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Charge Transfer Complexes of Some *N*-Methylated Thiohydantoins with Molecular Iodine

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ABSTRACT

Using a series of N*-methylated thiohydantoins as substrates, the donor properties of the sulfur atom are measured by determining the stability constants* (K) *of their adducts with molecular iodine. The* K*'s have been determined by recording the UV-visible spectra of several* CH_2Cl_2 *solutions with different amounts of the reagents. The experimental data fit the 1:1 adduct model for all the compounds. The* K *values, compared with those previously found for the unsubstituted hydantoins and with those obtained for 5-methyl-2-thiohydantoin, show that the hydrogen-bonding interaction between the NH hydrogen and the S-bonded iodine plays an important role in determining the stability of the adduct.*

The K *values obtained for several pentaatomic rings, all containing the thioureido group —HN—C(=S)—NH—, are discussed on the basis of the influence of the substituents at C-4 and C-5 on the donor properties of the sulfur atom.*

INTRODUCTION

For several years [1–5] we have been doing thermodynamic studies on the 1:1 adduct formation between molecular iodine and several series of heterocyclic ligands having the thio- and/or seleno-amido groups (D) according to the equilibrium:

$$D + I_2 \rightleftharpoons D \cdot I_2$$

This investigation has allowed the following general remarks: 1) selenium compounds bind iodine much more strongly than the sulfur ones; 2) for the same donor atom, the stability constant (K) values of the above equilibrium strongly depend on the chemical environment, even though K values are spread over a very large interval; in fact, small charge variations produce high variations in the K's; 3) the values of ln K show a linear correlation with the binding energies of the lone pair of the donor atom, measured by UPS spectroscopy; 4) the reducing abilities of the thio- or seleno-amido group increase as the K values increase. Hence, knowledge of the K's can be used to predict whether a ligand containing the thioamido group is able to stabilize transition metal ions in oxidation states different from the lowest.

At first, these studies were stimulated by the great interest in charge-transfer complexes between heterocyclic antithyroid drugs and molecular iodine in studies on hyperthyroidism [6–7]. More recently, it was found that sulfur-iodine charge-transfer complexes are also of great interest in the field of electrical properties and in particular in their superconducting ability [8].

We will report the results obtained for some *N*-methyl-substituted hydantoins (**1–3, 7, 8**) and compare them with those previously obtained for the unsubstituted series (**4–6**) [5]. Furthermore, the results will cover, in addition to the compounds listed in Scheme 1, 5-methyl-2-thiohydantoin.

RESULTS AND DISCUSSION

Although the hydantoin derivatives have two chalcogen atoms capable of coordinating molecular io-

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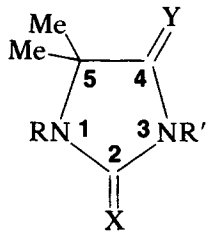


	X = S Y = O	S S	O S
R, R' = H, Me	1	2	3
H, H	4	5	6
Me, H	7	8	—

SCHEME 1

dine, only a 1:1 adduct seems important in CH_2Cl_2 solutions, as this model fits the experimental data fairly well. The 1:1 model was also verified for compounds in which the two chalcogen atoms are both either sulfur or selenium, where the competition in forming two coordinate bondings with two molecules of I_2 is higher than in (S, O), (Se, O) and (Se, S) couples. In all the above cases, the complete absence of other equilibria besides the 1:1 was also tested experimentally by isosbestic points.

The presence of isosbestic points in *N*-methylated hydantoins [9] also excludes formation of adducts with a ratio different from 1:1 (see Figure 1 for **2**). Table 1 shows the UV absorption maxima of the free ligands and the isosbestic points obtained between the visible band of iodine and its blue shifted band due to the adduct formation.

As described in a previous paper [3], for the simultaneous determination of the equilibrium constant (K) and the molar extinction coefficients (ϵ) of $D \cdot I_2$, we have followed the criteria outlined by Carta and Crisponi [10]; we have therefore enlarged the experimental range of the saturation fraction as far as possible in order to minimize the errors on K and ϵ (see Table 2).

The K and ϵ values with the relative standard deviations, calculated at the temperatures of 17°C and 35°C, are shown in the same Table. To improve the reliability of the K's, the calculation has been carried out on four different wavelengths. As a test of reliability of the calculation, the sum of the squared deviations (χ^2) between the experimental and calculated absorbances is reported.

The comparison between the stability constants K (dm^3mol^{-1}), interpolated at 25°C, with those previously obtained for the unsubstituted thiohydantoins [5] allows us to make the following observations: 1) sulfur bonded to C-2 (X = S, Y = O) binds molecular iodine much more strongly than sulfur at C-4 (X = O, Y = S); 2) the comparison between the two series with X = S shows the different influence of oxygen and sulfur at C-4: that is, the electron-withdrawing effect of the C=S group is higher than that of the C=O groups; this induces a decrease in the donor properties of the sulfur in the series with Y = S with a subsequent decrease of the K values; 3) in every case the substitution of the NH hydrogen with a methyl group induces a de-

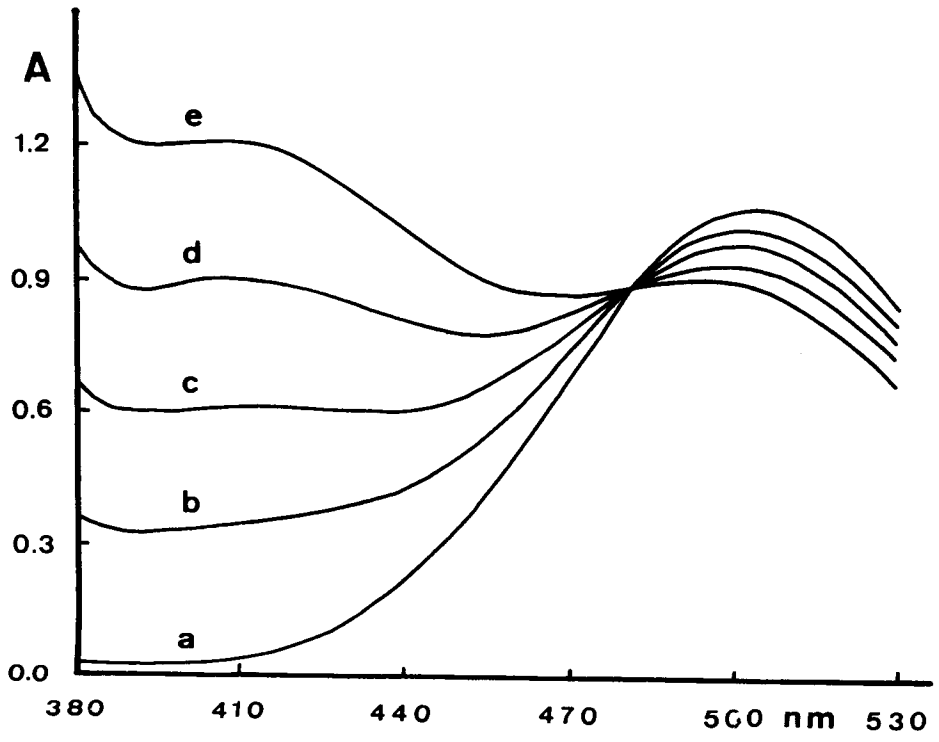
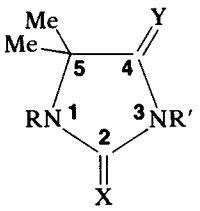


FIGURE 1 Isosbestic Point Obtained between the Visible Band of the Free I_2 and Its Blue Shifted Band in the Adduct with 3,5,5-Trimethyl-2,4-dithiohydantoin (**2**): $[I_2] = 1.044 \times 10^{-3}$ M and [**2**] = 0, 5.20×10^{-4}, 1.10×10^{-3}, 1.82×10^{-3} and 2.60×10^{-3} M for a, b, c, d, and e respectively.

TABLE 1 UV Absorptions (nm) (log ϵ in parentheses) of the Free Molecules and Isosbestic Points (nm) Obtained between the I_2 Visible Band and Its Blue Shifted Band (CH_2Cl_2 solutions).

Compound	UV absorptions	Isosbestic points
1	266(4.32) 304(2.95)	476
2	303(4.51) 392(1.80)	463
3	278(4.22) 368(1.52)	—
7	266(4.25) 297(3.48) 378sh(0.95)	483
8	299(4.48) 388(1.68)	487

TABLE 3 Comparison of the Stability Constants K (dm^3mol^{-1}) of the Adducts between Molecular Iodine and All the Studied Thiohydantoins (25°C; CH_2Cl_2 solutions).



	X = S, Y = O	S, S	O, S
R, R' = H, Me	171	126	12
R, R' = H, H	201	143	69
R, R' = Me, H	149	53	—

crease in K values, in contrast with the inductive effect of the methyl; the steric hindrance of the methyl and the possibility of a hydrogen-bonding interaction between the NH group and the S-bonded iodine seem to be responsible for these variations. The hydrogen-bonding interaction can be evaluated by IR spectroscopy, by comparing the frequency of the ν(NH) vibration of the free molecule with that of the iodine adduct. Shifts of about 60 cm^{-1} toward lower frequencies on passing from the free molecule to the adduct can be observed; for example, in CH_2Cl_2 solution, the ν(NH) vibration of **2** shifts from 3430 cm^{-1} to 3373 cm^{-1} in the adduct; 4) the steric hindrance of the methyl and the absence of the hydrogen-bonding interaction can explain the value of 12 dm^3mol^{-1} obtained for **3**, a value that is remarkably lower than the others.

To conclude, it is interesting to compare the K values obtained for the different substrates containing the thioureido group —HN—C(=S)—NH—, as reported in Table 4.

Since substrates under consideration are pentaatomic rings, with C-4 and C-5 differently substituted, the differences in K values could be attributed essentially to electronic effects. The stability constant of 5-methyl-2-thiohydantoin [11] is also included in Table 4.

Having stated that, in all cases, the donor atom is the thioureido sulfur, it can be seen that the imidazolidine-2-thione shows the highest value of the stability constant with molecular iodine. The benzene ring condensed with the pentaatomic lowers K by a factor of 10. The presence of another chalcogen atom bonded to C-4 further lowers the donor

TABLE 2 Molar Extinction Coefficients (ϵ) at the Wavelengths (λ) Used for the Calculation, Association Constants (K), Ranges of the Saturation Fraction (s), and Sum of the Squared Deviations (χ^2). Standard Deviation in Parentheses.

		17°C				35°C			
	λ (nm)	ϵ (cm^2mol^{-1})	K (dm^3mol^{-1})	s	χ^2	ϵ (cm^2mol^{-1})	K (dm^3mol^{-1})	s	χ^2
1	440	2432(20)	243(8)	0.15–0.89	0.01	2377(29)	114(6)	0.08–0.67	0.01
	420	3172(20)				2954(31)			
	400	2967(25)				2724(35)			
	380	2546(23)				2510(37)			
2	450	2491(58)	169(11)	0.21–0.81	0.05	2473(52)	89(5)	0.13–0.69	0.01
	430	3488(44)				3256(34)			
	410	3868(40)				3546(39)			
	390	3796(80)				3597(57)			
3	440	2364(82)	15(2)	0.06–0.69	0.27	2269(112)	9(2)	0.04–0.57	0.15
	420	2710(132)				2623(137)			
	400	2855(177)				3033(196)			
	380	2491(333)				2201(293)			
7	422	2943(64)	190(22)	0.09–0.88	0.21	2395(58)	112(14)	0.06–0.82	0.11
	402	2638(69)				2160(65)			
	380	2811(81)				2487(81)			
	360	6312(120)				5796(123)			
8	422	4701(85)	69(11)	0.06–0.70	0.49	4429(73)	38(5)	0.04–0.57	0.14
	406	4732(73)				4566(85)			
	382	6456(178)				6565(161)			
	366	12150(313)				12750(223)			

TABLE 4 Comparison of the Stability Constants K (dm^3mol^{-1}; 25°C; CH_2Cl_2 solutions) of the Adducts with Molecular Iodine of Several Pentaatomic Rings ϕ—HN—C(=S)—NH.

—ϕ—	K	Ref.
—CH_2—CH_2—	$5.06 \cdot 10^4$	[1]
—1,2—C_6H_4—	$4.57 \cdot 10^3$	[4]
—CO—CMe_2—	201	[5]
—CO—CHMe—	111	this work
—CS—CMe_2—	143	[5]

properties of the sulfur. This decrease is greater in the case in which the chalcogen is a sulfur atom.

The comparison between the *K* values 201 and 111 dm^3mol^{-1} obtained for 5,5-dimethyl- and 5-methyl-2-thiohydantoin shows the influence of the inductive effect of the C-5 methyl group on the stability constant. On the other hand, in this regard, the substitution of different alkyl groups at C-5 seems to play a remarkable role in determining the biological properties of this type of molecule [12].

EXPERIMENTAL

Materials

Iodine was purified by sublimation from KI and stored in a desiccator.

3,5,5-Trimethyl-2-thiohydantoin (**1**).

2 was refluxed with HgO in a 1:1 molar ratio in dilute HCl solution for 24 h. **1** was then extracted with chloroform and recrystallized several times from this solvent. The analytical data agree with the formula $C_6H_{10}N_2OS$ (mp 135–137°C).

3,5,5-Trimethyl-2,4-dithiohydantoin (**2**)

This compound was synthetized via 3,5,5-trimethylhydantoin. 5,5-Dimethylhydantoin was refluxed with one equivalent of MeI and NaOH in H_2O/EtOH (1:2 vol) for 1.5 h. From the reaction mixture, concentrated to a third of the original volume, 3,5,5-trimethylhydantoin was obtained by cooling and purified by recrystallizing from benzene after treatment with charcoal. The analytical data agree with the formula $C_6H_{10}N_2O_2$ (mp 147°C).

2 was then obtained by reacting 3,3,5-trimethyl-hydantoin with P_2S_5 in the molar ratio 1:2.5 in THN for 2 h and purified by crystallization from benzene. The analytical data agree with the formula $C_6H_{10}N_2S_2$ (mp 171°C).

3,5,5-Trimethyl-4-thiohydantoin (**3**)

When the reaction to yield **2** was carried out in dioxane rather than in THN, **3** was the main product. After 2 h of reaction the solvent was completely evaporated and the residue treated with boiling water and charcoal. **3** was obtained after filtration and cooling, as confirmed by the analytical data.

1,5,5-Trimethyl-2-thiohydantoin (**7**) *and 1,5,5,-Trimethyl-2-,4-dithiohydantoin* (**8**)

These compounds have been obtained by the same procedure used for **1** and **2**, by starting from 1,5,5-trimethyl-hydantoin prepared according to the literature [13]. The analytical data agree with the formulas $C_6H_{10}N_2OS$ and $C_6H_{10}N_2S_2$ for **7** and **8** respectively.

5-Methyl-2-thiohydantoin

This compound was prepared via 1-acetyl-5-methyl-2-thiohydantoin, as described in [14].

Spectrophotometric Measurements

The spectrophotometric measurements were carried out in CH_2Cl_2 solutions (spectrophotometric grade) by recording the spectra at 17°C and 35°C in the 300–500 nm range. The choice of the reagent concentrations of the solutions was made according to the criteria outlined in [10] and widely discussed in our previous papers [4–5].

Data Treatment

Data analysis was carried out with a program based on a non-linear least-squares method [15]. The method assumes that the best values of *K* and ϵ are those minimizing the sum of the function $\chi^2 = \Sigma(A_c - A_s)^2/(N-2)$, where A_c and A_s are the calculated and experimental absorbances and *N* is the number of data points. The optimization of *K* was carried out on four wavelengths, selected in dependence of the absorptivities of the adduct and the free reagents.

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