Theoretical study of the structure of 2-acyl- and 2-methoxycarbonylcycloalkanones

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The most preferred tautomers of 2-formyl-, 2-acetyl-, and 2-methoxycarbonylcyclopentanones, as well as -cyclohexanones, were calculated by means of the quantum chemical CNDO/2 method using a gradient optimization. Whereas in 2-formyl-, 2-acetyl-, and 2-methoxycarbonylcyclopentanones the keto-exoenol tautomer, stabilized by hydrogen bond, is energetically most advantageous, in 2-formyl- and 2-acetylcyclohexanones delocalization of electrons occurs due to strong hydrogen bond leading thus to a planar, quasi-aromatic, six-membered system. Not so extensive is delocalization in 2-methoxycarbonylcyclohexanone where the resultant optimum structure most approaches to the keto-endoenol tautomer. The results obtained are in agreement with the known experimental findings.

Методом градиентовой оптимализации в рамках CNDO/2 были рассчитаны наиболее выгодные таутомеры 2-формил-, 2-ацетил- и 2-метоксикарбонилциклопентанона и -циклогексанона. В то время как у 2-формил-, 2-ацетил- и 2-метоксикарбонилциклопентанона энергетически наиболее выгодным является кето-экзоенол таутомер, стабилизированный водородной связью, у 2-формил- и 2-ацетилциклогексанона вследствие прочной водородной связи происходит делокализация электронов с образованием плоской квазиароматической шестиатомной системы. У 2-метоксикарбонилциклогексанона делокализация не столь значительна и результирующая оптимальная структура ближе всего кето-эндоенол таутомеру. Полученные результаты согласуются с доступными экспериментальными данными.

Based on numerous experimental as well as theoretical studies, the existence of several tautomeric forms is supposed in β-dicarbonyl compounds. Under favourable electron and also structural conditions, the system becomes stabilized *via* intramolecular hydrogen bond, which is mainly in acyclic derivatives associated with formation of a stable, quasi-aromatic, delocalized system. 2-Acylcycloalkanones, representing a transition case between cyclic and acyclic β-dicarbonyl compounds, can be presumed to exist in the following four forms (Scheme 1):
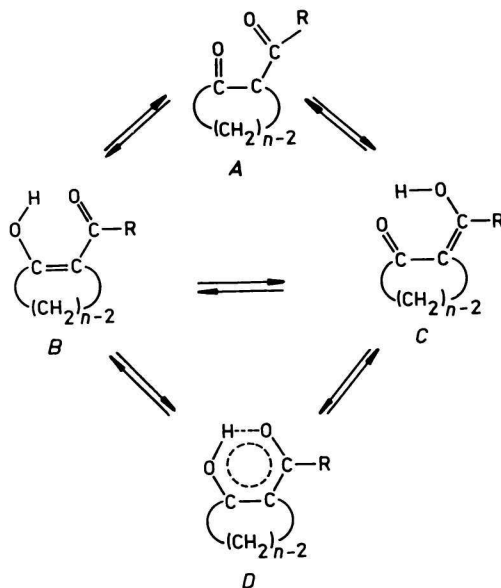
Scheme 1

diketo form A, keto-endoenol form B, keto-exoenol form C, and a delocalized form D. The populations of individual tautomers are determined by chemical structure of the compound, that is by the substituent R and the size of the ring n. On the basis of ^{1}H-n.m.r. data [1] a fast equilibrium between the forms B and C is assumed, the position of which is controlled by the size of the ring n. For $n = 5$ it is believed that the content of keto-exoenol form is 78 %. With increasing n the contribution of this form decreases (*e.g.* for $n = 10$ the content is 18 %). An anomalous percentage (24 %) occurs for $n = 6$. Similar conclusions follow from ^{17}O-n.m.r. measurements [2] showing, for example, 70 % of the form C for $n = 5$, R = CH$_3$ and 30 % of the form C for $n = 6$. The occurrence of the delocalized form D has been studied using ^{13}C-n.m.r. spectroscopy by *Barna* [3] who found in six-membered rings ($n = 6$) formation of a delocalized, though not perfectly symmetric, form D. In cases of R being an alkoxy group, experimental data show for $n = 5$ preference of diketo form A, whereas for $n = 6$ the enol form prevails [4].

The aim of this study was to examine theoretically the structure of 2-acylcycloalkanones depending on the ring size ($n = 5, 6$) and the nature of the substituent R (R = H, CH$_3$, OCH$_3$).

Method of calculation

For the purpose of this study we chose the quantum chemical semiempirical method CNDO/2 [5—7]. With respect to a possible existence of several tautomer forms (Scheme 1) we applied optimization of geometric parameters by the gradient method [8, 9]. The input geometry for the optimization process was obtained from experimental data of structurally similar compounds [10]. We started from the structures A, B, and C (Scheme 1) and the result of optimization procedure was the minimum energy structure. In case of diketo form A we took into consideration both axial and equatorial positions of acyl or methoxycarbonyl groups. In the forms B and C there occurs an intramolecular hydrogen bridge. Rotating the bridge hydrogen atoms by 180° round the C—O bond, the theoretical structures without hydrogen bridge can be obtained; such forms were also submitted to optimization. The difference in energy between the corresponding structures with and without hydrogen bonding represents stabilization energy, *i.e.* the sum of hydrogen-bond energy and delocalization energy. The relative total energy is represented by CNDO/2 calculated energy with regard to the most stable, optimized tautomer form of the respective compound.

Results and discussion

Using a gradient optimization of the above-mentioned compounds we found the forms stabilized by a hydrogen bridge to be energetically preferred, which is in agreement with the known experimental data. In each of the cases considered, the diketo form A is of higher energy than the most stable enol form. In the diketo

Table 1

The calculated values of relative total and stabilization energies of the tautomers under study

Tautomer		R	Relative total energy	Stabilization energy
			kJ mol⁻¹	kJ mol⁻¹
IB	5	H	19.6	30.99
IC	5	H	0	71.80
IIB	6	H	45.1	53.51
IIC	6	H	0	47.86
IIIB	5	CH₃	48.9	38.90
IIIC	5	CH₃	0	68.93
IVB	6	CH₃	31.6	73.31
IVC	6	CH₃	0	98.90
VB	5	OCH₃	29.6	50.50
VC	5	OCH₃	0	32.73
VIB	6	OCH₃	41.1	84.90
VIC	6	OCH₃	0	43.61

form *A*, there are possible two conformers having R in axial or equatorial positions. The more stable is the axial conformer, in which a lesser steric interaction occurs between the ring carbonyl oxygen and the substituent R. In the next, we shall consider only the enol forms *B* and *C*. The calculated values of relative total and stabilization energies for optimized forms are presented in Table 1. Designation *B* and *C* refers to the starting enol forms according to Scheme 1. The values of optimized geometric parameters for each individual form are given in Fig. 1. A theoretical index, which characterizes the strength of chemical bond, is represented by a Wiberg's bonding index [11]. The calculated values for these indices are given in parentheses in Fig. 1. At first glance it is evident that optimum forms differ from the starting geometries represented by structural formulas in Fig. 1.
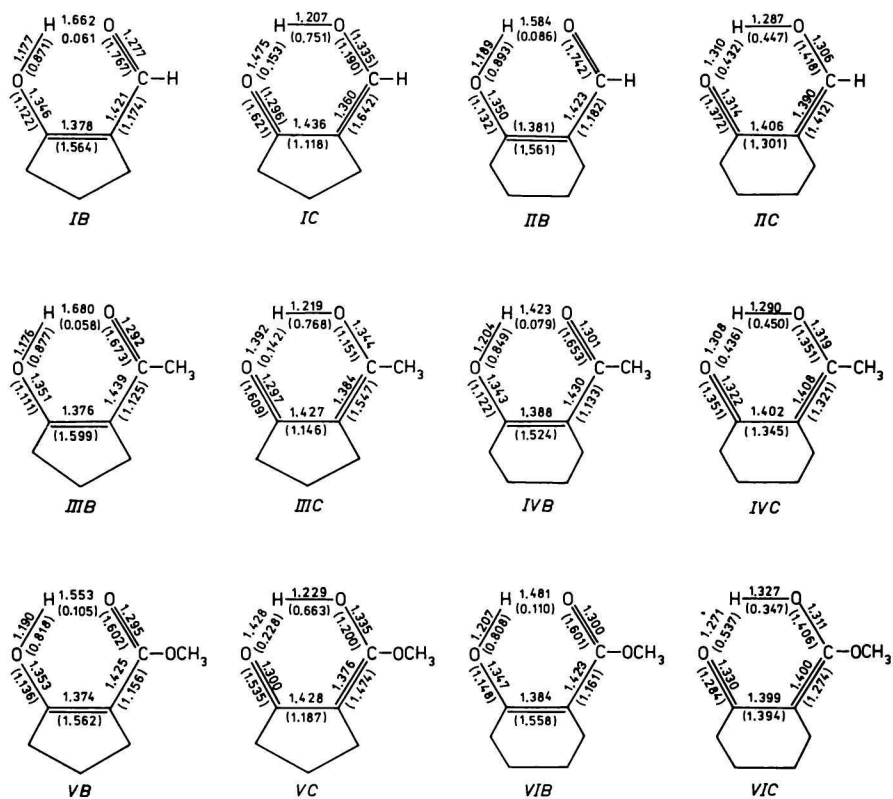

Fig. 1. The calculated values of optimum bond length and Wiberg's bonding index.

Cyclopentane derivatives ($n = 5$)

In 2-acylcyclopentanones, according to our calculations, the exoenol tautomer C is energetically the most advantageous. Its values of bond length and Wiberg's index (Fig. 1) indicate only a partial delocalization of electrons. The major contribution to stabilization of the structure C infers from the intramolecular hydrogen bond, as suggest the values of Wiberg's index between the carbonyl oxygen and enol hydrogen atoms as well as the relatively high values of stabilization energy (Table 1). The endoenol form B embodies the relative energetical minimum, however as regards the value of relative total energy, this form is less stable than the tautomer C. Geometric data as well as the values of Wiberg's index indicate the presence of a weaker hydrogen bond. Also the stabilization energy is lower than that of the tautomer C.

According to our calculations, keto-exoenol form VC is favorized also in 2-methoxycarbonylcyclopentanone. Accessible experimental data [4] report the diketo form A to be the most stable in analogous 2-ethoxycarbonylcyclopentanone. As calculated herein, energy of the axial 2-methoxycarbonylcyclopentanone is higher by 24.2 kJ mol^{-1} than that of the tautomer VC. It should be noted that whereas CNDO/2 calculations refer to an isolated molecule in gaseous state, the experimental measurements were performed in condensed phase with involvement of a solvent which can introduce also some other types of interactions.

Cyclohexane derivatives ($n = 6$)

The case of cyclohexane derivatives is considerably different. Of the lowest energy is again the conformer C, but the resulting geometry does not correspond at all to the starting exoenol form, represented by structural formulas IIC, IVC, and VIC. There occurs a strong delocalization and the C—O bonds are almost equivalent, similarly as are the C—C bonds. The system is stabilized by a strong hydrogen bond; in derivatives IIC and IVC the hydrogen atom is located almost symmetrically between the both oxygen atoms. Rather closer to reality is the structure D in Scheme 1. On the other hand, in ester VIC the endoenol tautomer suits best to the calculated optimum geometry. The existence of a strong hydrogen bridge is confirmed also by relatively high values of Wiberg's bonding index for O...H.

Starting from the endoenol tautomer B, we obtained by optimization a resulting structure representing the relative energetical minimum. The tautomer B is less stable in all three cases (IIB, IVB, and VIB). Also a partial delocalization of the system takes place, but it is less pronounced than in the foregoing case. Also the hydrogen bridge is weaker. The resulting structure represents the endoenol form B.

The preferred form of 2-methoxycarbonylcyclohexanone best corresponds to keto-endoenol structure, it means that the delocalization is not so extensive as in the analogous 2-acylcyclohexanones. The enol form was predicted also from experimental measurements [4, 12].

Conclusion

2-Formyl- and 2-acetylcycloalkanones exist predominantly in enol forms. Whereas in cyclopentane derivatives an exoenol tautomer with localized bonds is operative, in analogous cyclohexane derivatives the delocalized form is energetically most stable. The latter forms a planar, quasi-aromatic system as a result of a strong, almost symmetrical hydrogen bond. These conclusions are consistent with, or complementary to the so far known experimental findings. The existence of a delocalized form might explain also an anomalous amount of keto-exoenol form C found in 2-acylcyclohexanones [1] with the aid of ^{1}H-n.m.r. spectroscopy.

The enol forms, according to calculations, are preferred also in 2-methoxycarbonylcycloalkanones. The localized keto-exoenol tautomer is the preferred form in 2-methoxycarbonylcyclopentanone. In case of 2-methoxycarbonylcyclohexanone delocalization is more pronounced, but does not reach the level characteristic of analogous 2-acylcyclohexanones; consequently, the resulting structure best corresponds to the keto-endoenol form.

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