

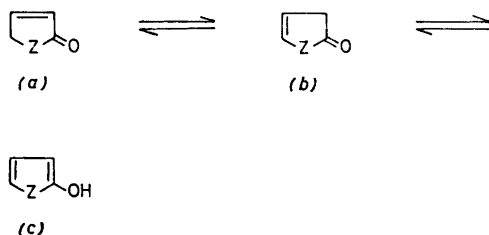
Ionisation Potentials in Tautomeric Analysis of 2-Hydroxy Derivatives of Thiophenes, Selenophenes, and Furans

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Ionisation potentials for tautomeric 2-hydroxy-thiophenes, -selenophenes, and -furans have been analysed by comparison with IP data for compounds derived from either tautomeric form. The enol isomer was not seen. Of the two possible α,β - and β,γ -unsaturated lactones the former was the major isomer; the ratios, however, depend on positional alkyl substitution and on the heteroatom.

The determination of appearance potentials (AP) and ionisation potentials (IP) has recently been found very useful in structure analysis of gaseous molecules in the mass spectrometer;¹⁻⁴ such data for the tautomeric hydroxy and amino pyridines have been interpreted in favour of the hydroxy and amino forms.¹⁻³ Five-membered heterocycles with a potential hydroxy group constitute another important class of tautomeric compounds (Scheme 1). The tautomeric behaviour of 2-hydroxy-thiophenes,^{5,6} selenophenes,⁷ and furans^{8,9} have been elucidated in solution, in solid and in liquid states. In this work we have used IP in structure analysis of the gaseous species from 2-hydroxy derivatives of these five-membered heterocycles.



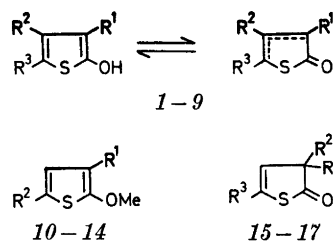
Scheme 1.

The IP values were obtained by the semilog-plot method as previously described.¹⁰ In most cases the molecular ion signal was the base peak in the spectrum; in the remaining cases the molecular ion signal was strong. For analytical interpretation of the IP data knowledge of the IP's for the possible tautomers is required. The data for the latter are obtained indirectly from the alkylated tautomeric derivatives; the alkylation prevents tautomeric interconversions. Data for such model compounds are presented in the tables. Before discussing the tabulated values it is pointed out that the influence of a substituent on the ease of ionisation depends on the nature of other substituents as well as on the ring system and relative position; generally an electron releasing substituent decreases the IP.^{1,11} The aromatic properties of thiophenes resemble closely those of corresponding benzenes; substituent influences in benzenes and thiophenes are therefore assumed to be similar, especially in derivatives derived from the hydroxy tautomer (c). Good models for the substituent effects in the lactones (a) and (b) are not available for comparison. Substituent effects on the ease of ionisation in these structures, however, will be seen in the discussion below to be of the same order as in the "aromatic" systems. The selenophene and the furan systems are treated in the same way. The thiophenes have been studied most extensively because of the availability of a considerable number of model compounds. Findings in the thiophene series are then applied in the structure analyses of the furan and selenophene series assuming similar substituent influences.

Introduction of a methoxy group into benzene decreases its IP with 0.7 to 8.83 eV (anisol);¹¹ the IP's for thiophene¹² and for 2-methoxythiophene (10) were found to be 8.80 and 8.14 eV, respectively. For methyl, ethyl, isopropyl, and *t*-butyl benzene the IP's have been determined by photoionisation; the successive decreases in IP from the previous member in the series were 0.42, 0.06, 0.07, and 0.01 eV.¹³ The IP values determined by photoionisation are generally lower than those obtained by electron impact methods;¹¹ the differences in a homologue series determined by the two different methods, however, are assumed to be similar. The IP difference between 2-methoxythiophene (10) and its 3-*t*-butyl homologue 12 is 0.47 eV (Table 1); the IP differences between 10 and the methyl homologue 11 and 13 are 0.09 and 0.13 eV, respectively. The presence of the methoxy group will by analogy to the benzene system slightly reduce the influences of the alkyl substituents. Non-bonded interaction between *ortho* substituents presumably has little influence on the ease of ionisation in the compounds studied since IP for *o*-methylanisole (8.68 eV) was found to be only 0.25 eV lower than the value reported¹¹ for *o*-cresol; the difference is in the usual range (0.2–0.3 eV) for reduction in IP on *O*-methylation.^{1,11} In the five-membered ring the substituents are further apart than in benzene and consequently non-bonded interaction between the vicinal substituents is expected to have less effect on IP than in benzene.

From Table 1 it is seen that IP of 2-methoxythiophene (10) is 8.14 eV; the estimated IP value for the enol (c) is thus of the order 8.4 eV (Table 2). IP for 3,3-dimethyl-4-thiolen-2-one (15) was measured to 8.77 eV; using the effect of the *O*-methyl group in the methoxy systems 11 and 13, the IP for the β,γ -unsaturated lactone (b) can be estimated to ca. 8.9–9.0 eV (Table 2); a similar estimation is arrived at from the methyl *t*-butyl derivative (16) by application of the alkyl substituent effects in 11 and 12. The model compound, 5,5-dimethyl-3-thiolen-2-one (18), for the α,β -unsaturated lactone (a) was not available; estimation of IP by the above technique was thereby prevented. Fortunately the unsubstituted structure 1 has significantly higher IP (9.78 eV) than the estimated IP's for (b) and (c). Hence IP for isomer (a) is at least 9.8 eV which shows that

Table 1. Ionisation potentials for thiophenes.



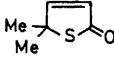



Com- pound	R ¹	R ²	R ³	IP ± 0.05 eV
1	H	H	H	9.78
2	Me	H	H	9.60
3	<i>t</i> -Bu	H	H	9.25
4	H	H	Me	9.16
5	H	H	Et	9.08
6	Me	H	Me	9.35
7	Me	Me	H	9.44
8	H	Me	Me	9.13
9	<i>t</i> -Bu	H	Me	9.07
10	H	H	—	8.14
11	Me	H	—	8.05
12	<i>t</i> -Bu	H	—	7.67
13	H	Me	—	8.01
14	Me	Me	—	7.78
15	Me	Me	H	8.77
16	Me	<i>t</i> -Bu	H	8.38
17	Me	Me	Me	8.53

1 exists almost entirely as the α,β -unsaturated lactone (a) in the gas phase. This conclusion parallels the results from studies in the non-gaseous states which showed only the presence of the α,β -unsaturated lactone (a) within experimental limits.⁵ It is also known from previous studies that the IP of a pure compound is rapidly decreased in a non-linear manner on admixture of an isomer with significantly lower IP.^{10,13} Therefore the high IP for 1 excludes the presence of lactone (b) in significant amounts.

The IP is a measure of the ease of ionisation. The tables operate with IP values which arise as a mathematical result from the semi-empirical evaluation technique of the ionisation efficiency curves for components with the same mass number.^{12,14} AP may therefore be a more correct term for these potentials. IP is used in this work, however, because the measured ionisations lead to molecular ions.

The estimated IP's for the three tautomeric forms (a), (b), and (c) of 1 show significant

Table 2. Estimated ionisation potentials.

	
(18)	(a) 9.8
	
(b) 8.9	(c) 8.4

differences (Table 2). These values are applied to the interpretation of the figures for the tautomeric compounds 1–9. The figures are all above 9 eV which excludes important contribution from the enol (c) (8.4 eV) in the gas phase. Hence further structural discussions are limited to the two lactone isomers (a) and (b). It is understood, however, that the IP technique does not exclude the presence of minor amounts of the enol (c). For the reasons discussed above the parent compound 1 is assigned the α,β -unsaturated lactone structure (a). An alkyl group in the 3-position will conjugate or hyperconjugate with an α,β -double bond; this effect adds to the stabilising effect from double bond-carbonyl conjugation in locating the double bond to the α,β -position. Not unexpectedly, therefore, IP for the 3-methyl derivative 2 shows that tautomer (a) is the dominant gaseous species, the IP is 0.18 eV lower than for 1 and corresponds to the expected influence from the first methyl group. The same conclusion is reached for the 3-*t*-butyl derivative 3.

It is seen from Table 1 that the IP for the 3-methyl derivative 2 is 1.5 eV higher than for the isomeric 2-methoxythiophene (10). For the other *C*-methyl isomer 4, however, the IP is 0.6 eV lower than for the parent compound 1. This difference is too large to be inherent in the methyl group and must reflect another lactone ratio than for the 3-isomer 2 in the gas phase. The IP for 4, however, is higher than the estimated value for the β,γ -unsaturated tautomer (b); it is concluded that the gaseous species are composed of both lactones (a) and (b). Solution studies have shown that hyperconjugation from a 5-alkyl group stabilises the β,γ -double bond. In fact, both lactone tautomers can be isolated separately. These readily rearrange, however, to a thermodynamic equilibrium mixture under acid or base catalysis.

Depending on substituents and medium, the equilibrium mixtures for simple 5-alkyl derivatives contain 10–20% of the β,γ -isomer.⁶ The available sample was such an equilibrium mixture which seems in accord with the gas phase data.

For an easily affected equilibrium mixture the question of thermal influence on the equilibrium position becomes important. The tautomeric compounds in this investigation were readily evaporated at 30–35 °C using the indirect insertion system. Intramolecular tautomeric changes in the gas phase are probably slow;¹⁵ any changes after evaporation will therefore have to occur on the heated walls of the instrument. The reservoir and its connecting line to the ion source were kept at 130 °C while the ion source temperature was varied from below this temperature to 285 °C; only a very slight increase in the recorded IP's were noticed with increase in temperature. The sample was kept in the reservoir for more than one hour to complete these measurements. The normal time for measurements is of the order 10–15 min and hence equilibration towards a gas equilibrium position in the reservoir is probably of little importance; nor is the equilibration rate in the liquid sample exceptionally rapid.⁶ The compounds were readily evaporated at 30–35 °C and consist essentially of the two lactone isomers which have similar boiling points; the α,β -unsaturated lactone (a) has the higher boiling point.⁶ Selective evaporation, therefore, probably plays only a minor role and hence the ratios of the lactones (a) and (b) are not very different in the gas phase and in the liquid sample. Support for this conclusion was demonstrated by using samples with different tautomeric compositions. The isomer ratio can be changed through the polarity of the solvent.⁶ Thus nitromethane decreases the amount of the less polar β,γ -isomer from the usual 15–20% in the liquid to 6–10%; in the mass spectrometer the IP for 4 was increased from 9.16 to 9.25 eV after pretreatment of the sample with nitromethane. Further support for direct evaporation is provided by the results in the furan series (Table 3); the available α,β -unsaturated and the β,γ -unsaturated 5-methyl tautomers had significantly different IP's as discussed below.

The IP for the 5-ethyl homologue 5 shows a

similar lactone ratio in the gas phase as for 4. A 4-alkyl substituent will conjugate with the double bond in either form. Not unexpectedly, therefore, the isomer distribution for the 4,5-dimethyl isomer 8 appears to be similar to 4. The IP for the 3,5-dimethyl isomer 6, however, is 0.22 eV higher reflecting a relative increase in the α,β -unsaturated lactone; either double bond is conjugated by only one of the methyl groups. A similar conclusion is reached from the IP value of the 3-*t*-butyl analogue 9. The highest IP (9.44 eV) for the dimethyl isomers was obtained for the 3,4-dimethyl isomer 7. The 4-methyl group in this isomer will stabilise either double bond while conjugative stabilisation from the 3-methyl group is limited to the α,β -double bond. The IP difference between 7 and the parent compound 1 is close to the expected substituent effect from two methyl groups. Hence the gas phase molecules consist mainly of isomer (a).

In the furan series (Table 3) available model compounds were restricted to 3,3,5-trimethyl-4-oxolen-2-one (21). By means of additional data from the thiophene series, however, structure analysis is possible. Thiophene and furan have closely similar IP's, 8.80 and 8.85 eV, respectively.¹² 2,5-Dimethyl-3-methoxythiophene and its furan analogue also have closely similar IP's, 7.89 and 7.86 eV, respectively.¹⁶ By analogy 2-hydroxyfuran is expected to have IP *ca.* 8.4 eV which on methyl substitution is reduced to *ca.* 8.3 eV; the observed values (9.62 and 10.12 eV) for the 5-methyl derivatives 19 clearly exclude the enol form as a major species in the gas phase.

The heteroatom effect on IP is pronounced,

Table 3. Ionisation potentials of furans.

	\rightleftharpoons		\rightleftharpoons	
(a)		(b)		(c)
		R	IP \pm 0.05 eV	
(19a)		Me	10.12	
(19b)		Me	9.62	
(20)		<i>t</i> -Bu	9.03	
		(21)		
		IP	9.00 \pm 0.05 eV	

Table 4. Ionisation potentials of selenophenes.

	\rightleftharpoons		\rightleftharpoons	
(a)		(b)		(c)
		(22)	IP	8.84 \pm 0.05 eV
		(23)		
		IP	7.98 \pm 0.05 eV	

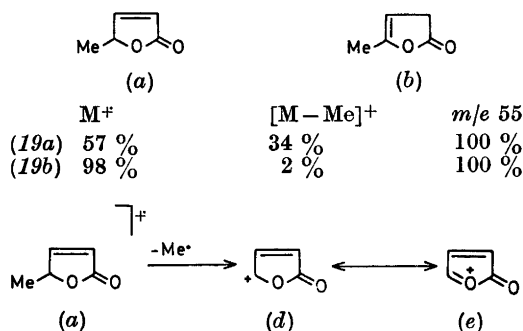
however, when the heteroaromatic system is broken. This is evident from a comparison of the IP data for 3,3,5-trimethyl-4-oxolen-2-one (9.00 eV), and the selen analogue (23, 7.98 eV) and the sulfur analogue (17, 8.53 eV). The same type of IP differences exist between the isomeric 2,2,5-trimethyl-4-thiolen-3-one and its selen and oxygen analogues.¹⁸ In six-membered oxygen and sulfur heterocyclic systems such differences have also been observed.¹⁷

The available lactone isomers 5-methyl-3-oxolen-2-one (19a) and 5-methyl-4-oxolen-2-one (19b) were found to have IP's 10.12 and 9.62 eV, respectively. The high value for 19a is consistent with the α,β -unsaturated formulation. The IP for the β,γ -unsaturated lactone is estimated to *ca.* 9.2–9.3 eV by adding the methyl group substituent effect onto the IP of 21; the experimental value lies between the estimated value and the experimental value for the α,β -unsaturated lactone 19a. It follows that the β,γ -unsaturated isomer has been partially tautomerised presumably before evaporation.

The IP (10.12 eV) for 19a suggests that IP for the unsubstituted α,β -unsaturated lactone (a, R=H) is *ca.* 10.2–10.3 eV which is in fair agreement with 9.8 eV as estimated for the sulfur analogue 1; almost the same IP difference is experimentally observed between the 3-methylthiophene 2 and 5-methylfuran 19a systems which both have been assigned the α,β -unsaturated lactone structure in the gas phase. The same comparison between the 5-methyl analogues 4 and 19a gives a much larger IP difference; it will be recalled that 4 was found to be a mixture of both lactone isomers in the gas phase.

The *t*-butyl sample 20 was an isomer mixture; the IP suggests that the β,γ -unsaturated lactone (b) is the major isomer.

The assignment of different isomer ratios in the gas phase from the two 5-methyl isomers 19 is supported by differences in fragmentation; of special interest is the relative intensities of the molecular ion and the [M-Me] fragment (Scheme 2). 19a has the lower molecular ion intensity but much larger [M-Me] fragment. This observation can be rationalised in terms of the carbonium ion fragment (d) where the positive charge is stabilised by conjugation from the double bond and from the heteroatom. A similar stabilisation by direct methyl group expulsion from the (b)-form cannot be visualised. The relative intensity differences also show that extensive tautomerisation does not occur in these molecules on ionisation after electron impact.



Scheme 2.

In the selenophene series (Table 4) the IP (7.98 eV) for the 3,3,5-trimethyl derivative 23 suggests that the β,γ -unsaturated lactone isomer (b) of the 5-methyl derivative 22 has IP ca. 8.2–8.3 eV. In the thiophene and furan series discussed the difference in IP between the lactone forms (a) and (b) is about 1 eV; if a similar difference is assumed in the selenophene series, the data lead to the conclusion that the α,β -unsaturated lactone (a) is the major isomer.

EXPERIMENTAL

The ionisation efficiency curves were recorded on an AEI MS-902 mass spectrometer and interpreted by the semi-log plot method.¹⁰ The ionising current was 20 μ A and the repeller was at cage potential. Xenon was the reference gas. The ion source temperature was 230 °C unless specially discussed in the text.

The IP data are the average of three determinations, the deviation being ± 0.05 eV under standardised conditions. The compounds were

introduced into the instrument by the indirect inlet system at 30–50 °C. The reservoir and the connecting tube to the ion source were at 130 °C.

The compounds used in this investigation were available from other work or were prepared according to the literature; 1, 4;⁵ 5;⁶ 3, 9, 12, 14–16, 23;⁷ 7, 8, 13, 21;⁸ 19, 20;⁹ 2;¹⁸ 6;¹⁹ 10;²⁰ 11;²¹ 22.²²

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REFERENCES

- Grønneberg, T. and Undheim, K. *Org. Mass. Spectrom.* 6 (1972) 823; *Tetrahedron Lett.* (1972) 3193.
- Undheim, K., El-Gendy, M. A. F. and Hurum, T. *Acta Chem. Scand. B* 28 (1974) 743.
- Grønneberg, T., Hurum, T. and Undheim, K. *Acta Chem. Scand. B* 28 (1974) 986.
- Jalonen, J. and Pihlaja, K. *Org. Mass. Spectrom.* 7 (1973) 1203.
- Gronowitz, S. and Hoffman, R. A. *Ark. Kemi* 15 (1960) 499.
- Hörnfeldt, A.-B. *Ark. Kemi* 22 (1964) 211.
- Cederlund, B. and Hörnfeldt, A.-B. *To be published.*
- Cederlund, B., Jespersen, Å. and Hörnfeldt, A.-B. *Acta Chem. Scand.* 25 (1971) 3656.
- Hörnfeldt, A.-B. *Ark. Kemi* 29 (1969) 229.
- Hvistendahl, G. and Undheim, K. *Org. Mass Spectrom.* 6 (1972) 217.
- Crabbe, G. F. and Kearns, G. L. *J. Phys. Chem.* 66 (1962) 436.
- Thorstad, O. and Undheim, K. *Chem. Scr.* 6 (1974) 222.
- Watanabe, K., Nakayama, T. and Mottl, J. *J. Quant. Spectrosc. Radiat. Transfer* 2 (1962) 369.
- Lossing, F. P., Tickner, A. W. and Bryce, W. A. *J. Chem. Phys.* 19 (1951) 1254.
- Beak, P. and Fry, F. S. *J. Amer. Chem. Soc.* 95 (1973) 1700.
- Thorstad, O., Undheim, K., Lantz, R. and Hörnfeldt, A.-B. *Acta Chem. Scand. B* 29 (1975) 652.
- Hvistendahl, G., Györösi, P. and Undheim, K. *Org. Mass. Spectrom.* 9 (1974) 80.
- Hörnfeldt, A.-B. and Gronowitz, S. *Acta Chem. Scand.* 16 (1962) 789.
- Cederlund, B. and Hörnfeldt, A.-B. *Acta Chem. Scand.* 25 (1971) 3324.
- Gronowitz, S. and Hoffman, R. A. *Ark. Kemi* 16 (1961) 515.
- Pedersen, E. B. and Laweson, S. O. *Tetrahedron* 27 (1971) 3861.
- Morel, J., Paulmier, C., Semard, D. and Pastour, P. *C. R. Acad. Sci. Ser. C* 270 (1970) 825.

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