agreement with other calculations and spectroscopic measurements.[9] The ring adopts the BC conformation. For the ketone a (++)BC and for the amine a (-+)BC form is found as the most stable conformer. For the amino ketone **1** three conformations are found to be rather close in energy: (++)BB, (++)BC and (-+)BC (see Figure 2). This result suggests that **1** forms an equilibrium of these three conformers. However, this is not in accord with spectroscopic findings. By NMR spectroscopy a BC form was found in aprotic solvents, but there is evidence that it may exist as a BB form in strong hydrogen-bonding solvents[10] (see also below). Since it is of prominent importance for our studies of transannular interactions[1] to determine the conformational properties of this compound with high reliability, also MNDO calculations have been executed. The obtained energies are included in Table I. Now the minimum corresponds to the crown conformer, which is 5.5 kJ/mol more stable than the (++)BC form.

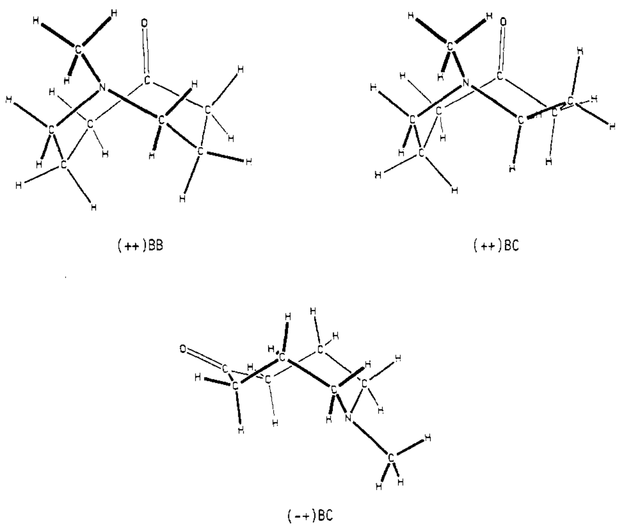

Figure 2. Most stable conformations of 1-methylhexahydroazocin-5-one (1) (MM2 results).

There is a further argument to estimate the conformations of this difunctional molecule. Ollis et al.,[11] on the basis of dynamic NMR data, estimated an upper limit of ca. 30 kJ/mol for the transannular attraction between an amino and a carbonyl group in an eight-membered ring. Compared with the standard energy of a N–C single bond, 292 kJ/mol,[12] this value corresponds to a virtual bond order of 0.10. This interaction obviously is more or less completely neglected by both theoretical methods. Since this attraction will favor a rather close contact of the two functional groups, a conformation with a short distance between the nitrogen and the carbonyl carbon atom allowing significant orbital overlap should result.

In fact, this distance varies appreciably in the above mentioned conformations (compare Figure 2). The greatest value (393 pm) is found in the crown, whereas the (++)BB (276 pm) and the (++)BC (286 pm) have rather small values. On this basis, the crown should be excluded as the most stable form, although it is favored by the MNDO method.

Additional MM2 calculations have been carried out for *N*-ethyl- (**2**), *N*-isopropyl- (**3**), and *N*-*tert*-butylhexahydroazocin-5-one (**4**). Here only the three most stable conformations found for the methyl compound have been considered. For these molecules the (++)BC conformation is found to be the most stable one. Structure parameters calculated for compound **4** are summarized in Table IV, together with the results of the X-ray analysis.

From the experimental (X-ray) and the MM2 structures of compound **4** a minimum estimate of the energy asso-

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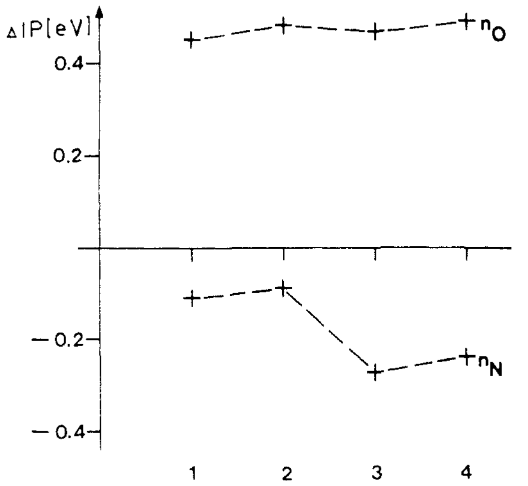

Figure 3. Shifts of IP_v values of amino ketones 1–4 relative to amines 5–8 and cyclooctanone.

Table II. Vertical Ionization Potentials (IP, eV) of Amino Ketones 1-4, Amines 5-8, and Cyclooctanone

compound	IP(n_N)	IP(n_O)
1-methylhexahydroazocin-5-one (**1**)	8.13	8.83
1-ethylhexahydroazocin-5-one (**2**)	8.02	8.80
1-isopropylhexahydroazocin-5-one (**3**)	7.96	8.81
1-*tert*-butylhexahydroazocin-5-one (**4**)	7.88	8.79
1-methyloctahydroazocine (**5**)	8.02	
1-ethyloctahydroazocine (**6**)	7.93	
1-isopropyloctahydroazocine (**7**)	7.69	
1-*tert*-butyloctahydroazocine (**8**)	7.64	
cyclooctanone		9.28

ciated with transannular amide resonance is possible: if all atoms, except hydrogens, are fixed at their experimental positions, an additional steric energy of 11.8 kJ/mol is calculated that has to be compensated by transannular attraction. This energy indicates a N···C bond order of 0.04.

PE Spectra. In part 1[1] of this series we have demonstrated that transannular interactions in amino ketones and aminoalkenes can be investigated by PE spectroscopy. Here we report on our results for the eight-membered amino ketones with different alkyl groups (Me, Et, *i*-Pr, *t*-Bu) on the nitrogen atom. The vertical ionization potentials of all investigated compounds are summarized in Table II.

In order to determine the interaction of the two functional groups in compounds 1–4 the n_N and n_O ionization potentials are compared with the respective values of the cyclic amines 5–8 and cyclooctanone. The ΔIP values, $\Delta IP(n_N) = IP_v(\text{amine}) - IP_v(\text{amino ketone})$ and $\Delta IP(n_O) = IP_v(\text{ketone}) - IP_v(\text{amino ketone})$, of compounds 1–4 are shown in Figure 3.

The data indicate nearly identical, comparatively large shifts (ca. 0.5 eV) of the n_O orbital for all these compounds. On the other hand, the n_N orbital is shifted only slightly in 1 and 2, whereas larger shifts are found in 3 and 4.

It has been pointed out that the IP (n_O) is a good indicator for transannular amide resonance[1] in a similar way as for resonance in amides and lactams.[13] Accordingly, the interaction between the two functional groups in 1–4 must be of similar size. This is an indication of equal conformations of these molecules. In contrast to this, the n_N orbital cannot be considered as a suitable measure of this interaction, because this orbital is largely affected by inductive effects[14] and by interaction with the π^*_{CO} MO.[1]

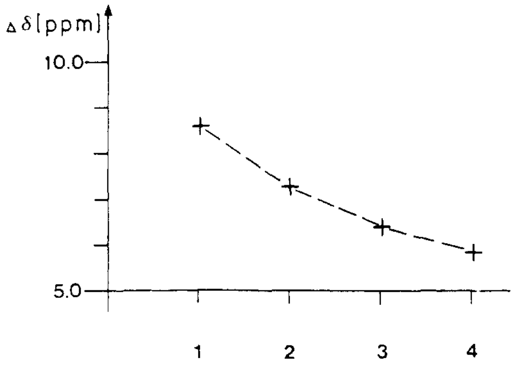

Figure 4. Shifts of the $\delta^{13}C$ values of amino ketones 1–4 relative to cyclooctanone.

Table III. ^{13}C NMR Values of the Carbonyl Group (δ) of Amino Ketones 1-4 and Cyclooctanone

1-methylhexahydroazocin-5-one (**1**)	206.4
1-ethylhexahydroazocin-5-one (**2**)	207.7
1-isopropylhexahydroazocin-5-one (**3**)	208.6
1-*tert*-butylhexahydroazocin-5-one (**4**)	209.2
cyclooctanone	215.0

Moreover, 1-alkyloctahydroazocines 5–8 have a (−+)BC conformation, while the amino ketones 1–4 prefer the (++)BC form. This conformational change on going from the amine to the amino ketone probably will also shift the n_N MO to a certain degree. Therefore, conformational analysis of this type of molecules has to rely on the n_O ionization.

^{13}C NMR Spectra. The sensitivity of ^{13}C NMR to transannular electron donation to carbonyl groups has been studied by Nakashima and Maciel[15] on 1-heteracyclooctan-5-ones. They concede that the observed effect of approximately 12 ppm in the case of 11-methyl-11-azabicyclo[5.3.1] undecan-4-one compared with cyclooctanone may partly be inductive, but the major part should be caused by transannular interaction.

At the same time Dahn et al.[16] have investigated the ^{17}O NMR spectra of eight- and nine-membered cyclic amino ketones. They found significant changes for the ^{17}O signal of the amino ketones relative to the corresponding ketones. Since the ^{17}O signal of the carbonyl group is only slightly affected by inductive interactions with other functional groups transannular orbital interaction must be present.

We have investigated the ^{13}C NMR spectra of amino ketones 1–4. The $\delta_{^{13}C}$ values of the carbonyl group for these compounds are collected in Table III.

Δδ values, defined as $\Delta\delta = \delta(\text{ketone}) - \delta(\text{amino ketone})$, are depicted in Figure 4. These data seem to indicate that transannular interaction in solution is decreasing with substituent size. This is in conflict with the PE results (see above). However, it has to be taken into account that spectra are measured of isolated molecules in the gas phase, while here solutions (30% in C_6D_6) are studied. It is well-known that chemical shifts are solvent dependent. For instance, benzene is able to stabilize electron-deficient regions of the molecules by solvation. The magnetic anisotropy of benzene will lead to an upfield or downfield shift of a certain signal depending on the spatial arrangement in the solvation complex. In the compounds

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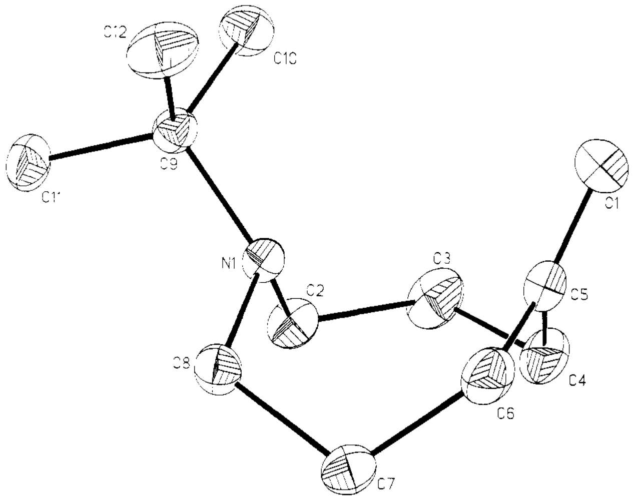

Figure 5. Molecular structure of 1-*tert*-butylhexahydroazocin-5-one (**4**) from X-ray structure analysis with thermal ellipsoids (50% probability level).

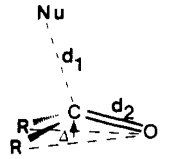

Figure 6. Approach direction of a nucleophile Nu to a carbonyl group.

Table IV. Selected Structure Parameters of 1-*tert*-Butylhexahydroazocin-5-one (4) from X-ray Analysis and MM2 and MNDO Calculations

	X-ray[a]	MM2	MNDO
	(a) Bond Distances (pm)		
O(1)–C(5)	122.5 (1)	121.1	122.6
N(1)–C(2)	147.0 (1)	147.5	148.0
N(1)–C(8)	146.2 (1)	147.2	148.1
N(1)–C(9)	148.6 (1)	148.9	150.1
C(2)–C(3)	153.1 (1)	154.0	155.3
C(3)–C(4)	153.4 (2)	153.6	153.7
C(4)–C(5)	151.6 (1)	152.0	153.6
C(5)–C(6)	151.2 (1)	152.1	152.9
C(6)–C(7)	153.2 (1)	153.7	153.9
C(7)–C(8)	152.6 (1)	154.2	155.0
	(b) Transannular Distances (pm)		
N(1)···C(5)	270.1 (1)	286.7	296.0
	(c) Bond Angles (deg)		
C(2)–N(1)–C(8)	111.8 (1)	111.0	113.3
N(1)–C(2)–C(3)	111.6 (1)	111.8	113.6
C(2)–C(3)–C(4)	112.1 (1)	114.4	116.7
C(3)–C(4)–C(5)	112.3 (1)	113.0	113.9
O(1)–C(5)–C(4)	120.3 (2)	120.3	121.2
O(1)–C(5)–C(6)	121.0 (1)	120.9	120.8
C(4)–C(5)–C(6)	118.3 (1)	118.8	117.9
C(5)–C(6)–C(7)	115.8 (1)	115.5	115.9
C(6)–C(7)–C(8)	111.4 (1)	113.7	119.6
N(1)–C(8)–C(7)	110.9 (1)	114.6	116.5
	(d) Torsional Angles (deg)		
C(8)–N(1)–C(2)–C(3)	−119.8 (2)	−116.9	−111.0
N(1)–C(2)–C(3)–C(4)	58.3 (2)	65.3	61.0
C(2)–C(3)–C(4)–C(5)	−62.0 (2)	−60.8	−60.7
C(3)–C(4)–C(5)–C(6)	106.6 (2)	103.4	105.2
C(4)–C(5)–C(6)–C(7)	−41.0 (2)	−46.5	−50.6
C(5)–C(6)–C(7)–C(8)	−66.1 (2)	−62.1	−53.9
C(6)–C(7)–C(8)–N(1)	49.1 (2)	54.4	47.3
C(7)–C(8)–N(1)–C(2)	−71.1 (2)	−60.1	−63.8

[a] Estimated standard deviations in parentheses.

studied here the solvation may be influenced by substituent size. Accordingly, we do not believe that the NMR data disprove the PE results with regard to equal conformations of **1**–**4**[17].

IR Spectra. It has often been found that conformational equilibria are dependent on the state of aggregation.[18] This phenomenon can be studied by vibrational spectroscopy, since different spectra are to be expected for the conformers. According to the low symmetry of the conformers of **1**–**4** all vibrations are infrared-active, but there should be differences in the frequencies of the carbonyl bands and some skeleton vibrations. Therefore, we have investigated the IR spectra (4000–400 cm^{-1}) of compounds **1** and **4** for the solid and liquid state as well as for 5% solutions in C_2Cl_4. The spectra of each compound show no significant deviations apart from small differences in band intensities on going from one state of aggregation to the other. Therefore, we conclude that phase transition is not accompanied by conformational changes for both compounds. Also a mixture of conformers is not likely to be present, otherwise one should expect considerable differences when comparing the spectra of the compounds in different phases.

X-ray Structure Analysis of 1-*tert*-Butylhexahydroazocin-5-one (4). Selected experimental structure parameters of the eight-membered ring of compound **4** are summarized in Table IV together with the respective calculated values. Full details of the structure analysis are given in the supplementary material. The numbering of the atoms is as shown in Figure 5.

The eight-membered ring adopts a (+ +)BC conformation. The oxygen atom is in a quasi-axial and the *tert*-butyl group in an equatorial position. This allows a rather close contact between the carbonyl and the amino group, the C···N distance d_1 being 270.1 pm (see Figure 6). This value is substantially smaller than the sum of the van der Waals radii of N and C (376.0 pm).[4] It is also clearly smaller than calculated by MM2 (286.7 pm) or MNDO (296.0 pm), an indication of attractive transannular interaction that is not reproduced correctly by the theoretical methods.

As has been expressed by the structure-correlation method of Dunitz and Bürgi,[19,20] intramolecular interactions can serve as models for intermolecular interactions. From the structures of several amino ketones they have analyzed the nucleophilic addition of amines to ketones. They found that the approach direction of the nucleophile is not perpendicular to the C=O bond but at an angle of about 105° and that the carbonyl group becomes pyramidal (Figure 6).

Our results for compound **4** are in good agreement with these findings: d_1 = 270.1 pm, d_2 = 122.5 pm, Δ = 48.7 pm, $\angle$N···C=O = 110.8°. Moreover, the distance d_1 can be correlated with the declination Δ. This correlation allows to determine the N···C bond order.[19] For **4** a value of 0.19 is obtained, which appears to be too large compared with the value calculated by comparison of experimental (X-ray) and MM2 structures, as well as the experimental findings of Ollis et al.[11] But one has to take into account that the calculated bond order of 0.04, as has been pointed out above, only represents a rough approximation. Moreover, it must be considered that Ollis et al.[11] have

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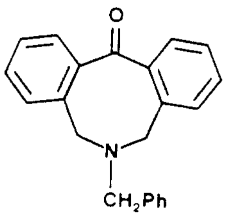
[17] C_6D_6 was used as solvent for experimental reasons. We will reinvestigate the ^{13}C NMR spectra using another solvent.

[18] Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw-Hill: New York, 1962.

[19] Bürgi, H. B.; Dunitz, J. D.; Sheffer, E. *J. Am. Chem. Soc.* **1973**, *95*, 5065.

[20] Bürgi, H. B.; Dunitz, J. D. *Acc. Chem. Res.* *1983*, *16*, 153.

investigated the transannular interaction for the dibenzo derivative **9** which is less flexible than the parent system and adopts the uncommon BB conformation.



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On the other hand, as is obvious from the data given in Table IV, there is fair agreement of the experimental structure parameters with the MM2 and MNDO results. Maximum deviations are less than 4 pm in bond lengths, 9° in bond angles, and 21° in torsional angles. MM2 results are generally a little closer to the experimental ones than the MNDO data. Average deviations for bond lengths are 0.9 (MM2) and 1.7 pm (MNDO), for bond angles 1.2° (MM2) and 1.6° (MNDO), and for torsional angles 4.5° (MM2) and 5.8° (MNDO).

Conclusion

Transannular interactions in 1-alkylhexahydroazocin-5-ones and similar compounds, extensively studied by Leonard et al. since 1954,[21,22] can be investigated by various experimental methods. In most cases these measurements are performed for solids, liquids, or solutions. Therefore, intermolecular interactions or interactions with the solvent may dominate possible intramolecular effects, whereas PE spectroscopy exclusively refers to isolated molecules in the gas phase, and only the properties of the pure substance are indicated. Furthermore, the electronic mechanism becomes more transparent than by other physical methods.

Theoretical methods like molecular mechanic (MM2) and semiempirical quantum mechanics (MNDO) fail to reproduce this type of interaction correctly. Therefore, it is difficult to analyze the conformational properties of such molecules by these methods. The MM2 method probably might be improved by including a special potential function for nonbonded N···CO interactions.

Experimental Section

MNDO calculations were run on an IBM 370 computer. For MM2 calculations an Olivetti M 24 personal computer was used.

The PE spectra have been recorded in the region of 6–21 eV by using a UPG 200 spectrometer of Leybold-Heraeus with He I excitation (21.21 eV). The calibration of the energy scale was performed with an Ar–Xe mixture. The accuracy of the measurements was ±0.02 eV for ionization potentials. NMR spectra were run on a Varian XL-200 spectrometer. ^1H spectra were recorded of 1% solutions in C_6D_6 with references to the solvent (C_6D_5H, 7.15 ppm). ^{13}C spectra were measured of 30% solutions in C_6D_6 with reference to the solvent. For IR spectra a Perkin-Elmer 397 was used and for mass spectra a Finnigan MAT312 (72 eV). Elemental analyses were carried out on a Heraeus EA301 C,H,N analyzer.

Compounds **1**–**4** have been obtained by the method of Leonard et al.[21] The amines **5**–**7** were synthesized by alkylation of heptamethylenimine. In the case of 1-*tert*-butyloctahydroazocine (**8**) this method was not successful;[23] this amine has been synthesized from the corresponding amino ketone by Huang–Minlon reduction.[21] Substances **3**,**4**,**7**, and **8** have been prepared—to our knowledge—for the first time. The purity of all compounds was checked by analytical GC.

1-Methylhexahydroazocin-5-one (1): mp 45 °C; IR (neat) ν 2800 ($N\text{-}CH_3$, $N\text{-}CH_2$), 1675 cm^{-1} ($C{=}O$); ^1H NMR (C_6D_6) δ 2.05–1.90 (m, 8 H, CH_2), 1.97 (s, 3 H, CH_3), 1.55–1.45 (m, 4 H, CH_2); ^{13}C NMR (C_6D_6) δ 206.4 (s), 54.7 (t), 43.5 (q), 40.7 (t), 28.4 (t); MS, *m/e* 141 (M^+).

1-Ethylhexahydroazocin-5-one (2): bp 225 °C (760 mm); IR (neat) ν 2810 ($N\text{-}CH_2$), 1680 cm^{-1} ($C{=}O$); ^1H NMR (C_6D_6) δ 2.25 (q, 2 H, CH_2), 2.10 (t, 4 H, CH_2), 1.99 (t, 4 H, CH_2), 1.65–1.50 (m, 4 H, CH_2), 0.79 (t, 3 H, CH_3); ^{13}C NMR (C_6D_6) δ 207.7 (s), 51.9 (t), 50.2 (t), 40.8 (t), 28.6 (t), 11.6 (q); MS, *m/e* 155 (M^+).

1-Isopropylhexahydroazocin-5-one (3): bp 246 °C (760 mm); IR (neat) ν 2810 ($N\text{-}CH_2$, $N\text{-}CH$), 1680 cm^{-1} ($C{=}O$); ^1H NMR (C_6D_6) δ 2.51 (sept, 1 H, CH), 2.06 (t, 4 H, CH_2) 1.96 (t, 4 H, CH_2), 1.60–1.45 (m, 4 H, CH_2), 0.76 (d, 6 H, CH_3); ^{13}C NMR (C_6D_6) δ 208.6 (s), 53.7 (d), 48.4 (t), 40.8 (t), 28.6 (t), 17.8 (q); MS, *m/e* 169 (M^+).

Anal. Calcd for $C_{10}H_{19}NO$: C, 70.96; H, 11.31; N, 8.27; Found: C, 70.62; H, 11.67, N, 7.92.

Picrate (from ethanol): mp 233 °C dec; IR (KBr) ν 3110 cm^{-1} (OH) [no carbonyl absorption].

Anal. Calcd for $C_{16}H_{22}N_4O_8$: C, 48.24; H, 5.57; N, 14.06. Found: C, 48.58; H, 5.33; N, 14.15.

1-*tert*-Butylhexahydroazocin-5-one (4): mp 41 °C; IR (neat) ν 2810 ($N\text{-}CH_2$); 1670 cm^{-1} ($C{=}O$); ^1H NMR (C_6D_6) δ 2.13 (t, 4 H, CH_2), 2.00 (t, 4 H, CH_2), 1.60–1.45 (m, 4 H, CH_2), 0.88 (s, 9 H, CH_3); ^{13}C NMR (C_6D_6) δ 209.2 (s), 55.0 (s), 47.8 (t), 40.5 (t), 29.1 (t), 26.3 (q); MS, *m/e* 183 (M^+).

Anal. Calcd for $C_{11}H_{21}NO$: C, 72.08; H, 11.55; N, 7.64. Found: C, 71.84; H, 11.67; N, 7.54.

Picrate (from ethanol): mp 164 °C dec; IR (KBr) ν 3150 cm^{-1} (OH) [no carbonyl absorption].

Anal. Calcd for $C_{17}H_{24}N_4O_8$: C, 49.51; H, 5.87; N, 13.59. Found: C, 49.89; H, 5.80; N, 13.37.

1-Methyloctahydroazocine (5). A solution of 5.00 g (44.2 mmol) of heptamethylenimine and 4.20 g (44.2 mmol) of methyl bromide in 50 mL of ethanol was heated under reflux with stirring for 3 h. K_2CO_3 (5 g) was added, and heating was continued for an additional 3 h. The solvent was evaporated under reduced pressure, and the residue was taken up in water. Ether extraction followed by drying and evaporation operations furnished a residue, which was purified by preparative GC [Chromosorb PNAW 60, 10% CW 20M + 2% KOH (column length 1.8 m, 150 °C): yield, 2.87 g (51.1%); IR (neat) ν 2780 cm^{-1} ($N\text{-}CH_2$, $N\text{-}CH_3$); ^1H NMR (C_6D_6) δ 2.35 (t, 4 H, CH_2), 2.22 (s, 3 H, CH_3), 1.70–1.40 (m, 10 H, CH_2); ^{13}C NMR (C_6D_6) δ 56.5 (t), 47.4 (q), 28.4 (t), 28.3 (t), 26.5 (t); MS, *m/e* 127 (M^+).

Picrate (from ethanol): mp 215 °C (lit.[24] mp 210 °C).

1-Ethyloctahydroazocine (6): IR (neat) ν 2800, 2760 cm^{-1} ($N\text{-}CH_2$); ^1H NMR (C_6D_6) δ 2.40 (t, 4 H, CH_2), 2.37 (q, 2 H, CH_2), 1.70–1.40 (m, 10 H, CH_2), 0.96 (t, 3 H, CH_3); ^{13}C NMR (C_6D_6) δ 54.1 (t), 53.3 (t), 29.0 (t), 28.2 (t), 26.6 (t), 13.8 (q); MS, *m/e* 141 (M^+).

Anal. Calcd for $C_9H_{19}N$: C, 76.53; H, 13.56; N, 9.92. Found: C, 76.21; H, 13.50; N, 9.79.

Picrate (from ethanol): mp 163 °C.

Anal. Calcd for $C_{15}H_{22}N_4O_7$: C, 48.65; H, 5.99; N, 15.13. Found: C, 48.77; H, 5.66; N, 15.13.

1-Isopropyloctahydroazocine (7): IR (neat) ν 2800 cm^{-1} ($N\text{-}CH_2$, $N\text{-}CH$); ^1H NMR (C_6D_6) δ 2.71 (sept, 1 H, CH), 2.40 (t, 4 H, CH_2), 1.80–1.40 (m, 10 H, CH_2), 0.90 (d, 6 H, CH_3); ^{13}C NMR (C_6D_6) δ 55.2 (d), 49.9 (t), 29.4 (t), 28.4 (t), 26.3 (t), 18.6 (q); MS, *m/e* 155 (M^+).

Anal. Calcd for $C_{10}H_{21}N$: C, 77.33; H, 13.65; N, 9.02. Found: C, 77.51; H, 13.75; N, 9.09.

Picrate (from ethanol): mp 141 °C.

Anal. Calcd for $C_{16}H_{24}N_4O_7$: C, 50.00; H, 6.29; N, 14.58. Found: C, 50.18; H, 6.54; N, 14.78.

1-*tert*-Butyloctahydroazocine (8). 1-*tert*-Butylhexahydroazocin-5-one (**4**) (2.00 g, 10.9 mmol) was reduced at 200 °C with an excess of N_2H_4 and KOH in triethylene glycol as solvent. Steam

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distillation followed by ether extraction, drying, and evaporation operations furnished a residue, which was purified by preparative GC [Chromosorb PNAW 60, 10% CW + 2% KOH (column length 1.8 m, 150 °C)]: yield, 1.06 g (57.4%); IR (neat) ν 2800 cm^{-1} (N–CH_2); ^1H NMR (C_6D_6) δ 2.44 (t, 4 H, CH_2), 1.80–1.40 (m, 10 H, CH_2), 0.97 (s, 9 H, CH_3); ^{13}C NMR (C_6D_6) δ 54.4 (s), 47.9 (t), 30.2 (t), 28.5 (t), 26.8 (q), 26.4 (t); MS, *m/e* 169 (M^+).

Anal. Calcd for $C_{11}H_{23}N$: C, 78.03; H, 13.69; N, 8.27. Found: C, 78.43; H, 13.67; N, 7.90.

Picrate (from ethanol): mp 159 °C.

Anal. Calcd for $C_{17}H_{26}N_4O_7$: C, 51.25; H, 6.58; N, 14.06. Found: C, 51.22; H, 6.56; N, 13.99.

X-ray Structure Analysis. Crystal Data: $C_{11}H_{21}NO$; $M = 183.29$; triclinic; $a = 5.966\ (3)$ Å, $b = 7.737\ (3)$ Å, $c = 12.492\ (5)$ Å; $\alpha = 101.83\ (3)°$, $\beta = 93.34\ (4)°$, $\gamma = 102.81\ (4)°$; $V = 547.14\ (4)$ $Å^3$ (at −155 °C, by least-squares refinement on diffractometer angles for 25 automatically centered reflections with $21° \leq 2\theta \leq 25°$, $\lambda = 0.71069$ Å); space group $P\bar{1}$ (No. 2); $Z = 2$; $D_x = 1.1129$ g cm^{-3}; crystal dimensions; 0.28 × 0.18 × 0.15 mm; μ(Mo Kα) = 0.65 cm^{-1}.

Data Collection and Processing: Syntex R3 four-circle diffractometer, ω scan mode, $2\theta_{max} = 70°$, ω scan speed 2.0–20.0° min^{-1}, graphite-monochromated Mo Kα radiation; $T = -155 \pm 0.5$ °C; 6091 reflections measured, merging to 4833 independent reflections ($R_{merg} = 0.024$), giving 3910 unique observed reflections, $F_o \geq 3.5\sigma(F)$.

Structure Analysis and Refinement. The coordinates of all non-hydrogen atoms were determined by direct methods and refined by using the SHELXTL program system[25] with the incorporated scattering factors on a NOVA 3/12 (Data General) computer. The positions of the hydrogen atoms were calculated on ideal geometry and refined as rigid groups (C–H distance, 96 pm; H–C–H angle, 109.5°). Their isotropic temperature factors were given the 1.2 fold of the U_{ij} tensor of the corresponding C atom. The refinement of 145 parameters converged to $R = 0.051$, $R_w = 0.057$, weighting scheme $w^{-1} = \sigma^2(F) + (8.3 \times 10^{-4})F^2$: residual maximum electron density 0.403 e/$Å^3$ between C(2) and C(3), residual minimum electron density 0.24 e/$Å^3$.

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Supplementary Material Available: Tables of atomic coordinates, thermal parameters, bond distances and angles, and anisotropic temperature factors and a figure showing the packing of the molecules (6 pages); observed and calculated structure factors (29 pages). Ordering information is given on any current masthead page.

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Experimental Evidence of Deviations from a Karplus-Like Relationship of Vicinal Carbon–Proton Coupling Constants in Some Conformationally Rigid Carbohydrate Derivatives

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The values of vicinal carbon–proton coupling constants for the conformationally rigid carbohydrate derivatives *N*-acetyl-3,4-di-*O*-acetyl-1,2-dideoxy-β-D-hexo(pento)pyranosyl[1,2-*d*]oxazolidin-2′-ones (**1–4**), 2,4-di-*O*-acetyl-1-acetamido-1-deoxy-1-*N*,3-*O*-carbonyl-α-L-arabinopyranose (**5**), and 2,3,4-tri-*O*-acetyl-1,6-anhydro-β-D-hexopyranoses (**6–12**) are reported. $^3J_{C,H}$ values were determined by the selective 2D heteronuclear *J*-resolved method proposed by Bax and Freeman. The values found were used as input parameters for simulating the coupled carbon spectra. From the final best values it may be concluded that both the number and relative orientation of substituents in a complex organic molecule may substantially modify the general shape of the existing Karplus-like relationship between $^3J_{C,H}$ and the corresponding dihedral angle. The crystal structures of *N*-acetyl-3,4-di-*O*-acetyl-1,2-dideoxy-β-D-gluco- and -xylopyranosyl[1,2-*d*]oxazolidin-2′-ones (**1** and **3**) and compound **5** have also been studied in order to determine the geometry of these molecules in the solid state.

Carbon–proton coupling constants are not yet routinely used in the conformational analysis of organic molecules due to experimental difficulties involved in their measurement by classical ^1H-coupled ^{13}C NMR spectroscopy and to the scarcity of reliable published data.[1] However, it has been shown that vicinal $^3J_{C,H}$ coupling constants are related to the torsion angle C–X–Y–H by a Karplus-like relationship[2] and, therefore, could give interesting conformational information in solution on molecules whose conformations cannot be investigated by ^1H NMR spectroscopy, such as those containing five-membered rings, peptides, oligosaccharides (conformation of the glycosidic bonds), etc. Theoretical studies have also demonstrated that there exists a general Karplus plot relating $^3J_{C,H}$ with torsion angle for propane[3] and substituted propanes,[4] al-

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