

## Synthesis and investigation of solvent effects on the ultraviolet absorption spectra of 1,3-bis-substituted-5,5-dimethylhydantoins

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**Abstract:** A series of 1,3-bis-substituted-5,5-dimethylhydantoins was synthesized using the reaction of 5,5-dimethylhydantoin with the corresponding alkyl halide in the presence of trimethylamine as catalyst and sodium hydroxide, according to a modified literature procedure. The experimental investigation included modification of the synthetic procedure in terms of starting materials, solvent, temperature, isolation techniques, as well as purification and identification of the products. The absorption spectra of the 1,3-bis-substituted-5,5-dimethylhydantoins were recorded in twelve solvents in the range 200–400 nm. The effects of the solvent polarity and hydrogen bonding on the absorption spectra were interpreted by means of linear solvation energy relationships using a general equation of the form  $\nu = \nu_0 + s\pi^* + a\alpha + b\beta$  and by two-parameter models presented by the equation  $\nu = \nu_0 + s\pi^* + a\alpha$ , where  $\pi^*$  is a measure of the solvent polarity/polarisability,  $\alpha$  is the scale of the solvent hydrogen bond donor acidities and  $\beta$  is the scale of the solvent hydrogen bond acceptor basicities. The solvent and substituent effects on the electronic absorption spectra of the investigated hydantoins is discussed.

**Keywords:** ultraviolet absorption spectra, solvent effects, linear solvation energy relationships, 1,3-bis-substituted-5,5-dimethylhydantoins.

### INTRODUCTION

The hydantoin ring system has been intensively studied in view of the study of naturally occurring hydantoins<sup>1</sup> and various hydantoin derivatives have been synthesized for use as pharmaceuticals.<sup>2–5</sup> Moreover, in the last twenty years 1,3-bis-substituted-5,5-dimethylhydantoins have been found to be suitable bonding agents in polymer chemistry.<sup>6</sup> Hydantoins are a class of bonding agents which provides an interaction of a filler with a resin to form a composite material. Selection of the substituents on the nitrogen atoms in the hydantoins is based on the resin and the reactivity of the substituents therewith. The functional group on the hydantoin must be reactive or compatible with the groups in the resin. 1,3-Disubstituted hydantoins are also suitable for bonding an explosive substance which is a special filler known as an oxidizer in the resins in order to form a special type of composite known as a composite propellant.<sup>6</sup>

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In our previous works,<sup>7,8</sup> the correlations between the wave numbers of the symmetric and asymmetric C=O stretching vibrations of 1,3-disubstituted-5,5-dimethylhydantoin with Taft's inductive  $\sigma^*$  constants have been reported. The results showed that the mechanism of the transmission of substituent effects in hydantoin systems depends on the nature of the substituents attached to the nitrogen atom. When electron releasing substituents are attached to the nitrogen atom, the stretching frequency increases with increasing electronegativity. However, the effect of strong electron-withdrawing substituents appears to be quite opposite, *i.e.*, the frequencies of the carbonyl stretching vibrations are decreased.

In this paper a series of 1,3-bis-substituted-5,5-dimethylhydantoin (Scheme 1) was synthesized according to modified literature procedures and the ultraviolet absorption spectra were recorded in the region 200–400 nm in twelve different solvents.



Scheme 1. The studied 1,3-bis-substituted-5,5-dimethylhydantoin.

The effects of solvent polarity and hydrogen bonding on the absorption spectra are interpreted by means of linear solvato energy relationships (LSER), a concept proposed by Kamlet and Taft,<sup>9</sup> using a general solvation Eq. (1) of the form

$$\nu_{\max} = \nu_0 + s\pi^* + a\alpha + b\beta \quad (1)$$

and by two parameter models presented by Eq. (2)

$$\nu_{\max} = \nu_0 + s\pi^* + a\alpha \quad (2)$$

where  $\alpha$ ,  $\beta$  and  $\pi^*$  are solvatochromic parameters,  $a$ ,  $b$  and  $s$  are the solvatochromic coefficients and  $\nu_0$  is the regression value of the absorption frequencies in the reference solvent cyclohexane.

In Eq. (1),  $\pi^*$  is the index of the dipolarity/polarisability, which is a measure of the ability of a solvent to stabilize a charge or a dipole by its own dielectric effects. The  $\pi^*$  scale was selected to run from 0.00 for cyclohexanone to 1.00 for dimethyl sulfoxide. The  $\alpha$  coefficient represents the solvent hydrogen bond donor (HBD) acidity, in other words it describes the ability of solvent to donate a proton in a solvent-to-solute hydrogen bond. The  $\alpha$  scale extends from 0.00 for non-HBD solvents to about 1.00 for methanol. The  $\beta$  coefficient is a measure of solvent hydrogen bond acceptor (HBA) basicity, and describes the ability of a solvent to accept a proton in a solute-to-solvent hydrogen bond. The  $\beta$  scale was selected to extend from 0.00 for non-HBD solvents to about 1.00 for hexamethylphosphoric acid triamide.

In this work the correlations of two and three parameters, with absorption frequencies is presented. The present paper demonstrates how the linear solvation energy relationship method can be used to unravel, quantify, correlate and rationalize multiple interacting effects of the solvents on the UV/Vis absorption spectra of 1,3-bis-substituted-5,5-dimethylhydantoins.

#### EXPERIMENTAL

5,5-Dimethylhydantoin, m.p. 176–178 °C, a key reactant in the synthesis of 1,3-bis-substituted-5,5-dimethylhydantoins, was prepared by the reaction of acetone cyanohydrin with ammonium carbonate. Acetone cyanohydrin was obtained from acetone, sodium cyanide and sulfuric acid (Ref. 10, m.p. 178 °C).

1,3-Bis(hydroxymethyl)-5,5-dimethylhydantoin, m.p. 98–100 °C, was prepared by the reaction of 5,5-dimethylhydantoin with 37 % formaldehyde. It was not obtained in the solid form after concentration under vacuum, as reported earlier.<sup>11</sup> In this work 1,3-bis(hydroxymethyl)-5,5-dimethylhydantoin was obtained as a suspension. This suspension was dried in air or under vacuum until solidification (Ref. 11, m.p. 100–102 °C).

1,3-Bis(2-hydroxyethyl)-5,5-dimethylhydantoin was prepared by hydroxyethylation of 5,5-dimethylhydantoin through the addition of ethylene oxide, according to literature data<sup>12</sup> without any changes. However, isolation of this product from the reaction mixture and the purification process as reported in the literature,<sup>12</sup> was not satisfactory from the point of view of the designated yields. Purification by distillation under vacuum at 205–210 °C (0.01995 bar), as reported in the literature,<sup>12</sup> caused decomposition of the 1,3-bis(2-hydroxyethyl)-5,5-dimethylhydantoin. The final purification of the crude product was modified in comparison to the method used in the literature.<sup>12</sup> The crude product was first diluted with water and the obtained mixture was extracted with diethyl ether. The ether was removed and 1,3-bis(2-hydroxyethyl)-5,5-dimethylhydantoin crystallized as solid with a melting point of 55–57 °C (Ref. 12, m.p. 57 °C).

1,3-Bis(2,3-epoxypropyl)-5,5-dimethylhydantoin was prepared by the reaction of 5,5-dimethylhydantoin with epichlorohydrin in the presence of triethylamine as catalyst and sodium hydroxide, according to the literature data.<sup>13</sup> However, isolation of this product and the purification process were modified. Namely, the crude product was not obtained as a solid compound as reported in the literature.<sup>13</sup> In this work 1,3-bis(2,3-epoxypropyl)-5,5-dimethylhydantoin was obtained as an oil. The crude product was dissolved in hot water, extracted with ether, the ether was removed and the product was crystallized by cooling the aqueous solution to 0 °C. The white crystals were obtained by filtration (m.p. 70–72 °C (Ref. 13, 72 °C)).

1,3-Bis(2-carboxyethyl)-5,5-dimethylhydantoin was prepared by the procedure described for the corresponding methyl ester.<sup>14</sup>

A mixture of 5,5-dimethylhydantoin, methyl acrylate, potassium hydroxide and hydroquinone catalyst was refluxed 3.5 h, distilled under vacuum to give dimethyl-5,5-dimethylhydantoin-1,3-bispropionate and then hydrolyzed to the corresponding acid. The isolation process and purification of this product were modified in the same way as for 1,3-bis(2,3-epoxypropyl)-5,5-dimethylhydantoin. The product melted at 110–112 °C (Ref. 14, m.p. 112 °C).

An attempt to synthesize 1,3-diallyl-5,5-dimethylhydantoin by the procedure described for 1,3-bis(2,3-epoxypropyl)-5,5-dimethylhydantoin did not give satisfactory results (5,5-dimethylhydantoin did not dissolve allyl bromide). 1,3-Diallyl-5,5-dimethylhydantoin was prepared by the modified method which we published earlier.<sup>7</sup> A mixture of hydantoin, allyl bromide and triethylamine was heated to boiling in tetrahydrofuran. In this synthesis, the same molar ratios were used as for the synthesis of 1,3-bis(2,3-epoxypropyl)-5,5-dimethylhydantoin. Tetrahydrofuran proved to be the best solvent in the series of solvents *N,N*-dimethylformamide, dimethyl sulfoxide, dioxane, tetrahydrofuran. This is probably because all the starting reagents are soluble in tetrahydrofuran and it is inert enough not to take part in the chemical reaction. Furthermore its boiling point provides the optimal temperature to avoid the eventual polymerization of the final product. The refluxing period was selected in a manner to enable the actual reaction and it is not recommended to prolong the heating longer than 3.5 h as decomposition of the product occurs. A strong base, sodium hydroxide, was added consequently to eliminate hydrogen halogenide, giving the 1,3-diallyl-5,5-dimethylhydantoin. After cooling to 0 °C, the potassium bromide was filtered off, the solvent was evaporated and the pure compound was obtained by distillation (b.p. 195–198 °C/0.0199 bar) of the reaction mixture under vacuum or by drying in air at the room temperature, yielding an oil showing all characteristics of 1,3-diallyl-5,5-dimethylhydantoin.

All the synthesized 1,3-bis-substituted-5,5-dimethylhydantoins were identified by melting or boiling points, FT-IR,  $^1\text{H}$  NMR and UV spectroscopic data.

#### RESULTS AND DISCUSSION

In this work, the ultraviolet absorption spectra were recorded for 1,3-bis-substituted-5,5-dimethylhydantoins in the region 200–400 nm on a Shimadzu 160 A spectrophotometer in twelve different solvents. The spectra were run in spectroquality solvents using concentrations of  $1 \times 10^{-4}$  M.

The effects of the solvents on the electronic absorption spectra of 1,3-bis-substituted-5,5-dimethylhydantoins can be explained as follows. The 5,5-dimethylhydantoin spectrum in which the electronic transitions on the  $-\text{CO}-\text{N}-\text{CO}-$  group lead to one absorption band was taken as the reference. The ultraviolet absorption data for 1,3-bis-substituted-5,5-dimethylhydantoins in twelve solvents are given in Table I. Examination of the data given in Table I shows that there is an identical trend in the UV absorption data of the investigated compounds in all solvents used. Increasing the chain length of the substituents generally results in bathochromic shifts of the long wavelength absorption maximum as compared to that of the reference system.

TABLE I. Ultraviolet absorption data for 1,3-bis-substituted-5,5-dimethylhydantoins

Solvent	$\lambda_{\text{max}}/\text{nm}$					
	H	$-\text{CH}_2\text{OH}$	$-\text{CH}_2\text{CH}_2\text{OH}$	$-(\text{CH}_2)_2\text{CO}_2\text{H}$	$-\text{CH}_2-\text{CH}=\text{CH}_2$	$-\text{CH}_2-\text{C}\equiv\text{C}-$
Methanol	209.0	209.6	211.8	209.4	218.4	211.0
Ethanol	211.6	213.0	214.4	211.4	218.4	213.2
Propan-2-ol	208.4	212.0	213.8	208.8	214.0	207.6
Butan-2-ol	210.0	212.4	214.0	209.0	215.0	209.6
2-Methyl-2-propanol	211.6	213.0	215.4	212.4	215.4	211.0
Ethylene glycol	207.2	208.0	209.0	211.0	215.2	206.8
<i>N,N</i> -Dimethylformamide	260.0	262.0	262.8	266.0	267.0	270.4
Ethyl acetate	252.4	254.0	254.2	252.4	254.4	256.4
Acetonitrile	205.2	205.4	205.6	—	238.2	244.6
Diethyl ether	207.6	207.8	208.2	208.4	220.2	213.2
Tetrahydrofuran	245.2	246.0	246.2	243.6	241.4	241.4
Dioxane	257.4	258.0	258.2	258.0	260.0	262.6

The effects of solvent polarity and hydrogen bonding on the 1,3-bis-substituted-5,5-dimethylhydantoins are interpreted by using a general solvation Eq. (1). The solvent parameters<sup>15</sup> are given in Table II.

The correlation of the spectroscopic data were performed by multiple linear regression analysis. Multiple linear regression of the  $\nu_{\text{max}}$  calculated from Table I ( $\nu_{\text{max}} = 1/\lambda_{\text{max}}$ ) and  $\pi^*$ ,  $\alpha$  and  $\beta$  solvent parameters gave poor results for all the examined hydantoins because the  $\beta$  parameter is not significant in these correlations. The best results were obtained

by two-parameter models in ten solvents (methanol, ethanol, propan-2-ol, butan-2-ol, 2-methyl-2-propanol, ethylene glycol, *N,N*-dimethylformamide, ethyl acetate, tetrahydrofuran and dioxane) as shown by Eqs. (2a)–(2f).

TABLE II. Parameters of the solvents<sup>15</sup>

Solvent	$\pi^*$	$\alpha$	$\beta$
Methanol	0.60	0.93	0.62
Ethanol	0.54	0.83	0.77
Propan-2-ol	0.48	0.76	0.95
Butan-2-ol	0.47	0.79	0.88
2-Methyl-2-propanol	0.41	0.68	1.01
Ethylene glycol	0.92	0.90	0.52
<i>N,N</i> -Dimethylformamide	0.88	0.00	0.69
Ethyl acetate	0.55	0.00	0.45
Acetonitrile	0.75	0.19	0.31
Diethyl ether	0.27	0.00	0.47
Tetrahydrofuran	0.58	0.00	0.55
Dioxane	0.55	0.00	0.37

5,5-Dimethylhydantoin:

$$\nu_{\max} = 41.12 - 2.58\pi^* + 9.84\alpha \quad (2a)$$

$$R = 0.9866, s = 0.798, n = 10, a/s = 3.81$$

1,3-Bis(hydroxymethyl)-5,5-dimethylhydantoin:

$$\nu_{\max} = 40.66 - 2.17\pi^* + 9.69\alpha \quad (2b)$$

$$R = 0.9877, s = 0.750, n = 10, a/s = 4.46$$

1,3-Bis(2-hydroxyethyl)-5,5-dimethylhydantoin:

$$\nu_{\max} = 40.41 - 1.86\pi^* + 9.29\alpha \quad (2c)$$

$$R = 0.9856, s = 0.779, n = 10, a/s = 4.99$$

1,3-Bis(2,3-epoxypropyl)-5,5-dimethylhydantoin:

$$\nu_{\max} = 41.40 - 3.86\pi^* + 10.33\alpha \quad (2d)$$

$$R = 0.9671, s = 0.834, n = 10, a/s = 2.67$$

1,3-Diallyl-5,5-dimethylhydantoin:

$$\nu_{\max} = 41.94 - 4.25\pi^* + 8.26\alpha \quad (2e)$$

$$R = 0.9626, s = 0.817, n = 10, a/s = 1.94$$

1,3-Bis(2-carboxyethyl)-5,5-dimethylhydantoin:

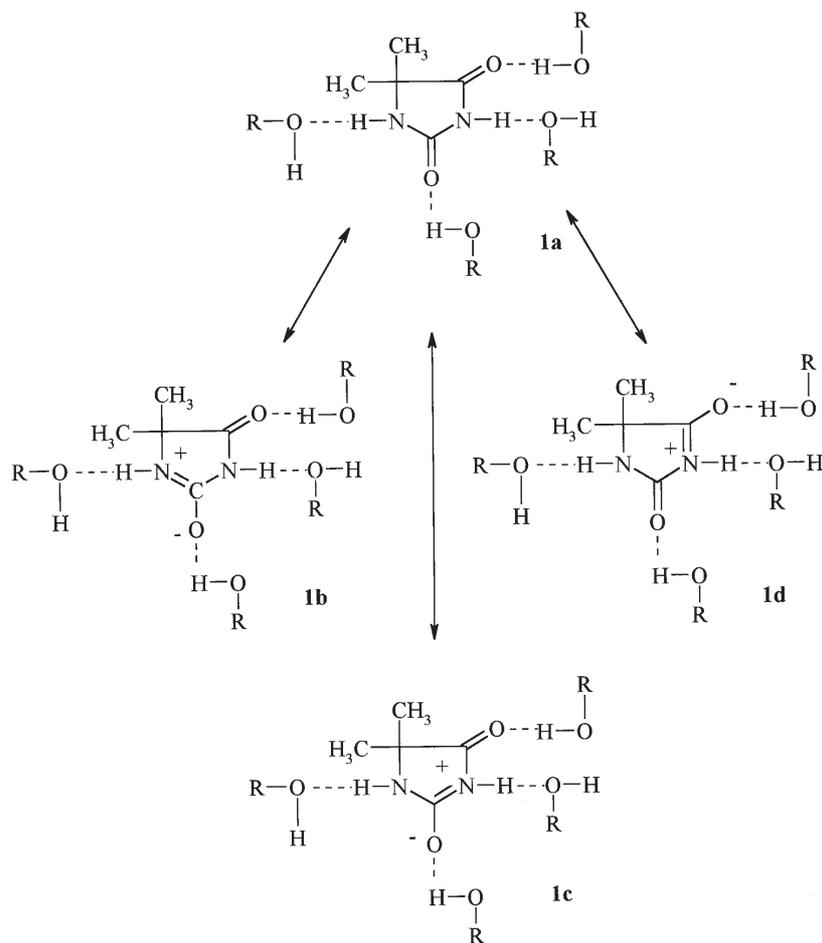
$$\nu_{\max} = 41.76 - 4.60\pi^* + 9.72\alpha \quad (2f)$$

$$R = 0.9854, s = 0.842, n = 10, a/s = 2.11$$

Eqs. (2a)–(2f) show that solvent effects on the absorption spectra of 1,3-bis-substituted-5,5-dimethylhydantoin include important contributions of the solvent polarity/polarizability and the solvent HBD (hydrogen bond donor) acidity. The latter effect undoubtedly arises from type A (solvent to solute) hydrogen bonding by protic solvents to the carbonyl oxygen of the hydantoin.

The overall hydrogen bonding situation for 5,5-dimethylhydantoin in amphiprotic solvents can probably be represented as in 1a, 1b, 1c, and 1d canonical structures (Scheme 2).

The canonical structures 1b, 1c, and 1d more closely resemble the resonance hybrid representing the electronic excited state and structure 1a can be expected to make a predominant contribution to the resonance hybrid representing the ground state. The positive



Scheme 2. Hydrogen bonding in 5,5-dimethylhydantoin in amphiprotic solvents represented by canonical structures.

sign of the coefficients in Eqs. (2a)–(2f) indicates a hypsochromic shift with increasing solvent hydrogen bond acidity. The negative sign of  $s$  in all the equations indicates a bathochromic shift with increasing solvent polarity/polarizability.

The results of the correlations of all of the examined 1,3-bis-substituted-5,5-dimethylhydantoins (Eqs. 2a–2f) show that most of the solvatochromism can be ascribed to the solvent acidity rather than the solvent polarity/polarizability. This suggests that structure 1a is stabilized to a greater extent than the structures 1b, 1c, and 1d by the dominant hydrogen bond donor acidity solvent effect. Increasing the chain length of the substituents attached to the nitrogen atoms generally leads to a decrease of the solvent HBD acidity effect compared to the reference system ( $a/s$  decreases). These results indicate that steric effects between the substituents and the carbonyl groups are important factors in the correlations between the structures in addition to solvent effects and the electronic transition energies of the studied 1,3-bis-substituted-5,5-dimethylhydantoins.

The satisfactory correlation of the ultraviolet absorption frequencies of the investigated hydantoins with the two-parameter model of the solvatochromic effects, Eq. (2), indicates that the correct model was selected. This means that this model gives a correct interpretation of the linear solvation energy relationships of the complex system of 1,3-bis-substituted-5,5-dimethylhydantoins in different solvents. We consider that the UV/Vis absorption results of 1,3-bis-substituted-5,5-dimethylhydantoins in different solvents presented in this work may be utilized to quantitatively estimate and separate the overall solvent effect into the contribution of structure 1a and structures 1b, 1c and 1d. This information is valuable when 1,3-bis-substituted-5,5-dimethylhydantoins are used as bonding agents in different composite materials.

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#### ИЗВОД

### СИНТЕЗА И ИСПИТИВАЊЕ ЕФЕКТА РАСТВОРАЧА НА UV СПЕКТРЕ 1,3-БИС-СУПСТИТУИСАНИХ-5,5-ДИМЕТИЛХИДАНТОИНА

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У оквиру рада је извршена синтеза серије 1,3-бис-супституисаних-5,5-диметилхидантоина из 5,5-диметилхидантоина и одговарајућег алкилхалогенида у присуству триметиламина као катализатора и натријум-хидроксида, по модификованом поступку из литературе. Синтетизовани хидантоини су идентификовани на основу тачке топљења, FTIR,  $^1\text{H-NMR}$  и UV спектроскопских података. Апсорпциони спектри 1,3-бис-супституисаних-5,5-диметилхидантоина су одређени у дванаест растварача различите поларности у опсегу 200–400 nm. Утицај поларности растварача као и ефекат водоничне везе проучавани су методом линеарне корелације солватационих енергија односно једначинама облика  $\nu_{\max} = \nu_0 + s\pi^* + a\alpha + b\beta$  и  $\nu_{\max} = \nu_0 + s\pi^* + a\alpha$ , у којима је  $\nu$  апсорпциона фреквенција,  $\pi^*$  мера ефекта солватације везана за поларност растварача,  $\alpha$  мера успостављања водоничне везе са протон-донорским растварањима, а  $\beta$  мера водоничне везе остварене са протонакцепторским растварањима. Резултати

презентовани у овом раду су веома значајни за сагледавање карактеристика 1,3-бис-супституисаних-5,5-диметилхидантоина због њихове велике примене у композитним материјалима као везујућих агенаса.

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#### REFERENCES

1. J. D. Dutcher, J. R. Johnson, W. F. Bruce, *J. Am. Chem. Soc.* **67** (1945) 1736
2. J. H. Bateman, in *Kirk-Othmer Encyclopedia of Chemical Technology*, vol 12, 1980, p. 692
3. S. H. Park, A. K. Bose, *Bull. Chem. Soc. Jpn.* **74** (2001) 1917
4. E. Pop, E. Shek, T. Murakami, N. S. Boder, *J. Pharm. Sci.* **78** (1989) 609
5. T. Murakami, E. Shek, E. Pop, N. Boder, *J. Pharm. Sci.* **78** (1989) 732
6. J. Consaga, US 4,214,928 (29.07.1980) and US 4,944,815 (31.07.1990)
7. G. Ušćumlić, M. Mišić-Vuković, *J. Mol. Struct.* **266** (1992) 315
8. G. Ušćumlić, S. Drmanić, V. Krstić, *Indian. J. Chem.* **36B** (1997) 193
9. M. J. Kamlet, J. L. M. Abboud, R. W. Taft, *Prog. Phys. Org. Chem.* **13** (1980) 485
10. E. Wagner, M. Baizer, *Org. Synth. Coll. Vol 3* (1955) 323
11. Y. Shimodoi, JP 4709 (15.03.1966)
12. J. Woellner, H-K. Heinemann, DE 1,912,026 (17.09.1970)
13. D. Porret, R. Aenisenslin, GB 1,148,570 (16.04.1969)
14. M. Sato, JP 15392 (20.08.1963)
15. M. J. Kamlet, J. L. M. Abboud, R. W. Taft, *J. Org. Chem.* **48** (1983) 2877.