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Rotational Barrier for 1-Acetyl-2-(*p*-Methoxy Benzyl)-3-Pyrroline*

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Calculation of the rotational barriers for the *trans*- and *cis*-forms of 2-(*p*-methoxy)-1-acetyl-pyrroline are presented in this paper. It is found that the *trans*-isomer is slightly more favourable energetically, while the rotations of the *cis*-form are highly impeded. Hence the relevant rotations are in the *trans*-form which stabilizes its energy by forming a weak inner proton bond between the carbonyl oxygen and the pyrroline ring. The acetyl rotational barrier is of the order of 8 kcal, which is well in accord with experimental data reported in the literature for other acetyl-amide derivatives.

Key words: Rotational barrier – Substituted pyrrolines – PCILO calculation

1. Introduction

1-Acetyl-2-(*p*-methoxybenzyl)-3-pyrroline is one of the intermediate products obtained in the synthesis of anisomycine [1]. Among the properties used for its characterization, those of the NMR spectrum are very important. In the NMR spectrum there is evidence of the existence of two conformational rotamers [2]: two simple signals which arise from the methyl group of the acetyl in the nitrogen atom are observed in the region of 1.98 – 2.2 ppm. The separation between these two signals is dependent on the temperature, thus showing that the free rotation of the acetyl group is impeded. This raises the problem of finding a theoretical description of the rotational barrier.

Furthermore, this substituted N-acetyl-pyrroline presents two isomer forms stemming from the inversion through the N-atoms. These are depicted in Figs. 1a and 1b and we shall henceforth refer to them as the *cis*- and the *trans*-forms. The fact that amines are not in general active as concerns polarized light waves, is connected with such an inversion.

2. Method

The rotational barriers are found by means of the PCILO (Perturbative Configuration Interaction using Localized Orbitals) method of Diner, Malrieu *et al.* [3 – 6]. PCILO is particularly adequate for conformational analysis and,

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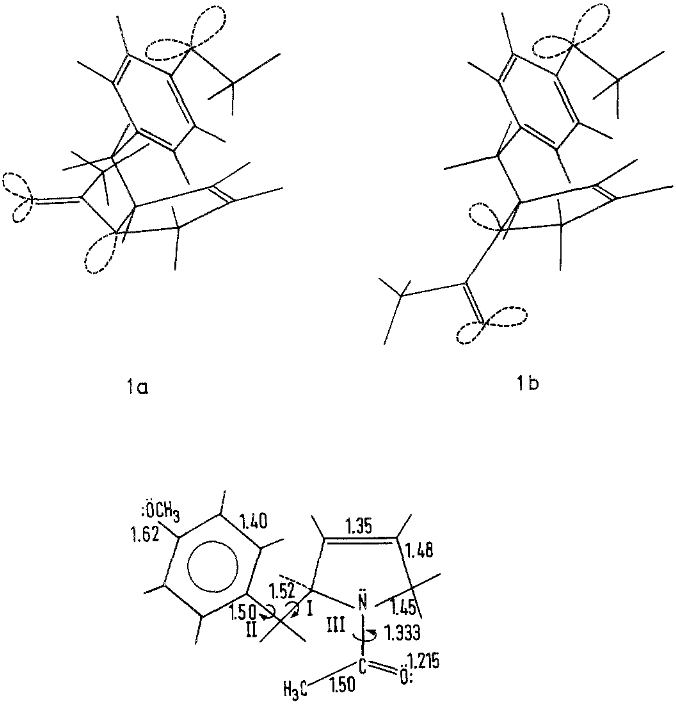

1c

Fig. 1. Structures of N-acetyl-2-(*p*-methoxibenzyl)-3-pyrroline showing a) *cis*-form, b) *trans*-form and the rotation axes. Dimensions in Å

furthermore, it is adapted to perform succesive rotations of different groups around bonds conveniently selected as the rotation axis.

The use of PCILO is particularly adequate for obtaining the ground state molecular properties. As Sinanoğlu [7, 8] has shown, the use of localized molecular orbitals can lead to a substantial improvement of the results.

Interatomic distances and bond angles were taken mostly from the literature [9] although a few, in particular in the pyrroline ring, were obtained in this work. These geometrical parameters are reported in Fig. 1c. As concern the benzene ring, the energy difference between the two Kekulé structures was calculated as 0.6 kcal. For the zero order function the one of lower energy was chosen. To calculate the rotational barriers, we proceeded first to perform a 30° by 30° rotation of the anisyl group around axis I of Fig. 1c, keeping the acetyl group static until a minimum value of third order perturbation energy was reached for the system. After completing this step we proceeded to rotate the benzene ring around axis II (Fig. 1c) until the energy was again minimized.

Then the rotation of the acetyl group by 15° increments was carried out. The axis was axis III of Fig. 1c and the starting position was as in Fig. 1a. This was done both for the *cis*- and *trans*-isomers.

3. Results and Discussion

The zeroth, second and third order perturbed energies for each of the positions of the acetyl group in both isomers are presented in Tables 1 and 2.

Cis-form. The energy versus rotation angle I has been plotted in Fig. 2. For the following discussion of the rotational barriers only the third-order perturbation energy will be used.

An enormous barrier (445 kcal/mol), which comes mostly from the excessive nuclear repulsion generated by the close approach of the methyl of the acetyl group to the benzylic protons, is immediately observed (position a) in Fig. 2. There is another barrier of magnitude 35 kcal/mol depicted in position b, Fig. 2, which stems from the approximation of the carbonylic oxygen to the benzyl group. These barriers are also conditioned by the interactions of both rotating groups with the pyrrolinic ring protons, of course.

This leads to the following conclusion: In the *cis*-configuration, the acetyl group cannot rotate freely because the methyl group cannot overcome the huge barriers; at best the carbonyl oxygen could flip between the two minima of Fig. 2. However, since the barrier for the *cis-trans* transition is only 2.5 kcal/mol, it seems far more likely that the molecule will go over to the *trans* configuration before any rotation of the acetyl group takes place.

Table 1. Energy (in kcal/mole) as a function of rotation angle I for the *cis*-form

Angle	Nuclear repul. energy	Localized total energy	2nd order total energy	3d order total energy
0°	393 270.70[a]	–100 187.80[a]	–101 424.89[a]	–101 245.48[a]
345°	394 746.90	–100 052.74	–101 297.36	–101 110.69
350°	396 032.88	–100 052.10	–101 318.40	–101 123.29
315°	397 072.37	– 99 970.01	–101 256.67	–101 054.33
300°	397 639.12	– 99 809.36	–101 083.26	–100 877.70
285°	397 223.92	– 99 949.97	–101 234.10	101 031.05
270°	396 287.52	–100 045.61	–101 312.09	–101 115.75
255°	395 114.28	–100 041.87	–101 281.36	–101 093.12
240°	393 755.61	–100 165.66	–101 398.46	–101 217.34
225°	392 676.24	–100 261.43	–101 486.47	–101 310.08
210°	392 089.50	–100 277.26	–101 498.70	–101 325.84
195°	391 919.41	–100 277.09	–101 498.08	–101 327.82
180°	392 086.70	–100 273.07	–101 496.24	–101 326.90
165°	392 493.94	–100 262.52	–101 489.93	–101 319.14
150°	392 978.42	–100 248.36	–101 478.68	–101 305.45
135°	393 333.26	–100 238.77	–101 471.45	–101 296.76
120°	393 392.09	–100 236.40	–101 470.92	–101 296.04
105°	393 095.33	–100 241.30	–101 470.04	–101 296.82
90°	392 519.16	–100 254.83	–101 476.57	–101 306.24
75°	391 861.10	–100 271.85	–101 487.50	–101 321.01
60°	391 353.87	–100 283.38	–101 493.60	–101 329.65
45°	391 169.89	–100 287.59	–101 497.95	–101 333.02
30°	391 402.84	–100 285.53	–101 501.77	–101 333.00
15°	392 096.59	–100 268.50	–101 494.10	–101 320.29

[a] kcal.

Table 2. Energy (in kcal/mole) for the *trans*-isomer

Angle	Nuclear repul. energy	Localized total energy	2nd order total energy	3d order total energy
0°	386267.71[a]	-100290.17[a]	-101499.12[a]	-101335.58[a]
15°	385786.78	-100292.01	-101497.73	-101335.43
30°	385339.43	-100293.73	-101495.28	-101334.67
45°	384998.07	-100294.93	-101493.03	-101333.88
60°	384809.02	-100295.35	-101492.20	-101333.60
75°	384781.39	-100294.98	-101493.23	-101334.07
90°	384887.76	-100293.85	-101495.58	-101335.01
105°	385073.95	-100292.19	-101497.99	-101335.83
120°	385277.29	-100290.31	-101499.14	-101335.90
135°	385447.82	-100287.63	-101497.91	-101334.32
150°	385555.69	-100284.19	-101494.93	-101331.45
165°	385590.94	-100283.13	-101493.85	-101330.50
180°	385577.06	-100283.86	-101493.96	-101330.54
195°	385557.69	-100284.18	-101492.51	-101328.82
210°	385572.18	-100286.38	-101492.31	-101328.19
225°	385663.47	-100290.79	-101494.68	-101330.06
240°	385870.73	-100292.86	-101496.04	-101331.05
255°	386189.52	-100290.82	-101494.93	-101329.86
270°	386559.02	-100286.73	-101493.01	-101328.10
285°	386888.41	-100284.82	-101493.49	-101328.84
300°	387103.75	-100284.43	—101494.80	-101330.37
315°	387156.51[a]	-100283.67	-101494.68	-101330.39
330°	387018.28	-100284.71	-101495.81	-101331.58
345°	386702.85	-100287.78	-101498.39	-101334.28

[a] kcal.

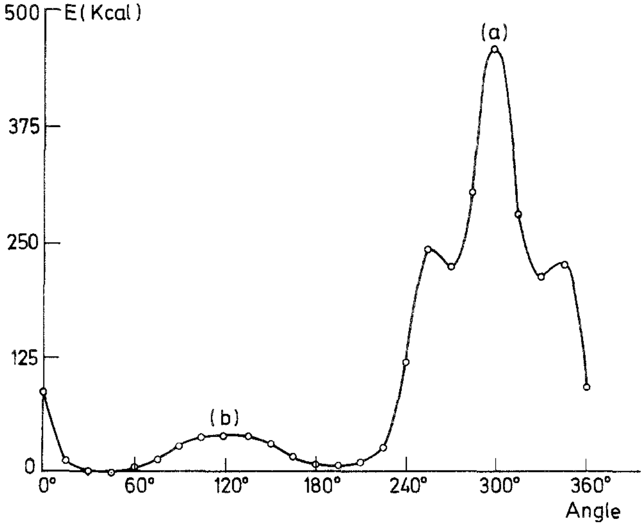

Fig. 2. Rotational energy barrier for the acetyl rotation in the *cis*-isomeric form. Only the third order energy of table I is plotted against the angle of rotation

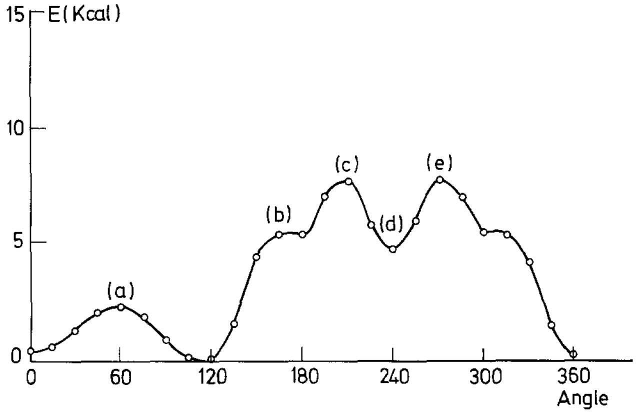

Fig. 3. Same as preceding figure, but for the *trans*-isomer. For the discussion of the characteristic points of these curves singled out with small letters see text

Trans-isomer. The acetyl rotation for the form denominated *trans* (see Fig. 1b) is presented in Fig. 3.

The sense of the rotation was sinistrorsum, taking as starting position that where the nitrogen, the non-substituted α-carbon, its *cis*-hydrogen with respect to the acetyl, the latter's carbon and oxygen are all in the same plane. This configuration turns out to be a minimum for the energy.

Starting from this configuration, as the rotation proceeds, the energy mounts until it reaches a maximum of 2.3 kcal/mol when the acetyl has rotated 60° around the N–CO bond (see position (a) in Fig. 3).

It is to be noted that position (a) is near a minimum as concerns *nuclear repulsion* (see Table 2), because the methyl is farthest from the pyrroline ring and the oxygen itself is conveniently far from its neighbours. However, the starting plane contains a hydrogen of the α-carbon, allylic with respect to the double bond of the pyrroline ring, at a postition and distance (1.88 Å) that are suitable for a hydrogen bond thus lowering the energy. The breaking of this inner proton bond is responsible for the increase that leads to the maximum at (a) which, moreover, corresponds to a position where the electron-rich regions of the pyrrolinic double bond and the oxygen are nearest. The value of this barrier, which is symmetric between 0° and 120°, is 2.3 kcal/mol, a typical value for a weak hydrogen bond.

As the rotation is continued, another barrier of about 7.7 kcal/mol is found which corresponds to the methyl groups interaction with the pyrrolinic proton. The following characteristic points are observed.

Position (b) (Fig. 3) corresponds to the nearest distance between one of the methyl protons and the pyrrolinic proton. Then at position (c) the pyrrolinic proton interacts simultaneously with the three methyl protons since it is equally close to all of them. In position (d), the methyl protons have passed beyond such an interaction. And lastly (e) corresponds to the repulsion of a methyl proton with both a pyrroline and a benzyl proton.

From the results a rotational enthalpy of the order of 8 kcal/mol is obtained. In Ref. [1] the rotational ΔG has been estimated to be 18 kcal/mol at 85° C.

As far we know, no experimental value for ΔH has been reported in the literature for this particular compound. However, many ΔH values or different acetylamides and related derivatives have been obtained experimentally by several authors [10 – 12]. Most of the values range from 6 or 7 kcal up to about 10 or 12 kcal [10 – 11], although larger values (as large as 19 kcal) exist [12]. We thenceforth consider the PCILO results reported here to be reasonable first estimation of the pyrroline barriers. Further calculations are being planned.

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