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DIPOLE MOMENTS OF 5-SUBSTITUTED ISOXAZOLES—I

DIPOLE MOMENTS AND TAUTOMERISM OF ISOXAZOLIN-5-ONES

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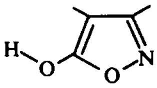
Abstract—The tautomerism of isoxazolin-5-ones was investigated by experimental determination of the dipole moments of several isoxazolin-5-ones, N-methylisoxazolin-5-ones and 5-methoxyisoxazoles. Experimental values were then compared with the theoretical ones obtained by vector addition of the σ and π moments.

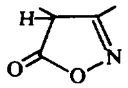
Our results show that isoxazolin-5-ones in dioxan can exist in all the three allowed tautomeric forms, though the ketonic forms are generally predominant.

The recent syntheses of 3,4-dimethyl-isoxazolin-5-one and its N-methyl and O-methyl-derivatives[1] has emphasized the problem of tautomerism of isoxazolin-5-ones,[2–4] which is of particular interest in connection with the aromaticity of the isoxazole ring.

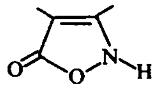
The isoxazolin-5-ones can be represented by one of the three tautomeric forms (I, II and III):



I



II



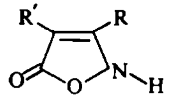
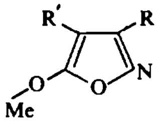
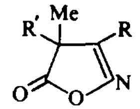
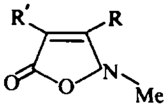
III

The passage from I to II and III implies the disappearance of isoxazole's aromatic sextet.

The aim of the present paper is (i) to report new data on the dipole moments of the isoxazolin-5-ones and the Me derivatives of the forms I, II and III in which protomeric changes have been rendered impossible and (ii) to use these data and published information[2] to discuss the problem of tautomerism. The data are summarized in Table 1.

As isoxazolin-5-ones tend to associate intermolecularly in non-polar solvents commonly used in the measurement of dipole moments, as shown by mol. wt. determinations and by the variation of the dipole moment with concentration, the tautomerism was studied in dioxan. From the data reported in Table 1 it is evident that all forms I, II and III must be considered in the tautomeric equilibrium of isoxazolin-5-ones: hence to interpret the results it was necessary to evaluate the moments of these forms. To achieve this aim, it was necessary to evaluate first the moments of

Table 1. Experimental dipole moments of isoxazolin-5-ones and their methyl derivatives of forms I, II, III in which tautomeric changes are inhibited

	 Isoxazolin-5-ones[a]		 5-methoxy-isoxazoles (I)		 C_4-methylisoxa-zolin-5-ones (II)		 N-methylisoxa-zolin-5-ones (III)	
	Benz.	Diox.	Benz.	Diox.	Benz.	Diox.	Benz.	Diox.
R = Me; R′ = H							5·89	
R = H; R′ = Me							5·15	
R = Ph; R′ = H	4·9[b]	5·13[b]	3·80[b]	3·896			5·974	
R = H; R′ = Ph		4·69	2·065				5·40	
R = Me; R′ = Me	(4·73)[c]	5·32	2·468	2·521	5·00[b]	5·11[b]	5·678	5·844[b]
R = Ph; R′ = Me		5·64[b]		2·83[b]	4·93[b]	5·10[b]	5·704	5·85[b]
R = Me; R′ = Ph		5·62[b]		2·32[b]		4·86[b]	5·640	5·95[b]

[a] Isoxazolin-5-ones are here written in form III, but they may of course exist in form I and II also.

[b] Ref. 2.

[c] The great difference between μ_{benzene} and μ_{dioxan} is to be attributed to molecular association in benzene solutions.

the Me derivatives of forms I, II and III in which tautomeric changes are inhibited and to obtain the best possible agreement with experimental results.

The present paper shows that dipole moment measurements can provide precise data about the relative amounts of different tautomeric forms present in the system.

DISCUSSION

Theoretical calculation of dipole moments. Table 1 shows that the moments of 5-methoxyisoxazoles range from 2 to 3D (except for 3-phenyl-5-methoxy which has a moment of 3·8D), those of C_4-methylisoxazolin-5-ones* are about 5D and those of N-methylisoxazolin-5-ones in the range 5·2–6D, while the moments of isoxazolin-5-ones range from 4·6 to 5·9D.

In order to interpret the moments of isoxazolin-5-ones in relation to their tautomeric possibilities it is necessary to estimate the moments of the three forms I, II, III. It is known that in the dipole moment calculation of conjugated compounds one must take into account the high polarizability of the π electrons, hence we treated the latter by the Hückel method. This method has been applied successfully to the calculation of some properties of different isoxazole derivatives.[11] However, we could not use the parameters suggested by Orgel *et al.*[12] as in Ref. 11, because they lead to dipole

---

* In the following test C_4-disubstituted-isoxazolin-5-ones will be referred to as C_4-methyl-isoxazolin-5-ones to emphasize that they are the methyl derivatives of form II in which tautomeric changes have been inhibited.

moment values of 2 or 3D higher than the experimental ones in such compounds as isoxazolin-5-ones in the carbonilic forms II and III.

In order to obtain the necessary agreement between experimental and calculated moments, on the basis of $h_{\dot{x}}$, $h_{\ddot{x}}$ and k_{x-y} values given by Streitwieser[13, 14] we determined a new set of parameters, which are valid not only for the above compounds, but also for all the ones treated in Refs 11 and 12. The parameters used are as follows:

$$
\begin{array}{llll}
h_{\ddot{O}} = 2{\cdot}6 & k_{C—O} = 0{\cdot}7 & & k_{C=O} = 1 \\
h_{\dot{O}} = 0{\cdot}65 & k_{N—O} = 0{\cdot}5 & & \\
h_{\ddot{N}} = 1{\cdot}9 & k_{C—N} = 0{\cdot}7 & k_{C=N} = k_{C\cdots N} = 1 & \\
h_{\dot{N}} = 0{\cdot}55 & & & \\
h_{CH_3} = 3 & k_{C—CH_3} = 0{\cdot}7 & k_{C—C_4} = k_{C_4—C_5} = 0{\cdot}7 & \\
\end{array}
$$

$$\delta_{\ddot{x}} = \tfrac{1}{20} \qquad \delta_{\dot{x}} = \tfrac{1}{10}$$

For the Me group we adopted the heteroatom model,[14] which gave values in very good agreement with experiment in the case of Me derivatives of isoxazole.

For $k_{C—C}$ the normally accepted value of 1 was assumed for the C—C simple bond in the ground state structure of aromatic rings (furane, pyrrole, isoxazole, etc.), while a value of 0·7 was used for $C_{isox.}—C_{phen.}$ bond in phenylisoxazoles and for $C_4—C_5$ bond in isoxazolin-5-ones.

In the absence of bond length values for most of the molecules studied, all rings were assumed to be regular polygons with sides 1·4 Å long. The calculation of the π moment of 1,2,5-oxadiazole with the experimental bond distances ($\mu_\pi = 1{\cdot}21$D)[15] shows that the above approximation does not bring about substantial difference in the results (1·33D for the regular pentagon).

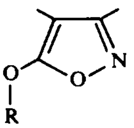
From molecules of similar structure we have taken the following bond distances[16] for the ring substituents:

$$
\begin{array}{ll}
C—CH_3 = 1{\cdot}53\,\text{Å} & C—O = 1{\cdot}36\,\text{Å} \\
C{=}O = 1{\cdot}22\,\text{Å} & C—N = 1{\cdot}47\,\text{Å}
\end{array}
$$

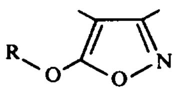
The σ bond moment was estimated by the vectorial sum from the following conventional magnitudes and directions of bond moments:[12, 17]

$$
\begin{array}{lll}
\overleftarrow{CH} = 0{\cdot}3 & \overleftarrow{NH} = 1{\cdot}31 & \overrightarrow{CN} = 0{\cdot}45 \\
\overrightarrow{CO} = 0{\cdot}86 & \overrightarrow{NO} = 0{\cdot}5 &
\end{array}
$$

In accord with $\mu_{CN} = 0{\cdot}45$D,[17–19] we adopted a value of $\mu_{CH} = 0{\cdot}3$D instead of 0·4D.[12] The NO moment was taken to be 0·5D[12] instead of Smyth's uncertain value of 0·3D.[17] For methoxy and hydroxyisoxazoles (form I) the σ moments were calculated for both possible configurations



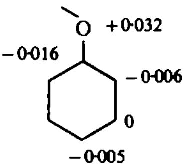
1



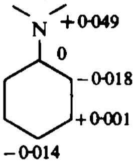
2

with the C—O—R angle of 120°.

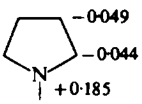
Table 2. Charge distributions in molecules taken in consideration to fix the set of parameters



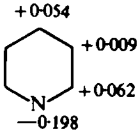
Phenol



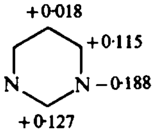
Aniline



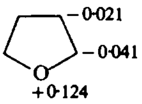
Pyrrole



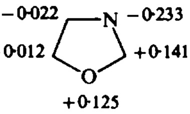
Pyridine



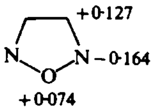
Pyrimidine



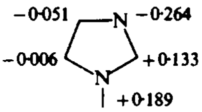
Furane



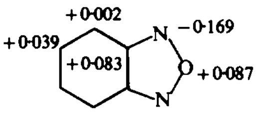
Oxazole



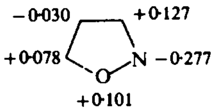
Oxadiazole



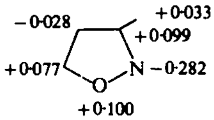
Iminazole



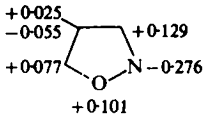
Benzfurazane



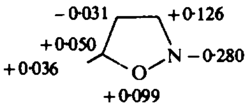
Isoxazole



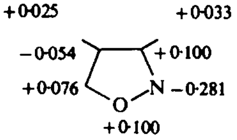
3-Methyl-isoxazole



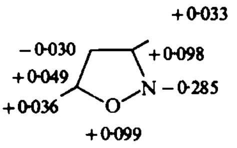
4-Methyl-isoxazole



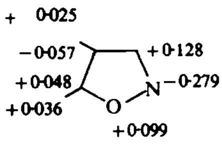
5-Methyl-isoxazole



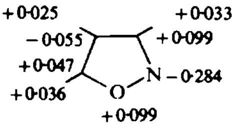
3,4-Dimethylisoxazole



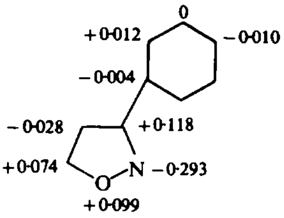
3,5-Dimethylisoxazole



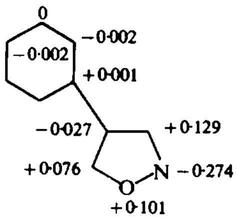
4,5-Dimethylisoxazole



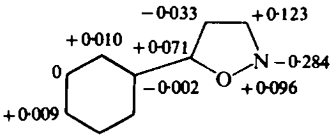
3,4,5-Trimethylisoxazole



3-Phenylisoxazole



4-Phenylisoxazole



5-Phenylisoxazole

The values under "calculated 1" in Tables 6 and 7 refer to these two configurations.

Charge distributions in the molecules calculated from our set of parameters are given in Table 2. The relative ratios of net charges on different atoms in each molecule are in general agreement with Orgel's results, but in our case it is not necessary to divide by 1·6 to obtain the π moment.

Table 3 shows the experimental and calculated values of the moments with the angle α relative to μ_{tot}.

Table 3. Comparison between experimental and calculated moments of molecules in table 2

	$\mu_{calc.}$				$\mu_{exp.}$[b]
	μ_σ	μ_π	μ_{tot}	α[a]	
phenole	1·58	0·50	1·44	0°	1·45–1·72
aniline	1·26	0·74	1·54	0°	1·30–1·55
pyrrole	0·47	1·35	1·82	0°	1·80
pyridine	0·75	1·34	2·09	180°	1·96–2·28
pyrimidine	0·75	1·30	2·05	180°	2·40
furane	1·24	0·76	0·48	180°	0·63–0·71
oxazole	0·80	2·13	1·53	76°	1·50[c]
oxadiazole	1·93	1·33	3·26	180°	3·38[d]
N-methyliminazole	0·77	2·76	3·38	83°	3·60
benzfurazane	1·96	2·18	4·14	0°	4·03
isoxazole	1·77	1·42	2·81	131°	2·76–2·84
3-methylisoxazole	1·77	1·35	2·88	136°	2·86
4-methylisoxazole	1·77	1·54	2·975	132°	3·12
5-methylisoxazole	1·77	1·72	3·00	126°	3·04
3,4-dimethylisoxazole	1·77	1·49	3·05	137°	3·15
3,5-dimethylisoxazole	1·77	1·63	3·04	131°	3·08
4,5-dimethylisoxazole	1·77	1·83	3·16	127°	3·23
3,4,5-trimethylisoxazole	1·77	1·75	3·21	132°	3·40
3-phenylisoxazole	1·77	1·37	2·99	141°	2·80–3·00
4-phenylisoxazole	1·77	1·32	2·70	131°	2·90
5-phenylisoxazole	1·77	1·89	3·12	123°	3·30
3-methyl-4-phenylisox.	1·77	1·25	2·77	134°	(e)
3-phenyl-4-methylisox.	1·77	1·53	3·17	128°	(e)

[a] α is measured clockwise from: (i) the upward symmetry axis in the charge diagrams of Table 2 for symmetric molecules except for benzfurazane, in which the axis is directed towards the oxygen (ii) the upward vertical axis passing through the position 1 of the ring for all the other ones.

[b] A. L. McClellan *Tables of experimental dipole moments* W. H. Freeman & Company, S. Francisco and London (1963).

[c] W. C. Mackrodt, *Chem. Comm.* 692 (1966).

[d] Ref. 15.

[e] This compound is not yet known.

The results in good agreement with the experimental include phenol and aniline (not considered by Orgel) and are better than those given by Orgel for furane, 1,2,5-oxadiazole (the value given in Ref. 12 is that for the 3,4-dimethyl derivative) and benzfurazane (recent dipole moment determinations give a value of 4·03D instead of 4·4D).

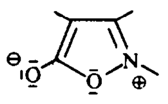
N-methylisoxazolin-5-ones and C_4-methylisoxazolin-5-ones. Table 4 shows the values of calculated and experimental moments for the above compounds, in which protomeric changes have been rendered impossible.

TABLE 4. EXPERIMENTAL AND CALCULATED MOMENTS OF N-METHYL AND C_4-METHYLISOXAZOLIN-5-ONES

Isoxazolin-5-ones	N-methyl				C_4-methyl			
	$\mu_{exp.}$		$\mu_{calc.}$	α	$\mu_{exp.}$		$\mu_{calc.}$	α
	Benz.	Diox.			Benz.	Diox.		
3-methyl	5·89		5·82	243°				
4-methyl	5·15		5·49	241°				
3-phenyl	5·974		5·94	241°				
4-phenyl	5·40		5·55	247°				
3,4-dimethyl	5·678	5·844	5·78	240°	5·00	5·11	4·37	209°
3-methyl-4-phenyl	5·640	5·95	5·84	244°		4·86	4·37	209°
3-phenyl-4-methyl	5·704	5·85	5·88	239°	4·93	5·10	4·72	197°

Agreement is excellent for N-methylisoxazolin-5-ones and very satisfactory for compounds with a substituent (Me or Ph) in position 4. Some deviations had been noticed earlier for 4-substituted phenylisoxazoles[11] and were confirmed by our calculations on these compounds.

In N-methylisoxazolin-5-ones, the value of the charge on the ring oxygen is substantially lower than those in form I and II derivatives. This supports Speroni's hypothesis[2] that the high dipole moment of N-methylisoxazolin-5-ones arises from a strong contribution of the polar form (a) in which the ring oxygen does not participate in the conjugation.



(a)

In the case of C_4-methylisoxazolin-5-ones, the agreement between experiment and calculations is not as good. This can be attributed both to the change of hybridization of the carbon atom in position 4 which cannot be taken into account in this calculation and to the fact that the π electron system does not extend over the entire molecule.

Table 5 shows the charge distributions of isoxazolin-5-ones and their Me derivatives of forms I, II and III in which tautomeric changes are inhibited.

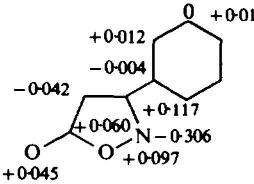
5-Methoxyisoxazoles. The interpretation of experimental moments was rendered difficult by the possible rotation of the MeO group around the C_5—O bond.

For this reason the theoretical moment of methoxyisoxazoles was evaluated by vector addition also. In this method, the moments of configurations **1**, **2** and that corresponding to free rotation were calculated by the formula

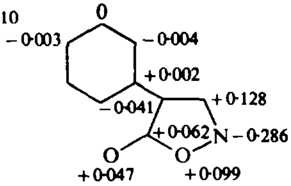
$$\bar{\mu}^2 = \mu_1^2 + \mu_2^2 + 2\mu_1\mu_2 \cos\phi \,.\, \cos\theta$$

TABLE 5. CHARGE DISTRIBUTIONS IN ISOXAZOLIN-5-ONES AND THEIR METHYL DERIVATIVES OF FORM I, II, III

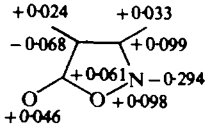
Form I



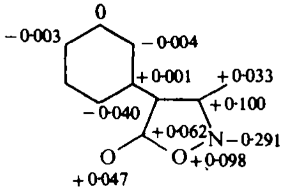
3-Phenyl



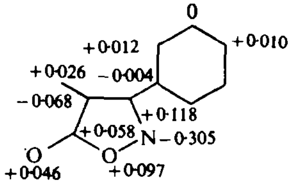
4-Phenyl



3,4-Dimethyl

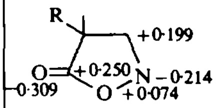


3-Methyl-4-phenyl

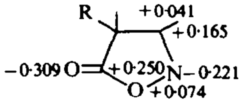


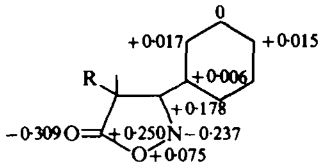
3-Phenyl-4-methyl

Form II



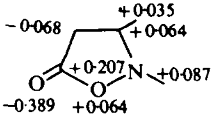
(*)



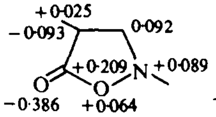


R = H; Me; C_6H_5.

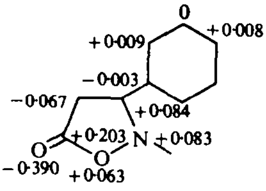
Form (II)



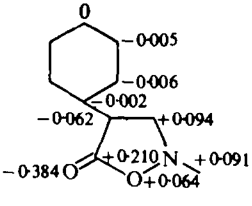
3-Methyl



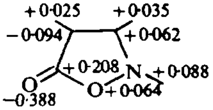
4-Methyl



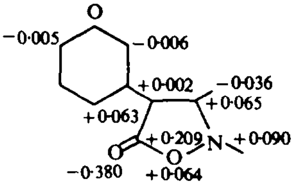
3-Phenyl



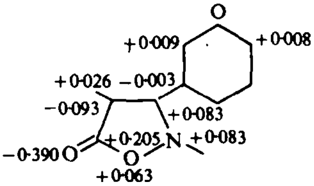
4-Phenyl



3,4-Dimethyl



3-Methyl-4-phenyl



3-Phenyl-4-methyl

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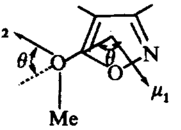
* This charge diagram has been reported because it is useful to calculate the π moment of form II of the corresponding isoxazolin-5-ones.

in which μ_1, μ_2 are group moments and ϕ, θ the angles in the figure below.



The values of μ_2 and $\phi(\mu_2 = 1{\cdot}25\text{D};\ \phi = 55°)$ were taken from Ref. 19 and μ_1 and θ were deduced from the theoretical values of μ_{tot} and α of the corresponding isoxazoles reported in Table 3 ($\mu_1 = \mu_{\text{tot}};\ \theta = 180° - \alpha + 72°$). The moments of the two methylphenylisoxazoles, which have not been synthesized, were also calculated. The moments of configurations **1** and **2** estimated with the present method and reported under "calc. 2" differ at most by 0·3D (Table 6) from those calculated by the previous theoretical method (calc. 1).

Table 6. Experimental and calculated moments of 5-methoxyisoxazoles

5-Methoxyisoxazoles	$\mu_{\text{exp.}}$		$\mu_{\text{calc.}}$				
			Calc.$_1$		Calc.$_2$		
	Benz.	Diox.	Conf. 1	Conf. 2	Conf. 1	Fr. rot.	Conf. 2
3-Phenyl	3·80	3·896	2·02	3·89	1·80	2·99	3·83
4-Phenyl	2·065		1·79	3·49	1·46	2·62	3·41
3,4-Dimethyl	2·468	2·521	2·11	3·93	1·83	3·00	3·83
3-Methyl-4-phenyl		2·32	1·79	3·59	1·54	2·71	3·52
3-Phenyl-4-methyl		2·83	2·19	4·07	1·92	3·01	3·80

From Stuart and Briegleb models, one can expect that configuration **2** is more sterically hindered whenever position 4 is occupied by a substituent. Thus, configuration **1** is expected to have a greater statistical weight than that of **2**.* This is consistent with the fact that the experimental moments are always between the moments calculated for configuration **1** and the free rotation model (Table 6). The exception is 3-phenyl-5-methoxyisoxazole, which is the only 5-methoxyisoxazole without a

Table 7. Experimental moments of isoxazolin-5-ones and calculated values for forms I, II, III

Isoxazolin-5-ones	$\mu_{\text{exp.}}$		$\mu_{\text{calc.}}$						
			Calc.$_1$				Calc.$_2$		
	Benz.	Diox.	C—H	N—H	O—H		O—H		
					Conf. 1	Conf. 2	Conf. 1	Fr. rot.	Conf. 2
3-Phenyl	4·90	5·13	4·72	6·34	1·87	4·23	1·41	3·14	4·22
4-Phenyl		4·69	4·03	5·97	1·74	3·84	1·10	2·79	3·78
3,4-Dimethyl	(4·73)	5·32	4·37	6·17	1·99	4·27	1·45	3·15	4·21
3-Methyl-4-phenyl		5·62	4·37	6·25	1·69	3·94	1·17	2·88	3·90
3-Phenyl-4-methyl		5·64	4·72	6·27	2·03	4·41	1·57	3·15	4·17

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* We plan to determine the dipole moments of our compounds at various temps in order to test this hypothesis.

substituent in position 4. Its experimental moment is about 1D higher than that of a free rotation model and agrees with the calculated value for configuration **2**.

Identical conclusions were obtained from calculations with Orgel's parameters.

Isoxazolin-5-ones. The difference between the moments of each tautomeric form of isoxazolin-5-ones and the moments of the corresponding derivative in which tautomeric changes have been rendered impossible can be attributed primarily to their different substituent group moment alone, that is to their different σ skeleton, while the π electron distribution remains constant. On the basis of this consideration and of the sufficient agreement between calculated and experimental moments for all the compounds treated until now, we can estimate the moments of the three tautomeric forms of isoxazolin-5-ones. The results are summarized in Table 7.

The moments of form I were calculated as for the OMe derivatives, taking $\mu_2 = 1{\cdot}6$ and $\phi = 62°$ for the OH group as in Ref. 19.

As in the 5-methoxyisoxazoles, the rotation of the OH group should be hindered whenever there is a substituent in 4 and hence the dipole moment of form I should be between the moments of free rotation models and those of configuration **1**, that is a value corresponding to MeO derivatives.

The experimental dipole moments $\mu_{exp.}$ of isoxazolin-5-ones is related to the moments μ_I, μ_{II}, μ_{III} of the three protomeric forms by

$$\bar{\mu}^2_{exp.} = N_I\mu_I^2 + N_{II}\mu_{II}^2 + N_{III}\mu_{III}^2$$

where N_I, N_{II}, N_{III} are the mole fractions of tautomers; that means

$$1 = N_I + N_{II} + N_{III}$$

Since these two relations alone are not enough to determine N_I, N_{II} and N_{III}, more details of the physico-chemical behaviour of isoxazolin-5-ones in dioxan were necessary to determine the tautomeric equilibrium.

Although IR and UV spectra of these compounds cannot give the relative amounts of the three forms, they can establish their presence in solution, especially in the case of forms II and III. In fact, both forms have strong and characteristic absorption bands in the C=O stretching frequencies of C_4-methyl and N-methylisoxazolin-5-ones.[2] On the other hand, the O—H stretching frequency is not suitable for identification of form I, since this band is very broad owing to association with dioxan and may overlap with the N—H stretching band of form III. The absence of one of the above C=O stretching bands in the IR of 3-phenylisoxazolin-5-one, 4-phenylisoxazolin-5-one and in 3-methyl-4-phenylisoxazolin-5-one suggests that the amount of the corresponding form is less than 5%.* Both absorption bands at ~1740 cm^{-1} and ~1800 cm^{-1} were present in the spectra of 3,4-dimethylisoxazolin-5-one and 3-phenyl-4-methylisoxazolin-5-one. For both compounds UV spectra in dioxan could only confirm the existence of form III without providing either its relative amount or conclusive evidence of the presence of forms I and II. In the NMR spectrum form II could be identified without doubt. Forms I and III also showed characteristic bands, but it was impossible to attribute them to either one of the two forms or to both forms in equilibrium due to rapid proton exchange.

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* This was confirmed by recording the spectra in dioxan solution of mixtures of C_4-methylisoxazolin-5-ones and N-methylisoxazolin-5-ones.

In the spectrum of 3,4-dimethylisoxazolin-5-one in dioxan* a doublet at 8·68 τ (J = 8·0 c/s) and a singlet at 7·93 τ were assigned to 4-Me and 3-Me substituents of form II respectively, while two singlets at 8·30 τ and 7·88 τ were assigned to the Me in positions 4 and 3 of either one of the two forms I and III or to both of them rapidly interconverting. A band at 0·79 τ was attributed to the NH/OH proton of forms I and III.

A value of 29 ± 1% for the relative amount of form II was calculated from the integrated areas of the Me groups. The spectrum of 3-phenyl-4-methylisoxazolin-5-one in dioxan showed the Ph group multiplet at 2·39 τ, a doublet at 8·55 τ (J = 7·7 c/s) which was assigned to the Me of form II and a singlet at 8·02 τ, which was assigned to the Me of form I and/or III. At 0·86 τ a very broad band (half height width = 22 c/s) was attributed to the NH/OH proton. The relative amount of form II was calculated to be 38 ± 1% from the integrated areas of the Me groups. For both compounds the CH proton of form II fell below the dioxan band: however its absorption was visible in $DCCl_3$. The τ values are in good qualitative agreement with the relative values of net charges for the Me, the only exception being the Me in position 3 of form II of 3,4-dimethylisoxazolin-5-one.

This confirms that the agreement with experimental in the case of form II is not as good as for forms I and III. Consequently, in the calculation of the relative amounts of forms I, II and III of isoxazolin-5-ones a much larger range of error was allowed for the calculated moments of form II and the moments of form I ranged between the experimental moments of the corresponding methoxyisoxazoles and the calculated values for the free rotation models. The results of our calculations are summarized in Table 8.

TABLE 8. PERCENTAGES OF FORMS I, II, III OF ISOXAZOLIN-5-ONES IN DIOXAN SOLUTION

	I	II	III
3-Phenylisoxazolin-5-one	7–0	90–100	0–3
4-Phenylisoxazolin-5-one	49–41	0–5	50–56
3,4-Dimethylisoxazolin-5-one	23–13	28–30	48–58
3-Methyl-4-phenylisoxazolin-5-one	24–19	0–5	74–78
3-Phenyl-4-methylisoxazolin-5-one	9–4	37–39	53–59

CONCLUSIONS

The tautomerism of 3,4-dimethylisoxazolin-5-one has been thoroughly investigated.[1] The ketonic structures II and III should be more stabilized than the enolic I, but on the other hand their delocalization energies are in the relative order I > III > II. Hence the three tautomeric forms can be expected to have a similar energy content. This may account for the dependence of the tautomeric equilibrium on the solvent: while in cyclohexane form II predominates, in dioxan (Table 8) all three forms are present and in highly polar solvents form III is preponderant.

In arylisoxazolin-5-ones the conjugation of the Ph group with the electronic system of the heterocycle is the pre-eminent factor: one of the three forms becomes less probable because its energy is much higher, hence the influence of the solvent

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* NMR spectra were recorded at the Dept. of Organic and Industrial Chemistry of the University of Bologna with a Varian DP-60 (56·4 Mc/s) in dioxan soln, using TMS as internal reference. Integrated areas were measured by a Varian 3521 integrator.

is less marked. Both in 4-phenylisoxazolin-5-one (Table 8)[7] and in 4-phenyl-3-methylisoxazolin-5-one (Table 8)[2,7], form II cannot be identified either in apolar or in polar solvents: the equilibrium is shifted towards form III in 4-phenyl-3-methylisoxazolin-5-one. In fact, the delocalization energies of forms I and III are much greater than that of form II, for in this case the Ph group cannot conjugate with the isoxazolinone ring.

The reason for the low contribution of form I to the tautomeric equilibrium of 3-phenylisoxazolin-5-ones is more obscure. Form II only of 3-phenylisoxazolin-5-one seems to be present in cyclohexane,[4,8] dioxan (Table 8), ether[2] and $CHCl_3$[4] and in very polar solvents only[2,4,8] small amounts of forms I and III do appear.[*]

Form II can be expected to be more stable than III for the steric hindrance existing in the latter, owing to the C_3—C_4 double bond. On the other hand, the greater delocalization energy of form I is probably not enough to overcome the stabilizing effect of the ketonic system on form II. In the case of 3-phenyl-4-methylisoxazolin-5-one, both forms I and III are sterically hindered, but the effect of the Me group on the conjugative system of form III is to bring its energy near to that of form II. This could explain why the tautomeric equilibrium between these two forms is so dependent on the solvent: while in cyclohexane and C_2Cl_4[2,4,8] form II is predominant, in $CHCl_3$ and dioxan (Table 8) almost the same amounts of forms III and II are present and in MeOH[2] and H_2O[4,8] form III becomes the preponderant one.

EXPERIMENTAL

Solutes. References to the syntheses, together with the m.p. or b.p., of compounds whose dipole moments have not been published are given in Table 9.

Solvents. Benzene and dioxan were used in the dipole moment measurements. They were purified and dried according to the usual methods.

Apparatus. Dielectric constants were determined with the apparatus described in Ref. 9 but modified by replacing the 500 pF and 100 pF variable condensers with two precision fixed capacitors of 100 pF and 200 pF and a G.R.C. 1422-ME variable capacitor. This change allowed measurements in two ranges 0–10·5 and 0–105 pF.

Results. The $_\infty P_2$ values in Table 9 have been calculated by the method of Halverstadt and Kumler.[10] The extrapolated data with their standard deviation were obtained by the least square method programmed on an IBM 1620 computer. Details of the computation method will be described later. All measurements were accomplished at 25°. For standardization, suitably purified benzene was used and its dielectric constant at 25° was assumed to be 2·2726. The definition of the symbols appearing in Table 9 are as follows:

f_2	molar fraction of solute [$f_2 = \pi_2 M_1/(\pi_2 M_1 + \pi_1 M_2)$], where M_1, M_2 are the mol. wts. in g of solvent and solutes respectively
ε_{12}	dielectric constant of the solution
d_{12}	density of the solution
n_{12}^2	square of refractive index of the solution
α	ε_{12} vs. f_2 slope
β	d_{12} vs. f_2 slope
γ	n_{12}^2 vs. f_2 slope
ε_1'	extrapolated value of ε_{12} at infinite dilution
d_1'	extrapolated value of d_{12} at infinite dilution
$n_1'^2$	extrapolated value of n_{12}^2 at infinite dilution
$_\infty P_2$	total molecular polarization at infinite dilution in cc
$\overline{MR_2}$	molar refraction in cc, taken equal to the electronic polarization P_E, calculated as the average value of $MR_2 = (MR_{12} - MR_1')/f_2 + MR_1'$,

[*] The spectrum of 3-phenylisoxazolin-5-one in methanol reported in Fig. 32 of Ref. 2 shows a max near 240 mμ (log ε = 4·1) and a shoulder near 285 mμ (log ε = 3·6), while the spectrum recently recorded shows a min at 222 mμ (log ε = 3·73), a max at 250 mμ (log ε = 4·12) and a shoulder at 290 mμ (log ε = 3·52).

MR'_1 being the molar refraction of the solvent calculated by the extrapolated data and MR_{12} that of the solution.

The moment in Debye at 25° is given by

$$\mu = 0{\cdot}2211\sqrt{({}_{\infty}P_2 - P_D)}$$

where P_D is 1·1 P_E.

Table 9. Dipole moment experimental and extrapolation data

3-*Methyl*-N-*methylisoxazolin-5-one* (m.p. 41–42°) (4)

Solvent: benzene ε_1 = 2·27171, d_1 = 0·87351, n_1^2 = 2·24402

f_2	ε_{12}	d_{12}	n_{12}^2
0·0016134	2·34966	0·87413	2·24416
0·0021794	2·37950	0·87438	2·24430
0·0037515	2·45544	0·87485	2·24442
0·0047499	2·50329	0·87510	2·24456
0·0057419	2·55139	0·87549	2·24468

Extrapolation data:

ε'_1 = 2·2724 ± 0·0009 d'_1 = 0·87365 ± 0·00004 $n_1'^2$ = 2·24395 ± 0·00001
α = 48·7 ± 0·2 β = 0·32 ± 0·01 γ = 0·126 ± 0·002
${}_{\infty}P_2$ = 744 ± 3 $\overline{MR_2} = P_E$ = 30·5 ± 0·2 μ = 5·89 ± 0·01

4-*Methyl*-N-*methylisoxazolin-5-one* (b.p. 65–66° 0·2 mm Hg) (5)

Solvent: benzene ε_1 = 2·27411, d_1 = 0·87343, n_1^2 = 2·24459

f_2	ε_{12}	d_{12}	n_{12}^2
0·0015378	2·32793	0·87392	2·24454
0·0028319	2·37382	0·87431	2·24451
0·0038417	2·41419	0·87469	2·24448
0·0049361	2·45222	0·87503	2·24445
0·0063645	2·50620	0·87548	2·24442

Extrapolation data:

ε'_1 = 2·270 ± 0·001 d'_1 = 0·87341 ± 0·00002 $n_1'^2$ = 2·244579 ± 0·000002
α = 37·0 ± 0·3 β = 0·326 ± 0·005 γ = −0·0254 ± 0·0007
${}_{\infty}P_2$ = 573 ± 4 $\overline{MR_2} = P_E$ = 28·02 ± 0·09 μ = 5·15 ± 0·02

3-*Phenyl-5-methoxyisoxazole* (m.p. 78–79°) (6)

Solvent: dioxan ε_1 = 2·20536, d_1 = 1·02795, n_1^2 = 2·01742

f_2	ε_{12}	d_{12}	n_{12}^2
0·0007144	2·22108	1·02820	2·01773
0·0016779	2·24229	1·02839	2·01850
0·0023959	2·25874	1·02855	2·01901
0·0033485	2·27943	1·02876	2·01984
0·0039656	2·29301	1·02890	2·02015

Extrapolation data:

ε'_1 = 2·20521 ± 0·00006 d'_1 = 1·028036 ± 0·000006 $n_1'^2$ = 2·01723 ± 0·00002
α = 22·15 ± 0·02 β = 0·216 ± 0·003 γ = 0·741 ± 0·009
${}_{\infty}P_2$ = 365·7 ± 0·3 $\overline{MR_2} = P_E$ = 50·3 ± 0·5 μ = 3·896 ± 0·004

TABLE 9—*continued*

3-*Phenyl*-N-*methylisoxazolin-5-one* (m.p. 43–45°) (5)

Solvent: benzene $\varepsilon_1 = 2{\cdot}27138$, $d_1 = 0{\cdot}87348$, $n_1^2 = 2{\cdot}24415$

f_2	ε_{12}	d_{12}	n_{12}^2
0·0008739	2·31672	0·87396	2·24469
0·0013968	2·34352	0·87430	2·24499
0·0021240	2·38023	0·87476	2·24538
0·0031250	2·43065	0·87521	2·24595
0·0038717	2·46836	0·87568	2·24628

Extrapolation data:

$\varepsilon_1' = 2{\cdot}2728 \pm 0{\cdot}0001$ $d_1' = 0{\cdot}87351 \pm 0{\cdot}00004$ $n_1'^2 = 2{\cdot}24424 \pm 0{\cdot}00002$
$\alpha = 50{\cdot}53 \pm 0{\cdot}06$ $\beta = 0{\cdot}56 \pm 0{\cdot}02$ $\gamma = 0{\cdot}54 \pm 0{\cdot}01$
${}_\infty P_2 = 785 \pm 1$ $\overline{MR_2} = P_E = 49{\cdot}9 \pm 0{\cdot}2$ $\mu = 5{\cdot}974 \pm 0{\cdot}004$

4-*Phenylisoxazolin-5-one* (m.p. 133–135° dec.) (7)

Solvent: dioxan $\varepsilon_1 = 2{\cdot}22084$, $d_1 = 1{\cdot}02760$, $n_1^2 = 2{\cdot}01714$

f_2	ε_{12}	d_{12}	n_{12}^2
0·0010587	2·25509	1·02810	2·01805
0·0019026	2·28365	1·02847	2·01873
0·0027568	2·31134	1·02879	2·01958
0·0035361	2·33484	1·02919	2·02032
0·0042900	2·35964	1·02939	2·02097

Extrapolation data:

$\varepsilon_1' = 2{\cdot}2218 \pm 0{\cdot}0008$ $d_1' = 1{\cdot}02770 \pm 0{\cdot}000015$ $n_1'^2 = 2{\cdot}01709 \pm 0{\cdot}00002$
$\alpha = 32{\cdot}2 \pm 0{\cdot}3$ $\beta = 0{\cdot}396 \pm 0{\cdot}005$ $\gamma = 0{\cdot}907 \pm 0{\cdot}006$
${}_\infty P_2 = 500 \pm 3$ $\overline{MR_2} = P_E = 45{\cdot}6 \pm 0{\cdot}2$ $\mu = 4{\cdot}69 \pm 0{\cdot}02$

4-*Phenyl-5-methoxyisoxazole* (m.p. 39–40°) (7)

Solvent: benzene $\varepsilon_1 = 2{\cdot}27333$, $d_1 = 0{\cdot}87361$, $n_1^2 = 2{\cdot}24430$

f_2	ε_{12}	d_{12}	n_{12}^2
0·0010251	2·28051	0·87426	2·24472
0·0018505	2·28602	0·87473	2·24514
0·0024911	2·29023	0·87501	2·24535
0·0034315	2·29650	0·87555	2·24580
0·0042145	2·30183	0·87586	2·24604

Extrapolation data:

$\varepsilon_1' = 2{\cdot}27365 \pm 0{\cdot}000045$ $d_1' = 0{\cdot}87377 \pm 0{\cdot}00004$ $n_1'^2 = 2{\cdot}24433 \pm 0{\cdot}00004$
$\alpha = 6{\cdot}67 \pm 0{\cdot}02$ $\beta = 0{\cdot}51 \pm 0{\cdot}01$ $\gamma = 0{\cdot}41 \pm 0{\cdot}02$
${}_\infty P_2 = 142{\cdot}3 \pm 0{\cdot}5$ $\overline{MR_2} = P_E = 50{\cdot}0 \pm 0{\cdot}1$ $\mu = 2{\cdot}065 \pm 0{\cdot}006$

4-*Phenyl*-N-*methylisoxazolin-5-one* (m.p. 144–146°) (5)

Solvent: benzene $\varepsilon_1 = 2{\cdot}27125$, $d_1 = 0{\cdot}87339$, $n_1^2 = 2{\cdot}24430$

f_2	ε_{12}	d_{12}	n_{12}^2
0·0008454	2·30558	0·87390	2·24472
0·0013795	2·32900	0·87420	2·24502
0·0018772	2·34966	0·87448	2·24550
0·0023940	2·37070	0·87490	2·24577
0·0028204	2·38740	0·87503	2·24613
0·0034819	2·41583	0·87570	2·24652
0·0038916	2·43011	0·87567	2·24679
0·0044177	2·45412	0·87613	2·24712

TABLE 9—*continued*

Extrapolation data:

$\varepsilon'_1 = 2{\cdot}2713 \pm 0{\cdot}0005$ $d'_1 = 0{\cdot}87336 \pm 0{\cdot}00005$ $n'^2_1 = 2{\cdot}24416 \pm 0{\cdot}00004$
$\alpha = 41{\cdot}4 \pm 0{\cdot}2$ $\beta = 0{\cdot}61 \pm 0{\cdot}02$ $\gamma = 0{\cdot}68 \pm 0{\cdot}01$
${}_{\infty}P_2 = 650 \pm 3$ $\overline{MR_2} = P_E = 49{\cdot}4 \pm 0{\cdot}1$ $\mu = 5{\cdot}40 \pm 0{\cdot}01$

3,4-Dimethylisoxazolin-5-one (m.p. 49–51°) (1)
Solvent: benzene $\varepsilon_1 = 2{\cdot}27269$, $d_1 = 0{\cdot}87354$, $n^2_1 = 2{\cdot}24459$

f_2	ε_{12}	d_{12}	n^2_{12}
0·0008339	2·30208	0·87385	2·24439
0·0015579	2·32512	0·87405	2·24427
0·0031641	2·38246	0·87462	2·24403
0·0043318	2·41932	0·87501	2·24397
0·0055918	2·45884	0·87533	2·24394
0·0065445	2·48693	0·87563	2·24400
0·0077338	2·51975	0·87602	2·24382
0·0089254	2·55523	0·87634	2·24373

Extrapolation data:

$\varepsilon'_1 = 2{\cdot}280 \pm 0{\cdot}003$ $d'_1 = 0{\cdot}87360 \pm 0{\cdot}00002$ $n'^2_1 = 2{\cdot}24436 \pm 0{\cdot}00005$
$\alpha = 31{\cdot}4 \pm 0{\cdot}5$ $\beta = 0{\cdot}311 \pm 0{\cdot}003$ $\gamma = -0{\cdot}071 \pm 0{\cdot}009$
${}_{\infty}P_2 = 488 \pm 7$ $\overline{MR_2} = P_E = 27{\cdot}6 \pm 0{\cdot}2$ $\mu = 4{\cdot}73 \pm 0{\cdot}03$

Solvent: dioxan $\varepsilon_1 = 2{\cdot}21953$, $d_1 = 1{\cdot}02778$, $n^2_1 = 2{\cdot}01714$

f_2	ε_{12}	d_{12}	n^2_{12}
0·0019796	2·30251	1·02800	2·01737
0·0031631	2·35338	1·02821	2·01762
0·0046424	2·40123	1·02852	2·01793
0·0058404	2·46236	1·02869	2·01825

Extrapolation data:

$\varepsilon'_1 = 2{\cdot}223 \pm 0{\cdot}007$ $d'_1 = 1{\cdot}02764 \pm 0{\cdot}00003$ $n'^2_1 = 2{\cdot}01691 \pm 0{\cdot}00003$
$\alpha = 40 \pm 2$ $\beta = 0{\cdot}183 \pm 0{\cdot}006$ $\gamma = 0{\cdot}226 \pm 0{\cdot}006$
${}_{\infty}P_2 = 608 \pm 25$ $\overline{MR_2} = P_E = 27{\cdot}41 \pm 0{\cdot}08$ $\mu = 5{\cdot}3 \pm 0{\cdot}1$

3,4-Dimethyl-5-methoxyisoxazole (b.p. 79° 22 mm Hg) (1)
Solvent: benzene $\varepsilon_1 = 2{\cdot}27262$, $d_1 = 0{\cdot}87365$, $n^2_1 = 2{\cdot}24459$

f_2	ε_{12}	d_{12}	n^2_{12}
0·0015153	2·28605	0·87403	2·24435
0·0028763	2·29747	0·87427	2·24376
0·0032606	2·30084	0·87446	2·24370
0·0051103	2·31484	0·87486	2·24343
0·0062342	2·32545	0·87519	2·24331

Extrapolation data:

$\varepsilon'_1 = 2{\cdot}2735 \pm 0{\cdot}0001$ $d'_1 = 0{\cdot}87366 \pm 0{\cdot}00003$ $n'^2_1 = 2{\cdot}2445 \pm 0{\cdot}0001$
$\alpha = 8{\cdot}34 \pm 0{\cdot}03$ $\beta = 0{\cdot}241 \pm 0{\cdot}006$ $\gamma = -0{\cdot}20 \pm 0{\cdot}03$
${}_{\infty}P_2 = 158{\cdot}5 \pm 0{\cdot}4$ $\overline{MR_2} = P_E = 32{\cdot}7 \pm 0{\cdot}3$ $\mu = 2{\cdot}468 \pm 0{\cdot}005$

TABLE 9—*continued*

Solvent: dioxan $\varepsilon_1 = 2·20966$, $d_1 = 1·02805$, $n_1^2 = 2·01742$

f_2	ε_{12}	d_{12}	n_{12}^2
0·0020707	2·22888	1·02810	2·01762
0·0029492	2·23676	1·02811	2·01771
0·0036245	2·24237	1·02810	2·01779
0·0052947	2·25806	1·02825	2·01802
0·0068507	2·27187	1·02814	2·01813

Extrapolation data:

$\varepsilon'_1 = 2·2102 \pm 0·0001$ $d'_1 = 1·02806 \pm 0·00008$ $n'^2_1 = 2·017400 \pm 0·000003$
$\alpha = 9·01 \pm 0·02$ $\beta = 0·02 \pm 0·01$ $\gamma = 0·1067 \pm 0·0009$
${}_\infty P_2 = 166·3 \pm 0·5$ $\overline{MR}_2 = P_E = 33·1 \pm 0·2$ $\mu = 2·521 \pm 0·005$

3,4-*Dimethyl*-N-*methylisoxazolin-5-one* (m.p. 39–41°) (8)

Solvent: benzene $\varepsilon_1 = 2·27237$, $d_1 = 0·87355$, $n_1^2 = 2·24430$

f_2	ε_{12}	d_{12}	n_{12}^2
0·0012445	2·32778	0·87399	2·24430
0·0023974	2·37984	0·87442	2·24436
0·0034879	2·42920	0·87471	2·24439
0·0045472	2·47704	0·87502	2·24445
0·0055383	2·52126	0·87545	2·24448

Extrapolation data:

$\varepsilon'_1 = 2·2718 \pm 0·0002$ $d'_1 = 0·87359 \pm 0·00004$ $n'^2_1 = 2·244251 \pm 0·000007$
$\alpha = 45·09 \pm 0·05$ $\beta = 0·33 \pm 0·01$ $\gamma = 0·042 \pm 0·002$
${}_\infty P_2 = 696·2 \pm 0·8$ $\overline{MR}_2 = P_E = 33·3 \pm 0·1$ $\mu = 5·678 \pm 0·004$

Solvent: dioxan $\varepsilon_1 = 2·21077$, $d_1 = 1·02798$, $n_1^2 = 2·01714$

f_2	ε_{12}	d_{12}	n_{12}^2
0·0013134	2·27434	1·02811	2·01765
0·0023578	2·32521	1·02818	2·01790
0·0036530	2·38786	1·02841	2·01827
0·0046986	2·43695	1·02848	2·01850
0·0060854	2·50543	1·02862	2·01884

Extrapolation data:

$\varepsilon'_1 = 2·2109 \pm 0·0001$ $d'_1 = 1·02794 \pm 0·00002$ $n'^2_1 = 2·017316 \pm 0·000005$
$\alpha = 48·41 \pm 0·04$ $\beta = 0·111 \pm 0·005$ $\gamma = 0·251 \pm 0·001$
${}_\infty P_2 = 734·9 \pm 0·5$ $\overline{MR}_2 = P_E = 33·12 \pm 0·04$ $\mu = 5·844 \pm 0·002$

3-*Methyl-4-phenyl*-N-*methylisoxazolin-5-one* (m.p. 111–113°) (5)

Solvent: benzene $\varepsilon_1 = 2·27288$, $d_1 = 0·87368$, $n_1^2 = 2·24430$

f_2	ε_{12}	d_{12}	n_{12}^2
0·0009413	2·31889	0·87420	2·24499
0·0017473	2·35741	0·87472	2·24544
0·0024561	2·38723	0·87514	2·24589
0·0031011	2·41683	0·87551	2·24628
0·0040692	2·46031	0·87632	2·24703

Extrapolation data:

$\varepsilon'_1 = 2·2759 \pm 0·0003$ $d'_1 = 0·87354 \pm 0·00006$ $n'^2_1 = 2·24433 \pm 0·00005$
$\alpha = 45·3 \pm 0·1$ $\beta = 0·66 \pm 0·02$ $\gamma = 0·64 \pm 0·02$
${}_\infty P_2 = 709 \pm 2$ $\overline{MR}_2 = P_E = 53·2 \pm 0·2$ $\mu = 5·640 \pm 0·008$

TABLE 9—*continued*

*3-Phenyl-4-methyl-*N*-methylisoxazolin-5-one* (m.p. 67–69°) (8)

Solvent: benzene $\varepsilon_1 = 2{\cdot}27154$, $d_1 = 0{\cdot}87334$, $n_1^2 = 2{\cdot}24430$

f_2	ε_{12}	d_{12}	n_{12}^2
0·0006175	2·30032	0·87371	2·24463
0·0011120	2·32264	0·87401	2·24493
0·0015860	2·34481	0·87430	2·24511
0·0021514	2·37062	0·87454	2·24532
0·0026615	2·39366	0·87484	2·24556
0·0031979	2·41920	0·87513	2·24589
0·0036113	2·43792	0·87535	2·24610
0·0041381	2·46229	0·87567	2·24634

Extrapolation data:

$\varepsilon'_1 = 2{\cdot}2717 \pm 0{\cdot}0001$ $d'_1 = 0{\cdot}87337 \pm 0{\cdot}00001$ $n_1'^2 = 2{\cdot}24434 \pm 0{\cdot}00003$

$\alpha = 46{\cdot}06 \pm 0{\cdot}05$ $\beta = 0{\cdot}550 \pm 0{\cdot}004$ $\gamma = 0{\cdot}48 \pm 0{\cdot}01$

${}_{\infty}P_2 = 725{\cdot}0 \pm 0{\cdot}7$ $\overline{MR}_2 = P_E = 54{\cdot}0 \pm 0{\cdot}1$ $\mu = 5{\cdot}704 \pm 0{\cdot}003$

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