

## A Calculation of the Equilibria in Keto-Enol Tautomerism

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A calculation of the equilibria obtaining in some simple cases of keto-enol tautomerism has been carried through with the aid of bond and resonance energies derived from

empirical data. The results obtained are in qualitative and semi-quantitative agreement with experiment.

THE energy of a molecule which can be represented by a single Lewis electronic structure is given with considerable accuracy by the sum of the energies of the various bonds which it contains. On the other hand, the energy of a molecule which can be represented adequately only in terms of two or more structures is, as a result of resonance, greater than would be predicted for even the stablest of them, on the basis of bond energies alone. The amount of this extra energy has been calculated from empirical data by Pauling and Sherman<sup>1</sup> for a number of cases, and has been shown to be fairly constant for a given type of resonance. We can, consequently, calculate the energy of an arbitrary molecule if we know the energy of each of its bonds and in addition the contribution made by any resonating systems that may be present.<sup>2</sup> Unfortunately, however, we do not have sufficient accurate data of this kind to proceed very far except in a few simple cases, and so we must usually resort to rough estimates and content ourselves with general results of a more or less qualitative nature. The purpose of the present paper is to apply this type of treatment to the problem of keto-enol tautomerism. The results obtained are quite satisfactory qualitatively and semi-quantitatively, and are of such nature as to lead one to expect that a more rigorous treatment

would give complete agreement with experiment. Since, however, this will have to wait until more powerful methods than are now available have been developed, it seems of interest in the meantime to carry the rougher and more qualitative methods as far as possible.

The calculations are simplified to a certain extent by the fact that the entropy change in the reaction keto→enol is apparently very small.<sup>3</sup> We can consequently neglect it entirely and put  $\Delta H = \Delta F$ . This is convenient since it makes possible a direct comparison between the values of  $\Delta H$  given by the calculation and the values of  $\Delta F$  derived from experimental data. In only a few cases are experimental  $\Delta H$  values known.

### SIMPLE KETO-ENOL SYSTEM



In the keto grouping I there is no possibility of resonance, and so the energy is simply the sum of the bond energies. This amounts to 357.2 Cal. if the C=O group is aldehydic, and to 360.6 Cal. if it is ketonic. In the enol grouping II, resonance between the two structures



is possible, but presumably the second structure does not make a very large contribution and the resonance energy is small. That some resonance does occur, however, is made probable by the

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<sup>1</sup> L. Pauling and J. Sherman, *J. Chem. Phys.* **1**, 606 (1933). All bond and resonance energies given without reference will be taken from this paper.

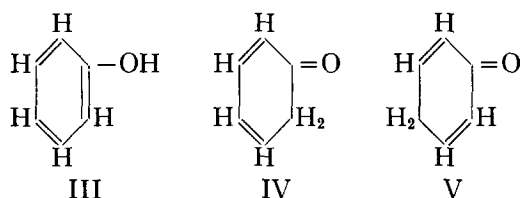
<sup>2</sup> This is rather an over-simplification since it leaves out of account the energy resulting from interaction between the dipoles in the molecule. This effect is usually small, and so we shall neglect it in the following discussion, except in a few cases where it becomes of special importance.

<sup>3</sup> J. B. Conant and A. F. Thompson, Jr., *J. Am. Chem. Soc.* **54**, 4039 (1932). Most of the data regarding the equilibria with  $\beta$ -diketones and  $\beta$ -ketonic esters are taken from this paper.

fact that the enols are considerably stronger acids than the alcohols. The bond energy for the enol grouping is 339.9 Cal. if the energy of the C—O bond is the same as for primary alcohols. Actually it is probably somewhat higher since an enol bears a rather closer resemblance to a secondary or tertiary than to a primary alcohol. The total energy of the enol grouping is then slightly greater than 339.9 Cal.—probably about 346.8 Cal. since in phenol similar effects raise the energy by 6.9 Cal. Thus ketones should be approximately 14 Cal. and aldehydes 10 Cal. more stable than the corresponding enols. This is in qualitative agreement with experiment; since the enols of this type are too unstable ever to have been isolated, a quantitative comparison cannot be made.

#### PHENOL

One enolic and two ketonic forms are possible.



(In the structure III the benzene ring is written, for the sake of convenience, as if it possessed the simple Kekulé form. Actually, of course, it resonates among several structures, of which this is only one.<sup>4</sup>) As far as the keto and enol groupings are concerned, the two keto forms IV and V should be more stable than the enol III by 14 Cal. The resonance energy remains to be considered, however. For the enol form this amounts to 39 Cal. (resonance within the benzene ring), and for the two keto forms to considerably less, probably between 13 and 19 Cal. The reason for this is as follows. The resonance energy of the system C=C—C=C can be calculated by the method described by Pauling and Wheland, and is found to be approximately 8 Cal. The resonance energy of the system C=C—C=O is probably a little less than 10 Cal.<sup>5</sup>—that is to say, practically the same as for C=C—C=C.

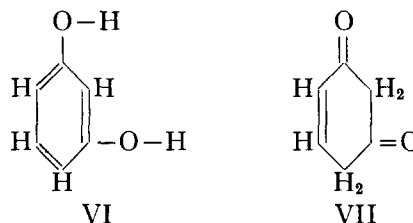
<sup>4</sup> L. Pauling and G. W. Wheland, *J. Chem. Phys.* 1, 362 (1933).

<sup>5</sup> This value is derived from data quoted by W. Hückel, *Theoretische Grundlagen der Organischen Chemie*, Vol. I,

Consequently it seems reasonable to assume that the resonance energies of the systems C=C—C=C—C=O and  $\begin{matrix} \text{C}=\text{C} \\ \diagdown \quad \diagup \\ \text{C}=\text{C} \end{matrix} \text{C}=\text{O}$  lie close to the values 17 Cal. calculated for C=C—C=C—C=C and 15 Cal. calculated for  $\begin{matrix} \text{C}=\text{C} \\ \diagdown \quad \diagup \\ \text{C}=\text{C} \end{matrix} \text{C}=\text{C}$ , respectively. It follows then that the enol form of phenol is more stable than either of the keto forms by 6–12 Cal. Again the agreement with experiment is qualitatively satisfactory, but a quantitative comparison is impossible on account of lack of experimental data.

#### RESORCINOL

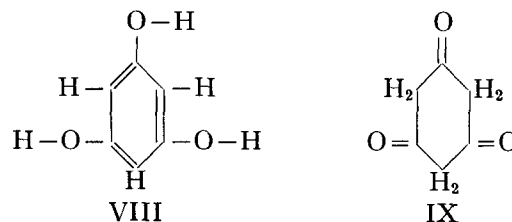
There is one dienolic and one diketonic form.



(The intermediate keto-enolic forms turn out to be less stable than either of the above.) If the resonance energy is neglected the diketonic form VII would be expected to be more stable than the dienolic VI by about 28 Cal. When the 39 Cal. resonance energy for the benzene ring and the 10 Cal. for the system C=C—C=O are considered, however, the dienol becomes more stable by 1 Cal. This is in qualitative agreement with the fact that resorcinol shows more of a ketonic behavior than phenol, but that its phenolic character is still predominant.

#### PHLOROGLUCINOL

There is one trienolic and one triketonic form.

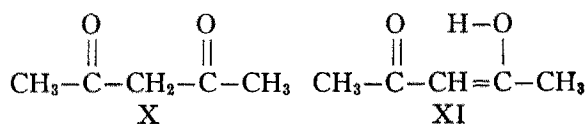


p. 304, Leipzig, 1931, regarding the heats of combustion of isomeric  $\alpha\beta$  and  $\beta\gamma$  unsaturated ketones.

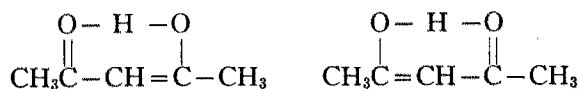
A calculation similar to the above gives the result that the triketonic form IX should be 3 Cal. more stable than the trienolic form VIII. This is again in good qualitative agreement with the fact that phloroglucinol possesses both phenolic and ketonic character, but the quantitative aspect is less satisfactory, as the phenolic character is apparently still predominant. The agreement would have been somewhat better if the dipole interactions had been considered. No great weight should be attached to the actual numerical values derived in this and the preceding calculations as they could hardly be expected to be accurate within a few kilocalories. The relative values, however, are probably significant.

## ACETYLACETONE

This is chosen as a typical example of a  $\beta$ -diketone. The keto and the enol forms (X and XI, respectively) are both known, and the free energy change accompanying the conversion of



the keto into the enol form has been found to be -1 Cal. With compounds of this type an additional complication enters in the fact that the enolic modification does not have the simple structure given above, but contains a chelate ring with a hydrogen bond. The resulting compound is then free to resonate between the two equivalent structures:

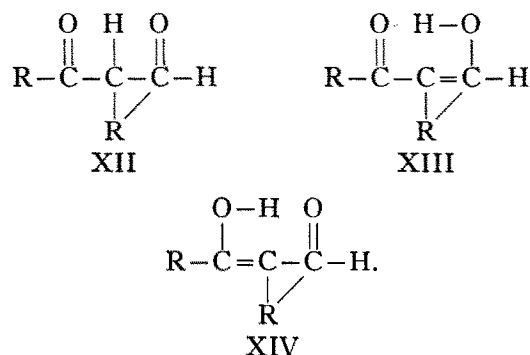


The amount by which this bond formation and resonance stabilizes the enol form can be calculated from the fact mentioned above that  $\Delta F$  for the reaction keto  $\rightarrow$  enol is -1 Cal. The keto form is readily seen to be 4 Cal. more stable than the open-chain enol form, and hence the formation of the chelate ring must stabilize the latter by an additional 5 Cal. This value is reasonable enough, but unfortunately cannot be checked by an independent calculation.

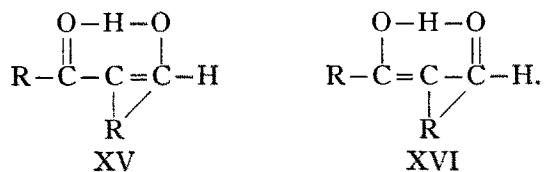
There is no provision in this treatment for the effect of substituent groups in the molecule (provided that at least one enolizable hydrogen is left), and in fact the calculation leads to the conclusion that the enolization should be independent of the presence of substituents. Actually this is not the case, but the effect of substitution is very small—less than 2 Cal. in all cases—and lies well within the accuracy of the method.

OXYMETHYLENE KETONES OR  
 $\beta$ -KETONIC ALDEHYDES

In compounds of this type enolization can take place in either of two ways and consequently there are (before formation of the chelate ring) two enol forms (XIII and XIV) in addition to the one keto form XII.



Since the energy of the C=O bond in aldehydes is 3.4 Cal. less than in ketones, it follows that the stability of the enol XIII is greater than that of XIV and nearly as great as that of the keto form XII. When the hydrogen bond is formed the resonance in the chelate ring will be less than in the case of the diketones as a result of the non-equivalence of the two structures

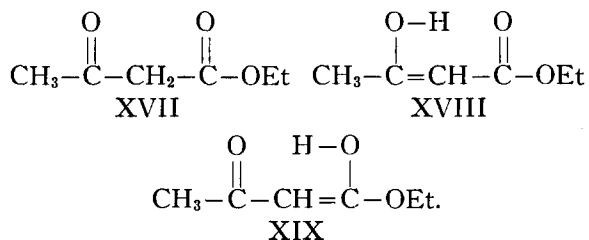


The effect of this will be twofold. In the first place, the energy of the ring will be less than 5 Cal., but probably still enough to make the enol form more stable than the keto; and in the second place, the structure XV will predominate over XVI since it represents the more stable

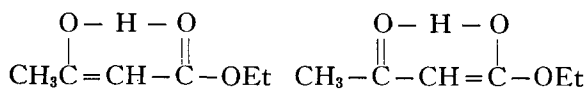
configuration. Experimentally, compounds of this type (for example, oxymethylene camphor) are found to possess the oxymethylene ketone structure, corresponding to the enol XIII or XV, in qualitative confirmation of the calculation. There are no accurate experimental data of quantitative nature for purpose of comparison.

#### ACETOACETIC ESTER

A  $\beta$ -ketonic ester can give rise to two (open-chain) enolic modifications (XVIII and XIX) in addition to the ketonic (XVII).



This problem is complicated by the fact that the carboxy group has a resonance of its own which makes the relatively large contribution of 28 Cal. to the energy of the molecule, and that this resonance is interfered with to an uncertain extent by any other types of resonance that may be present. In the keto form this effect does not enter since there is no other resonance than that of the carboxy group. In the enol form XVIII it is apparently of very minor importance since in a few cases for which data are available<sup>6</sup> the resonance energy of  $\alpha\beta$  unsaturated acids is essentially the same as if the  $\text{C}=\text{C}-\text{C}=\text{O}$  and the carboxyl groups were entirely independent of each other. In the enol form XIX, however, the carboxy group and its resonance energy have been destroyed, and hence this structure represents a relatively unstable molecule. The conclusions to be drawn from these considerations are: first, that the  $\beta$ -ketonic esters should be somewhat less enolic than the  $\beta$ -diketones, as a result mainly of damping of resonance in the chelate ring; and second, that the first of the resonating structures of the chelate compound

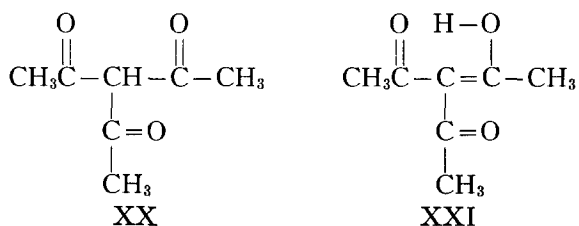


<sup>6</sup> For example, the heats of combustion of  $\alpha\beta$  and  $\beta\gamma$ -pentenoic acids differ by 8.5 Cal. See M. S. Kharasch, Bur. Standards J. Research 2, 359 (1929).

should predominate over the second. Both conclusions are in agreement with experiment. Acetoacetic ester is less enolic than acetyl acetone by about 1 Cal. ( $\Delta F=0$  Cal.), and the position of the  $\text{C}=\text{C}$  double bond has been determined by ozonization.<sup>7</sup> The  $\beta$ -ketonic esters are perhaps somewhat more enolic than might be expected from the discussion, but the agreement with the calculation is really quite satisfactory.

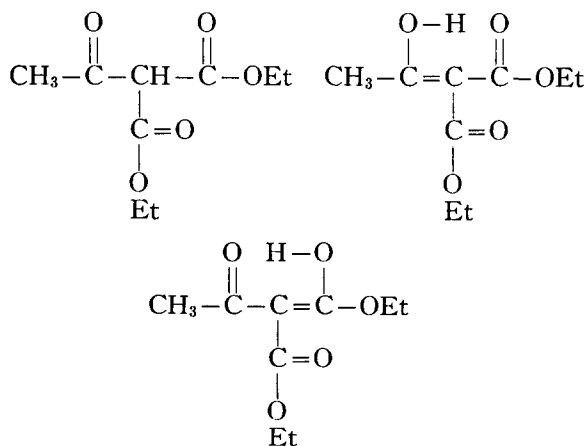
#### TRIACETYL METHANE

In this case there is only one keto and one enol form (XX and XXI, respectively).



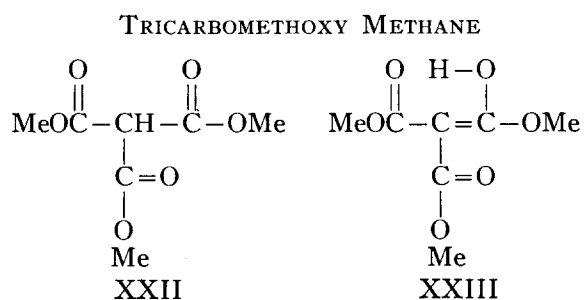
We see that this compound will be more enolic than acetylacetone by the amount by which the resonance of the system  $\text{C}=\text{C} \begin{array}{l} \text{C}=\text{O} \\ \text{C}=\text{O} \end{array}$  exceeds that of the system  $\text{C}=\text{C}-\text{C}=\text{O}$ . An estimate of about 4-8 Cal. seems to be reasonable for this figure and to agree satisfactorily with what little experimental data there are. The compound is usually considered to be completely enolic, but the equilibrium has never been measured accurately.

#### ACETYLMALONIC ESTER



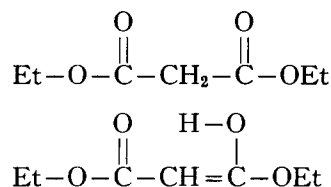
<sup>7</sup> J. Scheiber and P. Herold, Ann. d. Chemie 405, 295 (1914).

This compound would be expected to be less enolic than triacetylmethane (for the same reason that acetoacetic ester is less enolic than acetylacetone) and to be more enolic than acetoacetic ester. Experimentally,  $\Delta F$  of enolization is found to be about  $-0.5$  Cal. A value between  $-4$  and  $-8$  Cal. would seem more reasonable, but the qualitative agreement is good.



The stability of the enol form XXIII is decreased very materially by the fact that in it one of the carbomethoxy groups is no longer intact. Just how great this effect will be, however, cannot be predicted with any assurance since, as a result of the resonance within the chelate ring, the relationships involved are very complicated. All that can be said definitely is that this compound should be less enolic than acetylmalonic ester. This is indeed the case, but the difference is very much less than might be expected. The enolic form is less stable than the ketonic by only about 1 Cal., while a value of 10–20 Cal. would seem more reasonable. The quantitative aspects of the present treatment are consequently very unsatisfactory at this point, although the qualitative agreement is still good. Two possible explanations for this discrepancy suggest themselves at once. In the first place, the value of 28 Cal. for the resonance energy of the carbomethoxy group may be considerably too high. This figure was arrived at<sup>1</sup> on the doubtful assumption that the energies of the C=O and the C–O bonds were the same as in ketones and primary alcohols, respectively, and consequently may very well be in error by several kilocalories. In the second place, the neglect of the large interaction between the dipoles in the carbomethoxy group is probably not legitimate.

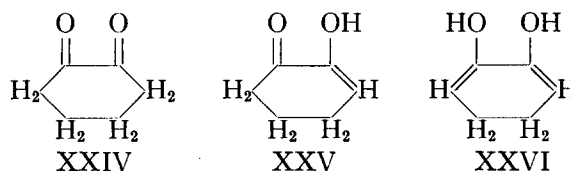
## MALONIC ESTER



This case differs from the preceding only in the substitution of the resonating system C=C–C=O for C=C  $\begin{array}{l} \text{C}=\text{O} \\ \text{C}=\text{O} \end{array}$  in the enol form. Consequently the stability of the enol relative to that of the keto should be decreased by the difference between the resonance energies of the two systems, i.e., by 4–8 Cal. This is in good agreement with the fact that  $\Delta F$  for the reaction keto→enol is known certainly to be greater than 6 Cal. and probably to be less than 14 Cal.<sup>8</sup>

## CYCLOHEXADIONE 1,2

Three structures are possible.



The calculation is simpler than in the case of  $\beta$ -diketones since the enol forms of  $\alpha$ -diketones do not form chelate rings, partly for steric reasons and partly on account of the impossibility of resonance within the ring. The resonance energy of the system O=C–C=O is not known, but presumably is not very different from that of C=C–C=O or of C=C–C=C. Consequently it would appear that the diketo form XXIV should be considerably more stable than the keto-enol XXV, which in turn should be more stable than the dienol XXVI. Actually, however, the compound appears to exist only in the keto-enol form. The reason for this discrepancy is probably to be found in the potential energy which results from the dipole repulsions of the carbonyl and the hydroxyl groups present, and which cannot be neglected in this case. The two

<sup>8</sup> J. B. Conant and G. H. Carlson, J. Am. Chem. Soc. 54, 4054 (1932).

dipoles are close together and are held in the *cis* position by the ring formation. The magnitude of this effect cannot be determined with any accuracy on account of the uncertainty in regard to the position and orientation of the dipoles and the dielectric constant of the medium. A rough calculation, however, shows that the effect is in the right direction and is of the correct order of magnitude.<sup>9</sup> It is probable that similar effects are responsible for other discrepancies in quantitative comparisons noted above.

#### DIACETYL

This case differs from the preceding in that the molecule is not kept rigid by the presence of a ring. Hence the dipoles are free to orient themselves in the more stable *trans* position where their effect upon the stability of the molecule is relatively small. This is in accord with the fact that the molecule exists only in the diketo form.

#### CONCLUSION

The results which have been obtained for the simple tautomeric systems treated above are in complete qualitative agreement with experiment

<sup>9</sup> For a somewhat similar calculation see H. M. Smallwood, *J. Am. Chem. Soc.* **54**, 3048 (1932).

and furnish considerable justification for the semi-empirical treatment used. In only two cases (tricarbomethoxy methane and malonic ester) are the quantitative aspects of the calculation unsatisfactory. These two compounds differ from the rest in that, with them, enolization necessarily destroys the characteristic resonance of a carboxyl group. As has been pointed out, this fact makes the problem very complicated, and so it is not surprising that quantitative agreement is lacking at this point. It is doubtlessly significant, however, that the calculations for the two compounds are in good quantitative agreement with each other.

This same treatment could be extended to a number of other cases, but since its success depends upon the possibility of estimating the resonance energies of various groupings in the molecules concerned, it rapidly becomes of less value as the complexity of the resonating systems increases. For this reason it does not seem profitable to attempt the treatment of such cases as dibenzoylmethane, etc., where the presence of the phenyl groups complicates the problem tremendously. The success obtained with the simpler systems, however, makes it seem quite probable that these could also be treated satisfactorily by the same method if sufficient empirical data were at hand.