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Studies on Enol Titration. III. Enol Contents of Cycloalkanones

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The enol contents of the cycloalkanones from C-4 to C-10 are reported. It is found that the enol contents alternate with the ring size, that cyclic ketones are generally more enolic than comparable open-chain ketones, and that cyclooctanone is especially rich in enol. Attempted explanations of these findings are presented.

In the preceding paper of this series[1] the enol contents of a number of simple open-chain ketones were reported, and it was observed that these enol contents alternate with the chain length, demonstrating a tendency for an even number of carbon atoms to occur between the terminal methyl group of an alkyl chain and a double bond, the latter being either the C=O group of the ketone or the C=C group of the enol. It was also noted that other workers[2] had found similar alternation in the series of 2-carbethoxyalkanones, and a hypothesis was offered according to which second-order hyperconjugation is responsible for this phenomenon in both cases.

Presently available data on the enol contents of simple cyclic ketones are restricted to cyclopentanone and cyclohexanone, and while here, too, cyclohexanone contains more enol than does cyclopentanone, two ketones are of course not enough to establish a trend. To fill this gap, the enol contents of the cyclic ketones from cyclobutanone to cyclodecanone were determined and are reported in Table I. This table also includes published data[1] on the enol contents of open-chain ketones with the same number of C atoms as the cycloalkanones, the latter being emphasized by italics.

Three important points may be observed in the enol contents assembled in Table I. First, the alternation which had been noted in the open-chain ketones and in the 2-carbethoxycycloalkanones is present also in the simple cycloalkanones: a cyclic ketone with an even number of carbon atoms in the ring contains more enol than either its next higher or its next lower homolog. In analogy to what was said[1] about the alternation in open-chain ketones, the same phenomenon in cyclic ketones may be described by the statement that some factor favors a situation in which both ends of a chain of an even number of carbon atoms are attached to a double bond. This situation is obviously realized only by the keto form in an odd-carbon ring, and by the enol form in an even-carbon ring. No factor other than second-order hyperconjugation is known to the author which would call for such a situation, therefore, until some better interpretation is forthcoming, second-order hyperconjugation seems to provide the most satisfactory explanation of the observed alternation of enol contents, as it also does in other similar cases.[3]

A second observation which clearly emerges from Table I is that the cycloalkanones uniformly contain more enol than do the corresponding open-chain ketones. Some effect appears to be at work in ring ketones which, compared to open-chain ketones, either favors the enol or opposes the ketone, or both. Conceivably, this effect could have to do with entropy. A double bond places a restraint on its vicinity because it forces all atoms directly attached to it into the same plane. From the point of view of the carbon chain, this restraint is greater in an enol than in its ketone because the ketonic double bond makes only three carbon atoms coplanar and the enolic double bond four. Thus one would expect the entropy factor to operate against the enol in all ketones. But open-chain ketones have more unrestrained mobility to lose than ring ketones which are restricted to a cyclic arrangement to begin with, and so the latter may be expected to oppose less resistance to enolization.

That the easier enolization of rings is more pronounced in larger than in smaller rings, as can be seen from the figures in Table I, is in harmony with this reasoning. The tendency toward puckering of rings opposes coplanarity, and this opposition should be strongest in small rings where the coplanar group of four carbon atoms in the enol makes up either the entire ring, as in cyclobutanone, or most of it as in cyclopentanone. In the latter compound, the half-chair form[4] is excluded in the enol and only the planar and envelope forms are possible, while in cyclohexanone the enol permits the half-chair form. Therefore, in cyclohexanone and in higher ketones there should be less opposition to enolization than in cyclobutanone and in cyclopentanone, and the results are in agreement with this expectation.

Finally, it seems that some eight-carbon ketones occupy a special position with respect to enolization. The enol content of cyclooctanone is, com-

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[1] A. Gero, *J. Org. Chem.*, **19**, 1960 (1954).

[2] G. Schwarzenbach, M. Zimmermann, and V. Prelog, *Helv. Chim. Acta*, **34**, 1954 (1951).

[3] M. J. S. Dewar, *The Electronic Theory of Organic Chemistry*, Clarendon Press, Oxford, 1949, p. 157 ff.

[4] F. V. Brutcher, Jr., T. Roberts, S. J. Barr, and N. Pearson, *J. Am. Chem. Soc.*, **81**, 4915 (1959).

TABLE I

ENOL CONTENTS OF KETONES WITH FOUR TO TEN CARBON ATOMS[a]

Number of C Atoms	Ketone	Enol Content, %
4	2-Butanone	0.12
4	*Cyclobutanone*	*0.55*
5	2-Pentanone	0.01
5	3-Pentanone	0.07
5	*Cyclopentanone*	*0.09*
6	2-Hexanone	0.11
6	3-Hexanone	0.05
6	4-Methyl-2-pentanone	0.27
6	*Cyclohexanone*	*1.18*
7	2-Heptanone	0.10
7	3-Heptanone	0.17
7	*Cycloheptanone*	*0.56*
8	2-Octanone	0.92
8	3-Octanone	0.01
8	*Cyclooctanone*	*9.3*
9	*Cyclononanone*	*4.0*
10	*Cyclodecanone*	*6.1*

[a] All enol contents are rounded off to the nearest 0.01%. The values for cyclopentanone, cyclohexanone, and the open-chain ketones are taken from an earlier paper.[1]

paratively speaking, truly enormous: this simple ketone is more highly enolic than ethyl acetoacetate. In addition, 2-octanone also contains almost 1% enol—the highest enol content this writer has found in any simple open-chain ketone. Possibly these observations can be interpreted on conformational grounds: Inspection of high-precision atom models[5] shows that while all cycloalkanones from cyclohexanone up are free of Baeyer strain, steric factors of a more subtle nature may still play a role. In particular, a model of the enol of cyclooctanone demonstrates that, except for the coplanar group, all C and H atoms are more or less in skew position and one H at C-5 is close enough to the enolic double bond to represent something like a transannular π complex (Fig. 1):

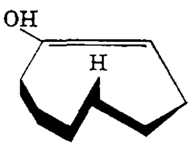

Figure 1

Such a fortunate situation does not exist in cyclodecanone where similar approach of a hydrogen to the double bond can be purchased only at the cost of excessive crowding of hydrogens elsewhere; and in the enol of cyclononanone, which is even better suited for a strain-free transannular π complex than that of cyclooctanone, second-order hyperconjugation works against the enol. Only in cyclooctanone does a high enol content seem to be favored by a unique combination of thermodynamic, steric, and electronic factors.

Models also offer an explanation of the high enol content of 2-octanone: that part of the chain from C-3 to C-8 can assume a conformation very much like that of the chair form of cyclohexane, with C-8 so placed that it can form a hydrogen bond with C-3 which is negative by the resonance of the enol group (Fig. 2):

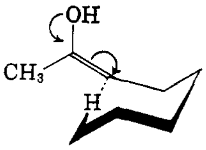

Figure 2

EXPERIMENTAL

The author is endebted to Dr. Alfred Bader of the Aldrich Chemical Company for providing him with some of the ketones used in this investigation. Cyclobutanone was prepared by oxidation of methylenecyclobutane,[6] cycloheptanone and cyclooctanone by ring enlargement from cyclohexanone with diazomethane,[7] and cyclononanone and cyclodecanone by ring closure from esters of the C-10 and C-11 dicarboxylic acids. All ketones were at least 98 % pure which, in view of the limitations of the method,[1] was considered more than sufficient.

The determination of enol contents was carried out as described in detail in the preceding paper of this series; therefore, no more will be said about it here except to emphasize once more the importance of the proper *p*H in the titration of the iodine with thiosulfate. Reproducible results can be obtained only when the *p*H of the titration mixture is just below 7, preferably 6.7 to 6.9. Use of the proper amount of bicarbonate is therefore essential. As the solvent in which the titration was carried out is 75 % methanol, it was difficult to measure the *p*H potentiometrically, but short-range *p*H paper (the author used Hydrion paper covering the *p*H range from 6.0 to 8.0) was satisfactory.

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(5) A. Gero, *J. Med. Pharm. Chem.*, **1**, 391 (1959).

(6) J. D. Roberts and C. W. Sauer, *J. Am. Chem. Soc.*, **71**, 3925 (1949).

(7) E. Mosettig and A. Burger, *J. Am. Chem. Soc.*, **52**, 3456 (1930).