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TRANS-ENOLIZATION

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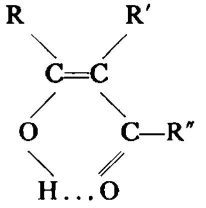
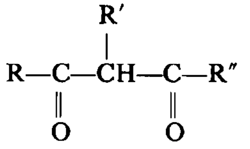
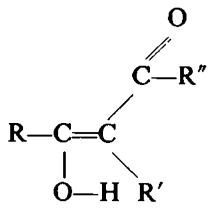
Abstract—The solvent effect on *trans*-enolization of different keto-enols is discussed. Ultra-violet and infra-red data are presented on keto-enol equilibrium in α-alkyltetronic acids, isopropylidene alkyl malonates, and α-alkyl-substituted alkyl acetoacetates, bromometrical evidence also being produced for the latter compounds. The limitations of Meyer's rule and Eistert and Reiss' hypothesis as to *trans*-enolization are shown and the general applicability of the relationship $K_T = EL + E'L'$ is demonstrated.

1. GENERAL CONSIDERATIONS

It has been established that solutions of β-dicarbonyl compounds with open chains generally contain at least the ketonic, *cis*- and *trans*-enolic forms in equilibrium.[1]


Cis-enol


$$\mathrm{R{-}\underset{\underset{\displaystyle O}{\|}}{C}{-}\overset{\overset{\displaystyle R'}{|}}{C}H{-}\underset{\underset{\displaystyle O}{\|}}{C}{-}R''}$$
Ketone


Trans-enol

This equilibrium of the three forms is determined by their ionization constants in a particular solvent, i.e. depends upon the acidic properties of the forms and their solvation.[2]

The enolic forms of ethyl acetoacetate and other related keto-enols are considered as chelated hydrogen bonded *cis*-forms.[3,4] Contrary to ketonic forms, they have a comparatively low boiling point and are more readily soluble in non-polar (hydrophobic) than in polar (hydrophilic) solvents. Hence, in full accordance with the Van't Hoff–Dimrot's rule,[5] the non-polar solvents shift the tautomeric equilibrium toward the enolic (*cis*-)forms and the polar solvents toward the ketonic forms. These relationships are expressed by the well known Meyer's equation[6] $K_T = EL$ where K_T is the keto-enol equilibrium constant of any keto-enol in solution, E is the enolizability of the keto-enol independent of the solvent, L is the enolizing capacity of the solvent equal to the equilibrium constant of the standard compound such as ethyl acetoacetate ($E = 1$). The value L changes from $4 \,.\, 10^{-3}$ for water to 1 for hexane. The graphic dependence of K_T on L for keto-enols obeying Meyer's equation is shown by straight lines passing through the origin.

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* Translated by A. L. Pumpiansky, Moscow.

[1] B. Eistert, F. Arndt and E. Ayça, *Chem. Ber.* **84**, 156 (1951).

[2] M. I. Kabachnik, *Izv. Akad. Nauk* 98 (1955).

[3] N. V. Sidgwick, *J. Chem. Soc.* **127**, 907 (1925).

[4] P. Nachod, *Z. Phys. Chem.* **A.182**, 208 (1938).

[5] O. Dimroth, *Liebigs Ann.* **377**, 134 (1910); **399**, 93 (1913).

[6] K. H. Meyer, *Ber. Dtsch. Chem. Ges.* **45**, 2846 (1912); **47**, 826 (1914).

The case becomes complicated when a considerable amount of *trans*-enolic form appears together with the *cis*-enolic form in the solution as first exemplified with ethyl formylphenylacetate.[7]

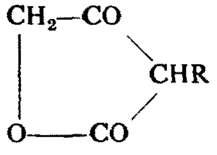
Henecka[8] has reported on a number of *trans*-enolic forms accounted for by their failing to give a colour reaction with ferric chloride. These compounds are found to deviate from Meyer's rule.

Trans-enolization was first discussed in detail by Arndt *et al.*[9] These authors found it controversial that hydrophilic solvents shift the tautomeric equilibrium toward the ketonic form rather than toward the most polar *trans*-enolic form containing an open hydroxyl group.

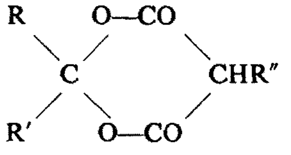
The authors answered the question "Warum nicht *trans*-Enol?" by assuming that the ketonic forms produce highly polar hydrates and semiacetals which react as ketonic forms. There are objections to this hypothesis[2,10] which is also invalid when investigating the effect of pressure on keto-enol equilibrium.[11]

Eistert and Reiss[12] have studied cyclic keto-enols containing both carbonyl groups in the same ring and hence unable to produce *cis*-enolic forms but producing "*trans*-fixed" enols. These authors consider that the effect of the solvent on keto-*trans*-enol equilibrium is opposite to Meyer's rule, i.e. the hydrophilic solvents must shift the equilibrium toward the enolic forms and the hydrophobic solvents toward the ketonic forms. The bromometrical analysis of solutions of such keto-enols in different solvents gave rather inaccurate and not easily reproducible results but did in general confirm the hypothesis.

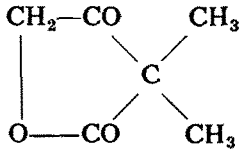
Thus in solutions of α-methyltetronic acid (I) in ether, methanol and water the percentage of enol amounted to 69, 97 and 100 whilst cyclic isopropylidene malonate (IV) ("Meldrum's acid") in benzene, methanol and water showed 37, 95 and 128 per cent, respectively.



I $R = CH_3$
II $R = C_2H_5$
III $R = C_3H_7$



IV $R = R' = CH_3$; $R'' = H$
V $R = R' = CH_3$; $R'' = C_2H_5$



VI

This hypothesis has been proved spectrometrically for a number of other cases, but it does not agree with the spectrometric data on α-ethyltetronic acid (II) obtained by other workers[13,14] as cited in the same paper. This hypothesis is, however, in accordance with ultra-violet evidence obtained by Russel[15] who found that solutions of β-cyanoketones whose enolic forms are sterically unable to exist as chelates and thereby

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[7] W. Dieckmann, *Ber. Dtsch. Chem. Ges.* **50**, 1376 (1917).
[8] H. Henecka, *Chem. Ber.* **81**, 192 (1948).
[9] F. Arndt, L. Loewe and R. Ginkök, *Rev. Fac. Soc. Istanbul* **A11**, 147 (1946).
[10] G. Brigleb and W. Strohmeyer, *Angew. Chem.* **64**, 409 (1952).
[11] M. I. Kabachnik, S. E. Yakushkina and N. B. Kislyakova, *Dokl. Akad. Nauk SSSR* **96**, 1169 (1954).
[12] B. Eistert and W. Reiss, *Chem. Ber.* **87**, 92 108 (1954).
[13] L. A. Dunkanson, *J. Chem. Soc.* 1210 (1953).
[14] R. W. Herbert and E. L. Hirst, *Biochem. J.* **29**, 1884 (1953).
[15] P. B. Russel, *J. Amer. Chem. Soc.* **74**, 2654 (1952).

contain an open hydroxyl group,[16,17] have more enolic forms in hydroxyl containing solvents than in hydrophobic ones. The data recorded by Russel were found to be much more involved. In the series of hydroxyl containing solvents such as water–methanol–ethanol–pentanol the enol content increases as the hydrophilic property of the solvent decreases. It reaches its maximum in pentanol, decreases in ether (yet remaining higher than in water), and then sharply drops in ether and hexane mixtures, being the lowest in hexane. This effect of the hydrophilic property of solvents cannot be accounted for either by Meyer's rule or the hypothesis under discussion.

Kabachnik[2] has considered the keto-*cis*-*trans*-enol equilibrium as acid–base equilibrium of three acids forming common anions. This equilibrium is in accordance with the acid-base equilibrium as formulated by Brønsted–Izmailov.[18–22] In solutions of keto-enols with an open chain both *cis*- and *trans*-enolic forms are present. The *trans*-enolic forms possess, however, considerably higher acidic properties. Therefore, their relative amount is always small and the keto-enol equilibrium is in agreement with Meyer's equation. But in polar solvents which dissolve the *trans*-form more readily, the overall decrease in enol content (at the expense of *cis*-enol) is accompanied by a relative increase of the *trans*-enolic form in the enolic fraction of keto-enol. Thus the discrepancy encountered by Arndt is explained.

In a more recent report on this subject[23] it has been shown that the effect of the solvent on the keto-*cis*-*trans*-enol equilibrium can be quantitatively accounted for in terms of an extended formula similar to that of Meyer but taking into consideration *trans*-enolization.

$$K_T = EL + E'L' \tag{1}$$

In this formula E and E' is the enolizability of keto-enol toward *cis*-enol (i.e. Meyer's constant) and *trans*-enol respectively; and L and L' is the enolizing capacity of the solvent toward *cis*-enol (L of Mayer) and *trans*-enol respectively. This relationship has been derived, like the Meyer's equation,[24] from the equation of Brønsted–Izmailov and is based on the assumption that the acid-base equilibrium theory is applicable to ketonic and *cis*- and *trans*-enolic forms as acids.*

To apply this formula, standard compounds must be chosen, one for *cis*-enolization ($E' = 0$; $E = 1$) and another for *trans*-enolization ($E = 0$; $E' = 1$). Ethyl acetoacetate may be used for *cis*-enolization, but the choice of a standard compound for *trans*-enolization is more difficult. Bromometrical[23] and spectrometric[25] investigation of the effect of the solvent on enolization of α-substituted acetoacetates described by Henecka[8] has shown that substances capable only of *trans*-enolization are characterized by a tautomeric equilibrium constant practically independent of the solvent. On the

* In formula (1) the parameters of L and L' remain constant in compounds of the same chemical type as this formula has been derived from $pK_{AS_1} = pK_{AS_2} + C$ with C is constant for acids of the same type.[20–21]

[16] S. B. Hendricks, O. R. Wulf, G. E. Hilbert and U. Liddel, *J. Amer. Chem. Soc.* **58**, 1991 (1936).

[17] G. S. Skinner, J. A. Gladner and R. F. Heitmiller, *J. Amer. Chem. Soc.* **73**, 2230 (1951).

[18] I. N. Brønsted, *Chem. Rev.* **5**, 291 (1928).

[19] I. N. Brønsted, *Z. Phys. Chem.* **A169**, 32 (1934).

[20] N. A. Ismailov, *Z. Phys. Chim. U.S.S.R.* **23**, 639, 643 (1949).

[21] N. A. Ismailov, *Z. Phys. Chim. U.S.S.R.* **24**, 321 (1950).

[22] N. A. Ismailov, *Izv. Univers. Kharkov* **10**, 5 (1953).

[23] M. I. Kabachnik, S. T. Yoffe and K. V. Vatsuro, *Tetrahedron* **1**, 317 (1957).

[24] M. I. Kabachnik, *Dokl. Akad. Nauk SSSR* **83**, 407, 859 (1952).

[25] M. E. Movsesyan, M. I. Kabachnik, S. T. Yoffe and K. V. Vatsuro, *Izv. Akad Nauk (Physical Series)* **22**, 1126 (1958).

other hand, the greater the *cis*-enolizability of the keto-enol, the more this constant depends on the solvent. Thus, for ethyl α-s-butylacetoacetate whose *cis*-enolic form is strongly hindered due to steric effects, the amount of enolic form proved to be practically constant in benzene, ethanol, methanol and 67 per cent aqueous methanol. This shows that for *trans*-enolization of such keto-enols, L' is practically constant and equation (1) may be more simply expressed as:

$$K_T = EL + E_1 \tag{2}$$

E_1 is a constant value denoting the *trans*-enolizability of α-substituted alkyl acetoacetates in any solvent. This conclusion is apparently substantiated by bromometrical estimation of the amount of enolic forms in solutions of some cyclic "*trans*-fixed" keto-enols carried out by the reversed Meyer's method.[23,*] The amount of *cis*- and *trans*-enolic forms in solutions of several α-substituted alkyl acetoacetates in various solvents may be calculated by application of formula (2).

The spectrometric investigation of enolization of some "*trans*-fixed" keto-enols was recently published by Eistert and Geiss.[26] Their results do not agree with the bromometric estimation of the amount of enolic forms in solutions of strongly acidic keto-enols determined by us[23] and by Eistert and Reiss.[12]

Thus, for example, in bromometric determinations,[12] isopropylidene malonate (IV) is 37–128 per cent enolized in different solvents and isopropylidene ethyl malonate (V) contains about 70 per cent of enol, whereas actually no enol form is present. As spectrometric data is regarded as more reliable in these cases it may be concluded that the bromometric method cannot be applied to these compounds. It is suggested that the bromometric method is unsuitable for strongly acidic cyclic β-dicarbonyl compounds as in addition to the bromination of anion there may be fast direct bromination of the ketonic form.[†]

Thus, it is necessary to consider:

(1) The actual effect of solvents on enolization of different "*trans*-fixed" cyclic keto-enols and the extent to which the hypothesis advanced by German authors on the reversion of Meyer's rule can be applied.

(2) The effect of solvents on *trans*-enolization of open chain ketones, the extent to which formula (2) is valid, and the substance which may be used as standard compounds for *trans*-enolization of β-keto esters.

These considerations led to additional experimental investigation which gave the following results.

2. RESULTS

α-Alkyltetronic acids

According to Eistert and Geiss[26] in solutions of α-ethyltetronic acid (II) and isoalkylidene malonates (IV) and (V) the only equilibrium observed is between ketonic forms and the corresponding enolate anion. The observed overlapping of ultra-violet absorption spectra of ethyltetronic acid in water, methanol and ethanol is explained by

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[*] In the work cited direct bromometrical titration procedure was mistakenly mentioned as applied for these compounds.

[†] On direct titration of benzene solution V and solution III in aqueous methanol with bromine solution in methanol or ethanol the amount of bromine consumed corresponds to 100 per cent enol content.

[26] B. Eistert and F. Geiss, *Tetrahedron* 7, 1 (1959).

Eistert and Reiss as being due to the occasional coincidence in the concentration of enolate anions in solutions investigated. No reference is made to the observations by Duncanson[13], Herbert and Hirst[14] and ourselves that the enolization of α-ethyltetronic acid is approximately constant in such different solvents as aqueous sulphuric acid and ethylene chloride.

We found that the infra-red spectra of crystalline α-ethyl- and propyl-tetronic acids (Fig. 1a and b) are markedly different at 1800 cm^{-1} and 2600 to 3000 cm^{-1} from those of the lactone of γ-hydroxy-α,α-dimethylacetoacetic acid (VI) of a similar structure but with fixed ketonic forms (Fig. 1c). In the spectrum of this lactone the 1745 and 1798 cm^{-1} bands definitely refer to the stretching vibrations of the ketonic and carbalkoxylic carbonyl.* Within the range of 2600–3300 cm^{-1} the spectrum of this compound reveals only characteristic C—H frequencies. The infra-red spectra of crystalline ethyl- and propyl-tetronic acids (II and III) showed a broad diffused band at 3050–2950 cm^{-1} and a sharp band at 2710 cm^{-1}. The character and position of these bands allow them to be assigned to the stretching vibrations of hydroxyl groups involved in intermolecular hydrogen bonds. The α-alkyltetronic acids under study have thus an enolic structure. This is in good agreement with the absorption bands of these compounds observed in the range of double bond stretching vibrations such as 1650 and 1715 cm^{-1}. The former band may be accounted for by the vibration of the C=C bond in the enolic form, the latter by that of the C=O bond.†

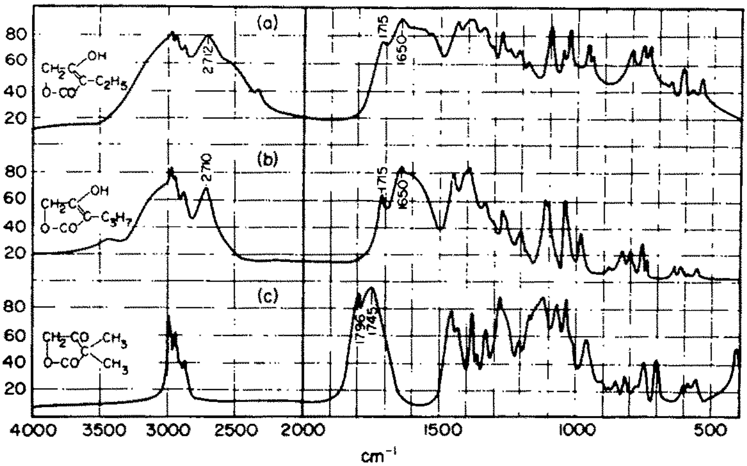

FIG. 1. Infra-red spectra of crystalline α-ethyl (a), α-propyl (b) tetronic acids and of lactone of γ-hydroxy-α-α-dimethylacetoacetic acid (c).

The lowering in the C=O frequency as compared to the vibration frequency of the

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* Higher values of these frequencies as compared to those of similar vibrations of non cyclic β-dicarbonyl compounds seems to be due to the peculiarity of the five-membered ring. It is known,[27] that the stretching vibration frequencies of carbonyl groups in cyclic compounds involving C=O increase as the ring becoming more strained.

† The C=C and C=O stretching vibration frequencies in II and III are to be compared with those of substituted acryloates. Thus the latter spectra show the C=C stretching vibration frequencies to be at 1630–1650 cm^{-1} whilst those of C=O at 1715 to 1725 cm^{-1},[28]

[27] V. Bellamy, *The Infra-red Spectra of Complex Molecules*. London (1954).

[28] R. W. F. Kohlrausch *Raman Spectren*. Leipzig (1943).

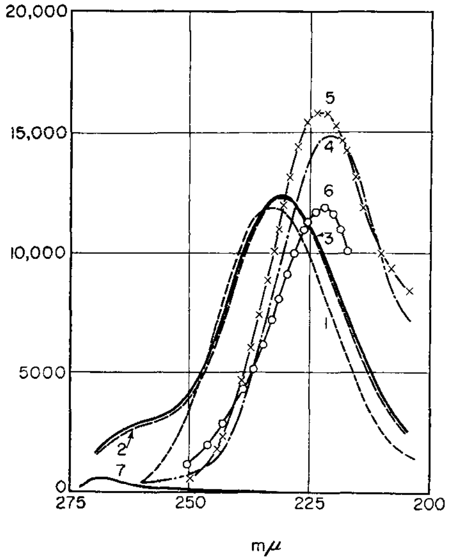

FIG. 2. Ultra-violet spectra of α-propyltetronic acid (conc. 5 · 10^{-4} mole/l.) in different solvents such as (1) water (– – – –) at pH 2·50 (2) methanol (— — — —) (3) ethanol (————) (4) ether (—·—·—·) (5) dioxan (—×—×—×—×) (6) dichloroethane (o—o—o—o) (7) lactone of γ-hydroxy-α,α-dimethylacetoacetic acid in methanol.

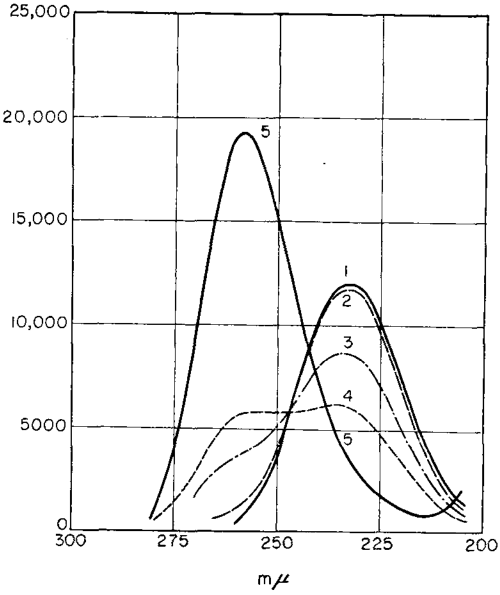

FIG. 3. Ultra-violet spectra of α-propyltetronic acid in water at different pH's (conc 5 · 10^{-4} mole/l.): (1) pH 2·50 (2) pH 2·90 (3) pH 3·35 (4) pH 3·75 (5) pH 11.20.

carbalkoxyl of the lactone mentioned above (spectrum 1c) to 1798 cm^{-1} is accounted for by the intermolecular hydrogen bonding and conjugation.*

The ultra-violet spectra of α-propyltetronic acid were investigated in water (at pH 2·50, 2·90, 3·35, 3·75, and 11·20) in methanol, ethanol, ether, dioxan, and dichloroethane (Figs. 2 and 3), that of lactone (VI) in methanol (Figs. 2 and 4).

As will be seen from the absorption curves the ultra-violet spectra of α-propyltetronic acid and that of reference lactone (VI) of a ketonic structure are markedly different both as to their position and the intensity of absorption bands. Hence in solutions of α-propyltetronic acid the tautomeric equilibrium is not shifted toward the ketonic form. In aqueous solution at high pH (11·20) one observes only one intensive maximum at 258 mμ that undoubtedly is characteristic of the absorption of the anion of α-propyltetronic acid.[13,14] The lowering of pH results in decrease of the intensity of this maximum. In acidic media there appears a fairly intensive absorption maximum at 233 mμ, that can only be assigned to non-dissociated molecules of α-propyltetronic acid, as not corresponding in character to the ketonic form are, therefore, attributable to the enolic form.† Thus the changes in the ultra-violet spectra observed with changing pH characterize the ionic dissociation equilibrium of the enolic α-propyltetronic acid. As the ultra-violet absorptions in acidified water, methanol, and ethanol as previously reported,[29] practically coincide (Fig. 2), the extent of enolization in these as well as in dichloroethane solutions are almost the same. The concentration of enolic form is higher in ether and is further increased in dioxan. Due to low absorption intensity of ketonic forms in the ultra-violet the data obtained cannot be used to determine the tautomeric equilibrium constant. It is, however, clear that it does not depend on the solvent and its variation is not explained by the hypothesis suggested by Eistert and Reiss.

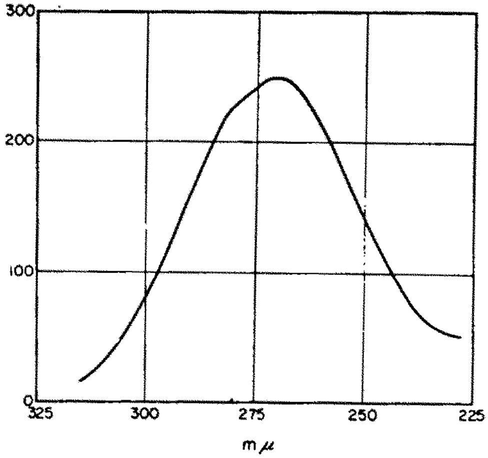

FIG. 4. Ultra-violet spectra of lactone of γ-hydroxy-α,α-dimethylacetoacetic acid in methanol (conc 5 · 10^{-4} mole/l.)

The ultra-violet evidence agrees with the infra-red data for 1 per cent solutions of

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* Conjugation usually lowers the C═O frequency by 20–40 cm$^{-1,28}$ and hydrogen bonding by 50–60 cm$^{-1,29,30}$ Simultaneous action of these factors can result in the overall lowering of C═O frequency down to 70–100 cm^{-1}.

† Absorption curves are reproducible whin passing back from acidic to basic solutions.

[29] R. S. Rasmussen and R. K. Brattain, *J. Amer. Chem. Soc.* **71**, 1077 (1949).

[30] R. S. Rasmussen, D. D. Tunnicliff and R. R. Brattain, *J. Amer. Chem. Soc.* **71**, 1068 (1949).

α-propyltetronic acid in chloroform, ether, tetrahydrofuran and saturated solutions in carbon tetrachloride (Fig. 5).

The spectrum of the solution in chloroform (Fig. 5b) reveals intensive bands at 1652 and 1730 cm^{-1}, which are similar to the corresponding bands of the crystalline compound and, therefore, are assigned to the enolic form. The spectra also show weak bands at 1768 and 1812 cm^{-1}, roughly corresponding to the frequencies of lactone (VI) and possibly accounting for the ketonic form. It can, therefore, be suggested that when the crystalline enolic form is dissolved in chloroform a minute amount of ketonic form is produced. Similarly, the spectrum of α-ethyltetronic acid in carbon tetrachloride solution (Fig. 5d) shows two enolic bands at 1650 and 1715 cm^{-1} and a band at 1761 cm^{-1} which may be assigned to the stretching C=O vibration of the ketonic form or to the C=O enol not involved in the hydrogen bonding. Its relative intensity is weaker than that of the corresponding band in chloroform solution and may be accounted for either by a lower content of the ketonic form or by a decrease in the number of molecules free from hydrogen bonding. Owing to poor solubility of the compound in carbon tetrachloride a fairly weak band at 1800 cm^{-1} assigned to the ketonic carbonyl was not observed. The spectrum of α-ethyltetronic acid in carbon tetrachloride has been described by Duncanson[13]. Besides the three bands mentioned, he observed a band at 1818 cm^{-1}, which supports the conclusion concerning the presence of ketonic forms in solutions of α-alkyltetronic acid in chloroform and carbon tetrachloride.

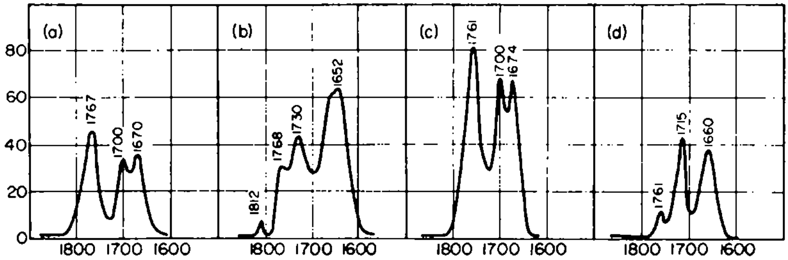

FIG. 5. Infra-red spectra of solutions of α-propyltetronic acid in (a) ether (b) chloroform (c) tetrahydrofurane (conc 1 per cent) (d) carbon tetrachloride (saturated solution).

The infra-red spectra of α-propyltetronic acid in ether and tetrahydrofuran (Fig. 5a and c) reveal three sharp bands at 1670, 1700, and 1760 cm^{-1}. It appears that the first may be assigned to the stretching vibration of C=C, and the second to C=O of the enolic form (hydrogen bonds). Concerning the 1760 cm^{-1} band, it may be assigned either to the C=O of the ketonic form, or to the hydrogen bond free enolic carbonyl. The second explanation is more acceptable as the presence of a ketonic form should produce a band at 1800 cm^{-1} which is not the case. The infra-red evidence confirms the existence of enolic α-propyltetronic acid in solution and one may reasonably expect the presence of a small amount of the ketonic form in the chloroform or carbon tetrachloride solutions.

Isopropylidene ethyl malonate

The infra-red spectrum of crystalline isopropylidene ethyl-malonate (V, Fig. 6a) reveals intensive absorption at 1740 to 1775 cm^{-1} corresponding to characteristic

C=O vibrations ofketonic carbonyls and carbalkoxyls. The ketonic structure of the crystalline molecules is also confirmed by the absence of hydroxyl absorption bands. The spectrum of this acid in carbon tetrachloride solutions shows a sharp line at 3535 cm^{-1} [31] which may be assigned either to free hydroxyl vibrations, indicating the presence of the enolic form, or to the C=O stretching vibration overtone. In the spectrum of the monodeuterated derivative in solution, the 3535 cm^{-1} line remains unchanged substantiating the latter suggestion. The isotopic substitution occurs at the ketonic α-carbon as evidenced by a marked decrease in the intensity of the band at 2895 cm^{-1}, as compared with the non-deuterated compound, and by the appearance of a band at 2145 cm^{-1} (Fig. 6b).

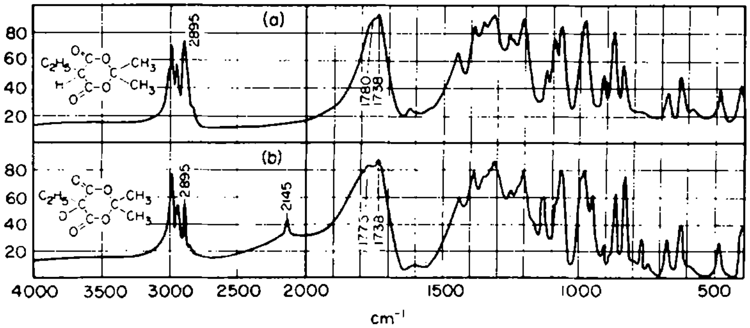

FIG. 6. Infra-red spectra of crystalline isopropylidene ethylmalonate (a) and isopropylidene monodeuteroethylmalonate (b).

The ultra-violet spectra of alkaline, neutral and acidic methanol solutions of isopropylidene ethyl malonate (Fig. 7) are similar to that observed by Eistert and Geiss[26]

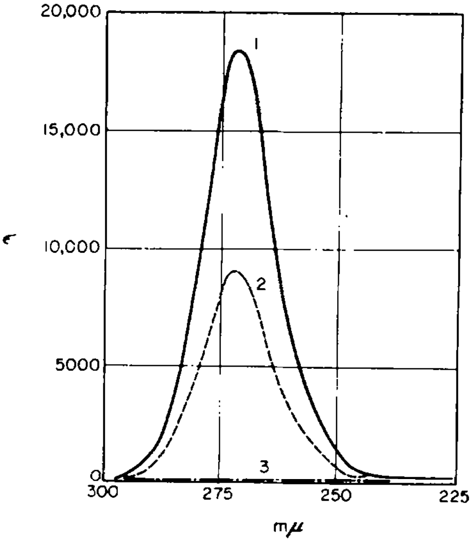

FIG. 7. Ultra-violet spectra of isopropylidene ethylmalonate in alkaline (1), neutral (2), and acidic (3) methanol.

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[31] M. E. Movsesyan, Dissertation, Moscow (1959).

in the spectra of its *spyro* analogs. In the alkaline solution an intensive absorption with a maximum of 272 mμ is observed, this is weaker in the neutral solution and non-existent in the acidic solution, but the maximum is again reached on addition of the required amount of alkali. In agreement with the German authors, this evidence shows that the ketonic form only is present in the crystalline state or when dissolved in non-polar solvents. In polar solvents the ketonic form is in equilibrium with the enolate anion, the concentration of which depends on the acidity of the medium. Under no conditions do these cyclic β-dicarbonyl compounds enolize and, therefore, do not obey either Meyer's rule or the hypothesis of Eistert and Reiss.

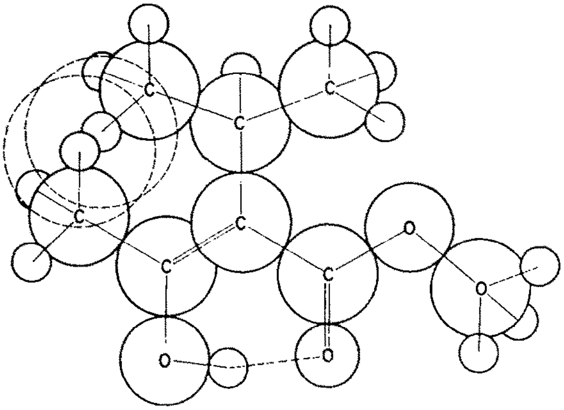


FIG. 8. *Cis*-enolic form of ethyl α-isopropylacetoacetate.

Alkyl α-alkylacetoacetates

Esters with α-alkyl substituents such as s-butyl-(XVI), cyclopentyl-(XXII), 2-pentyl-(XVIII), 3-pentyl-(XVII), 2-hexyl-(XIX), and 2-heptyl-(XX) were spectroscopically investigated. In all these compounds the appearance of a planar *cis*-enol form with intramolecular hydrogen bonding is accompanied by strong steric hindrance due to the overlapping of α-alkyl- and γ-methyl-groups (cf. Henecka[8]). This is shown in Fig. 8 which roughly pictures the relationships.

When considering the infra-red data for these compounds, particular attention was paid to the assignment of frequencies of different tautomeric forms.

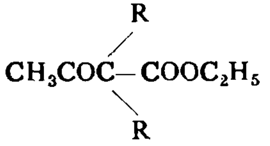
The α,α-disubstituted acetoacetates (XXIV), with "fixed" ketonic forms have spectra with two intensive bands over the range of 1710–1730 cm^{-1} and 1740–1760 cm^{-1}, which are assigned to C=O carbonyls and carbalkoxyls, respectively.[28] In the spectra of *cis*-fixed ketoenols such as those of cyclohexanone- (or cyclopentanone-)carboxylates (XXV) four bands are observed in the 1600–1800 cm^{-1} range.[25] Two of them are within the frequency range of 1710–1730 cm^{-1} and 1740–1760 cm^{-1} and are assigned to the ketonic isomer. Two other bands at 1610–1630 cm^{-1} and 1650–1660 cm^{-1} may refer to the enolic form, inasmuch as their intensity increases with increasing enolizing capacity of the solvent, and at the same time the band intensity of the ketonic form decreases.[25,30,31] The weaker absorption band at 1610–1630 cm^{-1} is assigned to the stretching vibration of the C=C bond and the intensive band at

$$\underset{\displaystyle R}{CH_3CO\overset{}{C}HCOOC_2H_5}$$

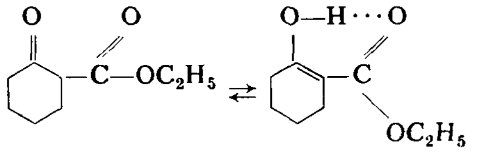
VII $R{=}CH_3$
VIII $R{=}C_2H_5$
IX $R{=}n\text{-}C_3H_7$
X $R{=}n\text{-}C_4H_9$
XI $R{=}n\text{-}C_7H_{15}$
XII $R{=}C_6H_5$
XIII $R{=}C_6H_5CH_2$

XIV $R{=}i\text{-}C_3H_7$
XV $R{=}i\text{-}C_4H_9$
XVI $R{=}s\text{-}C_4H_9$
XVII $R{=}(C_2H_5)_2CH$
XVIII $R{=}C_3H_7(CH_3)CH$
XIX $R{=}C_4H_9(CH_3)CH$
XX $R{=}C_5H_{11}(CH_3)CH$

XXI $R{=}C_6H_{13}(CH_3)CH$
XXII $R{=}cyclo\text{-}C_5H_9$
XXIII $R{=}cyclo\text{-}C_6H_{11}$



XXIV



XXV

1650–1660 cm^{-1} to the C=O vibration of the carbalkoxy group involved in intramolecular hydrogen bonding and conjugated with the double bond.

The infra-red spectra of α-alkylacetoacetates (Fig. 9) show three bands over the range of 1600–1750 cm^{-1}, their frequencies and assignment are given in Table 1.

The absence of absorption bands within 1650–1660 cm^{-1} characteristic of *cis*-configuration points to the *trans*-enolization of these compounds. The presence of

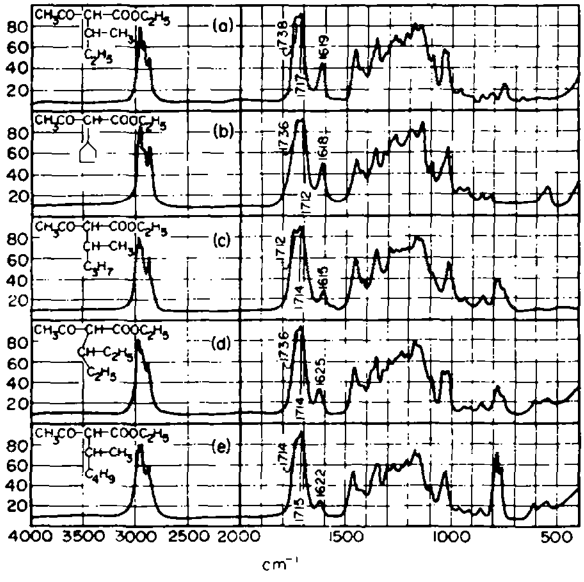


FIG. 9. Infra-red spectra of ethyl α-alkylacetoacetates.

TABLE 1. ASSIGNMENT OF FREQUENCIES OVER THE RANGE OF 1600–1800 cm^{-1} TO THE VIBRATION OF BONDS OF C=O AND C=C TAUTOMERIC FORMS OF ETHYL α-ALKYL ACETOACETATES

Compound	Ketonic form		Enolic form
$CH_3COCHRCOOC_2H_5$	I Carboxyl $\nu_{C=O}$	II Carbonyl $\nu_{C=O}$	III $\nu_{C=C}$
R = Sec-C_4H_9	1738	1717	1619
R = cyclo-C_5H_9	1736	1712	1618
R = $C_3H_7(CH_3)CH—$	1742	1718	1615
R = $(C_2H_5)_2CH—$	1738	1714	1625
R = $C_4H_9(CH_3)CH$	1738	1715	1622

enolic forms in *trans*-configuration is confirmed by the lack of a marked colour reaction with ferric chloride. The spectra exhibit no separate absorption band corresponding to C=O enolic forms which should appear in the 1700–1730 cm^{-1} range and are suppressed by intensive absorption bands of ketonic forms, the content of which was bromometrically shown to exceed considerably that of enolic forms. The ready solubility of alkyl-α-alkyl acetoacetates in various solvents permits the quantitative estimation of enolization and elucidates the solvent effect on these compounds.

As in the case of ethyl acetoacetate,[25] the solvents do not affect the molar absorption coefficient ratio of tautomeric forms within the accuracy of the experiment. In this case the ratio of optical densities of absorption bands of two tautomeric forms in infra-red spectra of solutions is proportional to the tautomeric equilibrium constant. In Fig. 10 the ratio (D III/D II) of optical densities of III(enolic) to II(ketonic) (Table 1) is plotted against the constant L (Meyer[6]) of the enolizing capacity of solvents. It is seen from Fig. 10 that in α-alkylsubstituted acetoacetate derivatives with branched alkyl groups, the content of enolic forms is essentially independent of the solvent. This agrees with the ultra-violet evidence obtained relating to the effect of such different polar solvents as water, alcohols, ether, and hexane. In Fig. 11 the ultra-violet spectra of ethyl-α-s-butylacetoacetate (XVI) solutions in acidified 67 per cent aqueous methanol (pH 2·5), methanol, ethanol, ether, and hexane are given. All curves agree well in intensity ($\varepsilon \simeq 2000$) and have a maximum at 233 to 240 mμ. *Trans*-enolization of keto-enols with an open chain is, therefore, independent, as far as α-alkylsubstituted acetoacetates are concerned, of the nature of the solvent, and

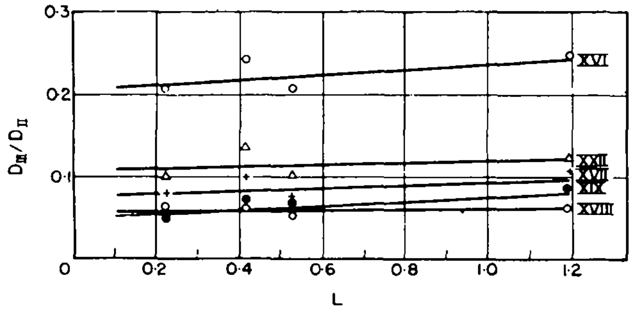


FIG. 10. A plot of D III/D II (optical densities of enolic and ketonic forms of ethyl α-alkylacetoacetates with branched substituents) against L.

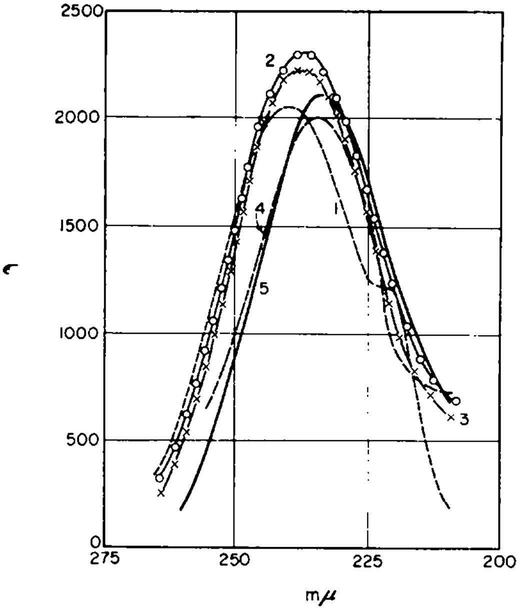


FIG. 11. Ultra-violet spectra of ethyl α-s-butylacetoacetate in (1) 67 per cent aqueous methanol at pH 2·50 (......) methanol (—o—o—o—o) (3) ethanol (×—×—×—×—) (4) hexane (— — — — —) (5) ether (————).

does not accord with either Meyer's rule or Arndt–Eistert and Reiss' hypothesis. The spectral data obtained fully coincide with direct bromometrical determination of the amount of enolic forms contained in different α-alkylacetoacetates. The compounds investigated are all weak acids and so the bromometrical procedure affords reliable results. In Tables 2, 3, and 4 the values obtained for esters with branched substituents together with those for esters with other alkyl and aryl substituents are listed.

TABLE 2. ENOL PERCENTAGE IN α-SUBSTITUTED ETHYL ACETOACETATES IN DIFFERENT SOLVENTS

Substituent R in $CH_3COCHRCOOC_2H_5$	Solvent					
	67%-CH_3OH	CH_3OH	C_2H_5OH	C_6H_6	$(C_2H_5)_2O$	CCl_4
C_2H_5	0·9	1·8	2·8	4·2		
n-C_3H_7	1·9	3·0	4·2	5·6		
n-C_4H_9	3·4	4·3	5·4	6·2		
n-C_7H_{15}	3·6	4·9	6·0	7·0		
iso-C_3H_7	2·6	3·0	3·1	3·6		
iso-C_4H_9	3·3	4·7	6·7	7·9		
s-C_4H_9	14·3	14·5	13·9	14·6		14·8
$(C_2H_5)_2CH$	6·2	6·7	7·2	8·0	9·3	
n-$C_3H_7(CH_3)CH$—	3·9	4·1	4·3	5·1	6·1	7·2
n-$C_4H_9(CH_3)CH$—	4·5	4·7	4·8	4·9	5·8	6·2
n-$C_5H_{11}(CH_3)CH$—	3·8	3·9	4·1	4·4		
n-$C_6H_{13}(CH_3)CH$—	3·9	4·5	4·4	4·7		
Cyclohexyl	1·7	1·6	2·3	3·1		
Cyclopentyl	10·9	11·7	11·7	12·1		11·6
$C_6H_5CH_2$	1·6	3·2	5·0	7·9		

TABLE 3. ENOL PERCENTAGE IN α-SUBSTITUTED ETHYL ACETOACETATES IN DIFFERENT SOLVENTS

Substituent R in CH_3COCH-$RCOOC_2H_5$	Solvent									
	67% CH_3OH	CH_3CO-OH	CH_3OH	$CHCl_3$	C_2H_5OH	CH_3CO-OC_2H_5	C_6H_6	$C_6H_5CH_3$	$(C_2H_5)_2O$	CCl_3
H	2·0	5·7	7·1	8·3	11·4	13·0	18·3	21·0	29·1	34·6
CH_3	1·1		2·5		3·9	4·0	5·2	9·0		
C_6H_5	8·4	22·5	19·0	32·0	26·0	40·1	51·5	56·1		68·9

TABLE 4. *Cis*-ENOL PERCENTAGE IN THE ENOLIC FRACTION OF α-SUBSTITUTED ETHYL ACETOACETATES IN DIFFERENT SOLVENTS

Substituent R in $CH_3COCHRCO$-OC_2H_5	E	E_1	Solvent						Reaction* with FeCl
			67% CH_3OH	CH_3OH	C_2H_5OH	C_6H_6	$(C_2H_5)_2O$	CCl_4	
CH_3	0·319	−0·001	100	100	100	100			
C_2H_5	0·177	0·005	46·6	74·8	83·1	89·5			+ +
n-C_3H_7	0·201	0·015	25·1	51·1	63·4	75·0			+ +
n-C_4H_9	0·156	0·033	10·6	26·9	37·9	51·5			+ +
n-C_7H_{15}	0·187	0·036	11·3	39·0	40·1	53·2			+ +
iso-C_3H_7	0·050	0·026	4·6	13·0	19·9	30·1			−
iso-C_4H_9	0·267	0·030	18·1	41·2	53·7	66·8			+
s-C_4H_9	0·016	0·165	0·3	0·8	1·3	2·2		5·0	−
$(C_2H_5)_2CH$—	0·097	0·065	3·5	10·4	16·1	25·1	37·9		+
n-$C_3H_7(CH_3)CH$—	0·072	0·037	4·5	15·5	20·1	30·4	44·4	50·7	−
n-$C_4H_9(CH_3)CH$—	0·037	0·046	2·0	5·9	9·4	15·5	24·7	29·9	−
n-$C_5H_{11}(CH_3)CH$—	0·035	0·038	2·2	6·8	10·6	17·1			−
n-$C_6H_{13}(CH_3)CH$—	0·039	0·041	1·9	7·0	11·0	17·7			−
Cyclohexyl	0·081	0·013	13·2	32·7	44·5	58·9			+
Cyclopentyl	0·008	0·13	0·2	0·5	0·8	1·4		3·3	−
$C_6H_5CH_2$	0·362	0·007	55·5	79·9	86·8	91·9			+ +

* + + —instantaneous colouration + —faint colouration, − —no colouration.

TABLE 5. *Cis*-ENOL PERCENTAGE IN THE ENOL-FRACTION OF ETHYL α-PHENYLACETOACETATE IN DIFFERENT SOLVENTS

E	E_1	Solvent				
		CH_3COOH	$CHCl_3$	$CH_3COOC_2H_5$	C_6H_6	$C_6H_5CH_3$
4·722	0·006	98·1	98·7	99·2	99·5	99·6

The esters with branched alkyl substituents (XVI–XXII) display a far-reaching constancy in bromine consumption in different solvents and give no colour reaction with ferric chloride (see Table 4). This confirms that L' remains constant in formula (1) for *trans*-enolization of α-substituted acetoacetates and hence formula (2) may be applied in the investigation of a quantitative determination of their keto-*cis*-*trans*-enol equilibrium. This removes the doubts expressed by Eistert and Geiss[26].

In Figs. 12, 13 and 14 the dependence of K_T on Meyer's L for these substances is given. In all instances studied good linear relationships corresponding to formula (2) are observed. For compounds with branched alkyl substituents the slope of the straight lines is gradual. It increases in passing to non-branched alkyls, reaches 45° with ethyl acetoacetate (standard compound) and becomes steeper still with ethyl-α-phenylacetoacetate. The data obtained were used to calculate in terms of formula (2) the constants E and E_1 and the percentage of *cis*-enolic forms in the enol fraction of keto-enols (see Tables 4 and 5).

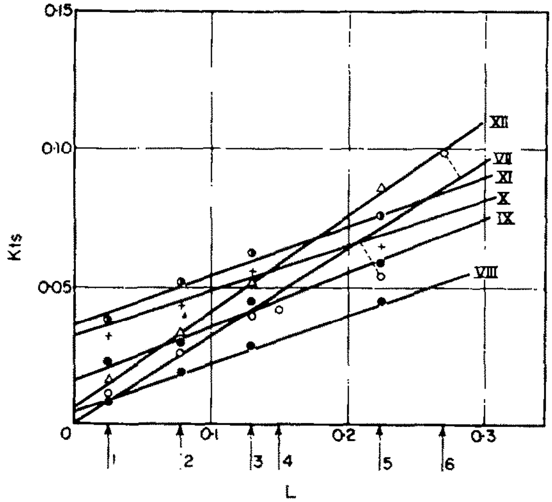


FIG. 12. Dependence of tautomeric equilibrium constant (K_T) on the solvent (constant L) for α-substituted ethylacetoacetates with non-branched substituents. $CH_3COCHRCOOC_2H_5$: VII $R = CH_3$, VIII $R = C_2H_5$, IX $R = n\text{-}C_3H_7$, X $R = n\text{-}C_7H_9$, XI $R = n\text{-}C_7H_{15}$, XIII $R = C_6H_5CH_2$ Solvents: (1) 67 per cent CH_3OH (2) CH_3OH (3) C_2H_5OH (4) $CH_3COOC_2H_5$ (5) C_6H_6 (6) $C_6H_5CH_3$.

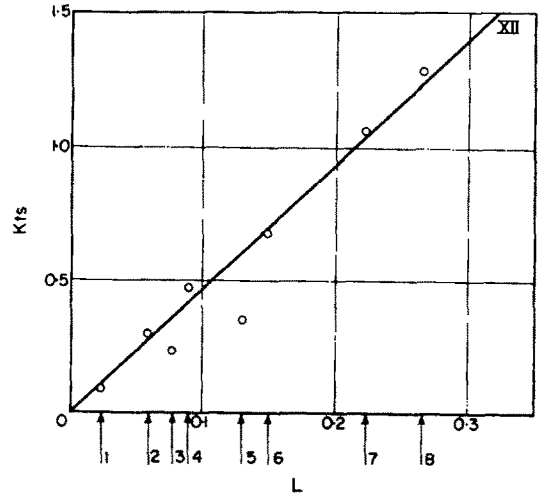


FIG. 13. Dependence of the tautomeric equilibrium constant (K_T) on the solvent (Constant L) for ethyl α-phenylacetoacetate. Solvents: (1) 67 per cent CH_3OH (2) CH_3COOH (3) CH_3OH (4) $CHCl_3$ (5) C_2H_5OH (6) $CH_3COOC_2H_5$ (7) C_6H_6 (8) $C_6H_5CH_3$

3. CONCLUSION

The solvent effect on *trans*-enolization is to a great extent dependent on the nature of the keto-enol yielding *trans*-enol, the keto-enols being classified as follows:

1. Cyclic β-diketones, such as dimedone, containing two carbonyl groups in the same ring.

These compounds have been studied in detail by Eistert *et al.* and their spectra were found to exhibit a solvent relationship not in accordance with Meyer's rule. Hydrophilic solvents show a dominance of the enolic (*trans*-) form and in hydrophobic

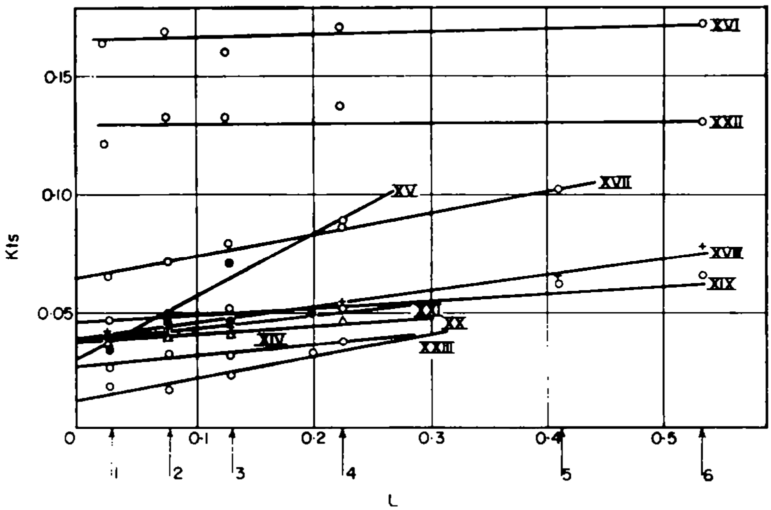


FIG. 14. Dependence of the tautomeric equilibrium constant (K_T) on the solvent (constant L) for α-substituted ethyl acetoacetates with branched substituents $CH_3CHRCOOC_2H_5$: XIV R = i-C_3H_7; XV R = i-C_4H_9; XVI R = s-C_4H_9 XVII R = 3-pentyl; XVIII R = 2-pentyl; XIX R = 2-hexyl; XX R = 2-heptyl; XXI R = 2-octyl; XXII R = cyclopentyl; XXIII R = cyclohexyl. Solvents: (1) 67 per cent CH_3OH (2) CH_3OH (3) C_2H_5OH (4) C_6H_6 (5) ether (6) CCl_4

solvents the ketonic form is present. Hence, Meyer's rule does not hold whilst the hypothesis of Eistert and Reiss is valid.

2. Cyclic β-ketolactones, such as alkyltetronic acid. The concentration of the enolic form is approximately constant in different solvents. The ethereal solvents (ether, dioxan) lead to an increased enol content, probably because in these solvents only the enolic (*trans*-) form is capable of hydrogen bonding with the ether oxygen atoms of the solvent.

In solvents containing hydroxyls, hydrogen bonds produce both ketonic (with O—H groups of the solvent) and enolic forms. Judging from the experimental results, this capacity of the two forms changes to an equal degree from one hydroxyl containing solvent to another. It is noteworthy that in dichloroethane the tautomeric equilibrium constant is the same as in water or alcohols. Neither Meyer's rule nor Eistert and Reiss' hypothesis can be applied to "*trans*-fixed" keto-enols of this type.

3. Cyclic acetals of malonic acid, such as isopropylidene alkylmalonates. Here enolization is negligible in all solvents and there is, therefore, no action of solvent on enolization. Meyer's rule and Eistert and Reiss' hypothesis do not hold.

4. Keto-enols with open chains, such as alkyl α-alkylacetoacetates. As in 2, *trans*-enolization is to a large extent independent of the solvent and ethereal solutions are characterized by a small increase in enolic forms. In the case of cyclic and non cyclic α-alkyl-β-keto-carboxylates L' may be regarded as constant in formula (1) and hence, for α-alkyltetronic acids and α-alkylacetoacetates with strong steric hindrances, EL is equal to zero and formula (1) becomes $K_T = E'L' = \text{Const}$, and (*trans*)-enolization is independent of the solvent there being virtually no *cis*-enol and the reaction with ferric chloride being negative.

For α-alkylacetoacetates with small substituents it is normal to have all three forms present in solution. It can be assumed that *trans*-enolization does not depend on the solvent as with α-alkyltetronic acids or α-alkylacetoacetates with branched substituents, that is $L' = \text{Const}$. They differ, however, in $EL \neq 0$, formula (1) being thereby converted to formula (2). Plot $K_T = f(L)$ is a straight line with a stronger or weaker slope that cuts on the ordinate axis an intercept characteristic of *trans*-enolization. As seen from Table 4 the amount of *cis*-enolic forms increases with decreasing

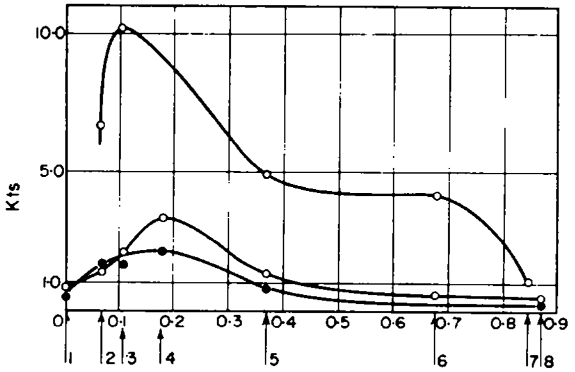


Fig. 15. Dependence of the tautomeric equilibrium constant (K_T) of cyanoketones on the solvent (constant L) with ethyl acetoacetate as standard compound.

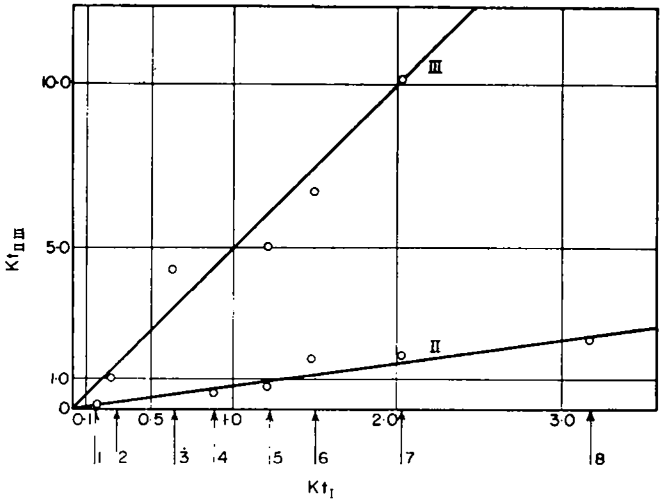


Fig. 16. Dependence of the tautomeric equilibrium constant (K_T) of cyanoketones on the solvent (constant L') with cyanodesoxybenzoin as standard compound. I-cyanodesoxybenzoin II α(2-furoyl) phenylacetonitrile; III α-(2-furoyl)-3, 4-dichlorphenyl-acetonitrile

steric hindrances caused by alkyl radicals. These compounds give a pronounced colour reaction with ferric chloride, enolization of such compounds being expressed in terms of formula (2).

5. *Enols produced from cyano-ketones studied by Russel.* In this case both the *trans*- and *cis*-enols have an open hydroxyl group and, as seen from Fig. 15 (co-ordinates K_T and L) the dependence of enolization on the solvent is very involved. The *cis*-enolizing capacity of the solvent (the Meyer's constant L) being increased, K_T passes

TABLE 6. PROPERTIES OF ETHYL α-ALKYL ACETOACETATES

Substituent R in $CH_3COCHRCOOC_2H_5$	b.p./mm	n_D^{20}	d_4^{20}	Literature data	Reference	Analyses C Found	C Calc.	H Found	H Calc.
CH_3	66–66·5/8	1·4200	0·9989	b.p. 75–76·5°/12 mm, n_D^{15} 1·4237	32	57·8;58·0	58·3	8·4;8·6	8·3
iso-C_4H_9	105–108/16	1·4300	0·9511	b.p. 104–106°/14 mm	33	64·7;64·6	64·6	9·7;9·7	9·7
n-$C_3H_7CHCH_3$	96–99/7	1·4350	0·9492	b.p. 226°	34	66·0;66·1	66·0	10·1;10·2	10·1
$(C_2H_5)_2CH$	100/9	1·4375	0·9568	—	—	66·2;66·1	66·0	10·1;10·1	10·1
n-$C_4H_9(CH_3)CH$	118–121/10	1·4370	0·9433	b.p. 130–132°/17 mm	35	67·2;67·2	67·2	10·4;10·3	10·3
n-$C_5H_{11}(CH_3)CH$	123–124/8	1·4388	0·9331	b.p. 250–260°	36	68·7;68·6	68·5	10·8;10·4	10·6
s-C_4H_9	68/3	1·4350	0·9584	b.p. 102/104°/15 mm	37	64·5;64·6	64·5	9·8;9·8	9·7
n-$C_6H_{13}(CH_3)$ CH	114–116/2	1·4397	0·9254	b.p. 280–282°	38	69·6;69·7	69·4	11·0;11·1	10·8
n-C_7H_{15}	122–124/3	1·4365	0·9291	b.p. 141·6/10 mm n_D^{15} 1·4376 d_4^{15} 0·9327	39	68·1;68·2	68·5	10·5;10·5	10·6
Cyclopentyl	115/7	1·4570	1·0155	b.p. 118–120°/12 mm; n_D^{20} 1·4646	40	66·7;67·0	66·6	9·1;9·3	9·2
Cyclohexyl*	95–96/3	1·4618	1·0386	b.p. 146–148°/12 mm	41	67·9;67·6	67·9	9·3;9·3	9·5
C_6H_5†	113–115/2·5	1·5170	1·0855	b.p. 130–134°/5 mm	42	69·9;70·0	69·9	6·8;6·9	6·8
$C_6H_5CH_2$	110·5–112/2	1·5056	1·0636	b.p. 164–165°/12 mm	43	70·6;70·4	70·9	7·3;7·3	7·3

* Obtained from ethyl acetoacetate, cyclohexanol, and BF_3

† Obtained via α-phenyl-α-acetylacetonitrile

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through the maximum. These curves become straight lines when applying L' (formula 1) instead of L, that is when substituting the standard compound. If any cyano-ketone is taken as standard, good linear relationships are observed and the straight lines pass through the origin (Fig. 16). Enolization to form a chelated enol being impossible in this case, $E = 0$ and formula (1) becomes similar to that of Meyer, $K_T = E'L'$ but differing from it as to the standard compound. Here again the relatively high enolizing capacity of ether may be due to its hydrogen bonding with the open hydroxyl group of the enolic form. Thus for this case both Meyer's rule and Eistert and Reiss' hypothesis do not hold true but when choosing a suitable standard compound formula $K_T = E'L'$ can be applied.

The above types of keto-enols do not exhaust all the possibilities of solvent effect on *trans*-enolization and even these examples point to the great variety of such effects; only types such as dimedon follow the hypothesis suggested by Eistert and Reiss.

Formula (1) is of a general character and its application depends on the right choice of standards for L and L'. Formula (2) is of a more limited value and can be applied only to those systems characterized by $L' = \text{Const.}$

EXPERIMENTAL

The α-substituted acetoacetates were produced by alkylating sodium ethyl acetoacetate with suitable alkyl halides, the properties of the compounds investigated are listed in Table 6.

Isopropyliden ethylmalonate m.p. 107° was obtained as described previously.[14] (Found: C, 56·1, 56·1; H, 7·2, 7·3. Calc. for $C_8H_{12}O_4$: C, 55·8; H, 7·0%).

Deuterated isopropylidene ethylmalonate, m.p. 107°. (Found: C, 55·4, 55·2; H, 7·0, 7·0. Calc. for $C_8H_{11}OD$: C, 55·5; H, 7·6%).

Ethyltetronic acid, m.p. 127–128° and propyltetronic acid, m.p. 126° were obtained as described.[45]

Lactone of γ-hydroxy-α,α-dimethylacetoacetic acid was synthesized according to Conrad[46] from ethyl γ-acetoxy-α,α-dimethylacetoacetate, b.p. 72·5°/5 mm; n_D^{20} 1·4483; d_4^{20} 1·1496. (Lit. b.p. 208–209°; d_{15}^{18} 1·147. (Found: C, 56·2, 56·3; H, 6·6, 6·6. Calc. for $C_6H_8O_3$: C, 56·2; H, 6·3%.)

The bromometrical titration of 1 per cent solutions was carried out according to Hesse and Krehbiel with alcoholic bromine solution.

The pH determination of solutions for spectral study was carried out with a potentiometer LP-5 with an accuracy of 0·05 pH units.

The infra-red spectra were obtained on a double beam spectrometer IKS-14. The samples of crystalline compounds were pressed together with potassium bromide.

The ultra-violet spectra were taken on spectrometer SFD-1. The concentration of solutions investigated is referred to in the text in subtitles.

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