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Original Scientific Paper

Synthesis, Spectroscopic Characterization and *ab initio* Investigation of Thioanalogues of Spirohydantoins

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Dithioanalogues of cycloalkanespiro-5-hydantoins were prepared by reaction of the respective spirohydantoins with Lawesson's reagent or P_4S_{10}. Cycloalkanespiro-5-(2-thiohydantoins) and cycloalkanespiro-5-(4-hydantoins) were also synthesized from cycloalkanespiro-5-(2,4-dithiohydantoins) *via* different reaction pathways. The structures of the compounds obtained were verified by ^1H, ^{13}C NMR and IR spectroscopy. Quantum-chemical calculations at the *ab initio* level of molecular nonlinear characteristics were performed. Increase of polarizability α and the second hyperpolarizability γ with enlarging the saturated ring was observed in all the structures studied.

Keywords
spirothiohydantoins
spirodithiohydantoins
Lawesson's reagent

INTRODUCTION

Azaspirohydantoins and their thioanalogues have been found useful in the medical treatment of disorders in mammalian central or peripheral nervous systems.[1,2] Spirothiohydantoin derivatives have been reported to show inhibiting activity toward muscular and liver glycogen phosphorilase.[3–6]

To our knowledge, three papers[7–9] on the synthesis of 2,4-dithiohydantoins have been published. Henze and Smith[7] treated 5,5-disubstituted hydantoins with phosphorus trisulfide in $NaHCO_3$ solution to obtain the respective 2,4-dithiohydantoins. Carington[8] reported that dithiohydantoins can be obtained when ketones react with CS_2 and NH_4CN. Twelve years later, Carington *et al.*[9] suggested modification of the Bucherer-Bergs reaction. These methods, however, produce low yields of dithiohydantoins.

Interest in heterocycles has increased due to their potential applications as bifunctional compounds for nonlinear optics.[10] Recently[11] hyperpolarizabilities of rhodanine-related compounds and 2-thiohydantoin, 4-thiohydantoin and 2,4-dithiohydantoin were calculated. It was found that the exocyclic heteroatoms have a much more pronounced effect on the molecular nonlinear characteristics than the ring heteroatoms.

This paper describes the preparation of mono- and dithioanalogues of cycloalkanespiro-5-hydantoins involving the use of sulfur-containing reagents. Theoretical in-

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TABLE I. Elemental analysis data of the compounds

Compound	Anal. calcd. (found) / %			
	C	H	N	S
1b	45.13 (45.04)	5.41 (5.39)	15.04 (14.88)	34.42 (34.23)
2b	47.96 (47.85)	6.04 (5.95)	13.99 (13.87)	32.01 (31.89)
3b	50.43 (50.28)	6.58 (6.54)	13.07 (12.92)	29.92 (29.86)
4b	52.59 (52.46)	7.06 (7.01)	12.27 (12.08)	28.08 (27.91)
5b	59.11 (58.93)	8.50 (8.37)	9.85 (9.74)	22.54 (22.38)
1c	50.68 (50.61)	7.09 (6.99)	19.70 (19.62)	15.03 (14.94)
2c	52.83 (52.78)	7.54 (7.44)	18.49 (18.42)	14.11 (13.95)
3c	54.74 (54.65)	7.93 (7.82)	17.41 (17.37)	13.29 (13.18)
4c	56.44 (56.41)	8.29 (8.19)	16.45 (16.39)	12.56 (12.43)
5c	61.69 (61.62)	9.38 (9.31)	13.49 (13.48)	10.29 (10.18)
1d	49.39 (49.28)	5.92 (5.90)	16.46 (16.28)	18.84 (18.64)
2d	52.15 (52.05)	6.56 (6.55)	15.20 (15.17)	17.40 (17.27)
3d	54.51 (54.31)	7.12 (7.08)	14.13 (14.03)	16.17 (15.98)
4d	56.57 (56.47)	7.60 (7.59)	13.20 (13.13)	15.10 (15.01)
5d	62.64 (62.51)	9.01 (8.87)	10.44 (10.24)	11.95 (11.76)
1g	49.39 (49.36)	5.92 (5.89)	16.46 (16.33)	18.84 (18.61)
2g	52.15 (52.01)	6.56 (6.48)	15.20 (15.12)	17.40 (17.29)

vestigations of their structure and nonlinear optical properties are aimed at following the dependence of the calculated hyperpolarizabilities on the size of the saturated ring in spiro-5-hydantoins.

EXPERIMENTAL

Synthesis of Cycloalkanespiro-5-(2,4-dithiohydantoins) ***1b–5b***

Cycloalkanespiro-5-hydantoins **1a–5a** were synthesized by the Bucherer-Lieb method.[12] Lawesson's reagent (LR) was synthesized according to Ref. 13. Dithioanalogues of the spirohydantoins were synthesized using two methods.

Method A: A suspension of 0.01 mol of the corresponding spirohydantoin **1a–5a** and 8.08 g (0.02 mol) LR in 50 ml toluene was refluxed for 6 hours and filtered immediately (Scheme 1). The product obtained was recrystallized from methanol/water solution.

Method B: A suspension of 0.01 mol of the corresponding spirohydantoin **1a–5a** and 4.45 g (0.01 mol) P_4S_{10} in 50 ml xylene was refluxed for 5 hours and filtered immediately. The precipitate formed was treated with a 10 % solution of Na_2CO_3 and then acidified with 6 mol dm^{-3} HCl. The product obtained was recrystallized from methanol-water solution. All cycloalkanespiro-5-(2,4-dithiohydantoins) **1b–5b** were obtained in 7–28 % lower yields compared to method A.

Synthesis of Cycloalkanespiro-5-(2-thiohydantoins) ***1d–5d*** *(Scheme 2)*

0.03 mol of the corresponding cycloalkanespiro-5-(2,4-dithiohydantoin) **1b–5b** and 3.50 ml 50 % aqueous solution of 2-aminoethanol were heated under reflux at 100 °C for half an hour. The mixture was left in a refrigerator for 24 hours. The product (**1c–5c**) was recrystallized from ethanol.

0.07 mol of 4-(2-hydroxyethylimino)-cycloalkanespiro-5-(2-thiohydantoin) **1c–5c** and 18 ml 20 % hydrochloric acid were refluxed for an hour. After cooling and 24 hours standing, product **1d–5d** was recrystallized from hot water.

Synthesis of Cycloalkanespiro-5-(4-thiohydantoins) ***1g, 2g*** *(Scheme 3)*

0.004 mol of the corresponding cycloalkanespiro-5-(2,4-dithiohydantoin), **1b** or **2b,** was added to 6 ml of 8 % NaOH. 0.46 ml dimethylsulfate was added to the mixture while it was stirred and cooled. Stirring was continued for 3 hours, whereupon the mixture was filtered and the filtrate was acidified with 20 % hydrochloric acid. The product was recrystallized from methanol-water solution.

All chemicals used were purchased from Merck, Fluka, Aldrich and Riedel.

The melting points were determined with a Koffler apparatus. The elemental analysis data were obtained with an automatic analyzer Carlo Erba 1106. All the products were analyzed for C, H, N and S, giving results within ± 0.2 % of the calculated values (Table I). The purity of the compounds was checked by thin layer chromatography on Kieselgel 60 F_{254}, 0.2 mm Merck plates, eluent systems (vol. ratio): (i) chloroform : acetone = 9 : 1, (ii) ethylacetate : petroleum ether = 1 : 5, (iii) chloroform : methanol : acetic acid = 9 : 2 : 1.

IR spectra were taken on spectrometers Bruker-113 and Perkin-Elmer FTIR-1600 in KBr discs. NMR spectra were taken on a Bruker DRX-250 spectrometer, operating at 250.13 and 62.90 MHz for ^1H and ^{13}C, respectively, using the standard Bruker software (zg, noediff, cosy45, invbtp, inv4lplrnd). Chemical shifts were referenced to tetramethyl-

silane (TMS). Measurements in DMSO-d_6 solutions were carried out at ambient temperature (300 K). Typical conditions for 1D ^{1}H spectra were: pulse width 30°, 1 s relaxation delay, 16K time domain points, zero-filled to 64K, hard pulse with 90° pulse width of 11.8 μs; 1D ^{13}C spectra: pulse width 30°, 1 s relaxation delay, 16K time domain points, zero-filled to 32K, hard pulse with 90° pulse width of 6.4 μs at a power level of 3 dB below the maximum output. Samples for the ^{1}H NOE (nuclear Overhauser effect) experiment were prepared by bubbling argon through the solutions for 10 min to remove traces of oxygen. The ^{1}H NOE experiments were performed in the difference mode with preirradiation time of 10 s. The 2D ^{1}H-^{1}H homonuclear correlation spectra (COSY) were typically performed with a spectral width *ca* 1500 Hz, relaxation delay 2 s, number of increments 256 or 512 and FT size 2K x 1K. The 2D ^{1}H-^{13}C Heteronuclear Multiple Quantum Coherence (HMQC) and ^{1}H-^{13}C Heteronuclear Multiple Bond Connectivity (HMBC) experiments were carried out with a spectral width of *ca.* 1000 Hz for ^{1}H and 7000 Hz for ^{13}C, relaxation delay 1.5 s, FT size 1K x 512W for the HMQC and 2K x 256W for HMBC.

Quantum-chemical Calculations

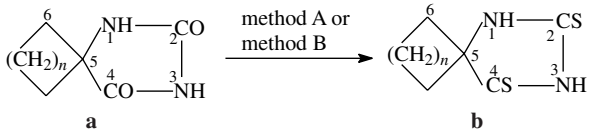
The *ab initio* molecular orbital calculations for compounds **1b–4b**, **1d–4d** and **1g–4g** were carried out with the GAMESS program package.[14] Geometric structures were fully optimized at the HF/3-21G$^{(*)}$ computational level. The CPHF (Coupled Perturbed Hartree Fock) method implemented in the GAMESS program was used for hyperpolarizability calculations at the HF/6-31++G** level using the HF/3-21G$^{(*)}$ optimized geometries of the compounds studied. The isotropic average polarizability and isotropic second hyperpolarizability were defined as $\langle\alpha\rangle = (\alpha_{xx} + \alpha_{yy} + \alpha_{zz}) / 3$ and $\langle\gamma\rangle = (\gamma_{xxxx} + \gamma_{yyyy} + \gamma_{zzzz} + 2\gamma_{xxyy} + 2\gamma_{xxzz} + 2\gamma_{yyzz}) / 5$, respectively. The first hyperpolarizability was defined as $\beta_{tot} = (\beta_x^2 + \beta_y^2 + \beta_z^2)^{1/2}$, where $\beta_i = \sum_j \beta_{ijj}$.

RESULTS AND DISCUSSION

The corresponding spirohydantoins **1a–5a** (Scheme 1) were thionated with 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide (Lawesson's reagent, LR) or P_4S_{10} following procedures developed by us and described in the Experimental.

Dithiospirohydantoins **1b–5b** were obtained when the reaction mixture of spirohydantoin and LR (mole ratio 1 : 2) in toluene was refluxed for 6 hours. The products were formed in high (82–96 %) yields. The procedure is described as method A in the experimental part. We also carried out a parallel synthesis of the same products *via* a similar pathway. Suspensions of appropriate amounts of spirohydantoin and P_4S_{10} in xylene were refluxed for 5 hours. However, this procedure (method B) resulted in 7–28 % lower yields of products than those obtained by method A.

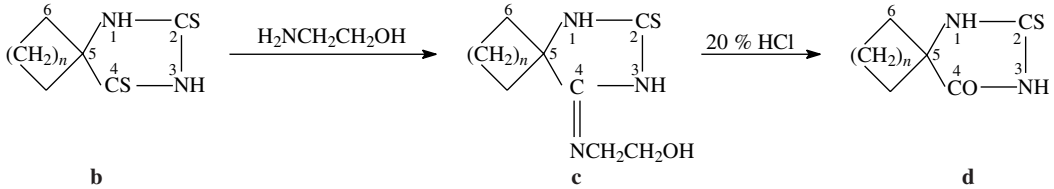
Cycloalkanespiro-5-(2-thiohydantoins) **1d–5d** were synthesized by us from cycloalkanespiro-5-(2,4-dithiohydantoins) **1b–5b** in two steps (Scheme 2).



a **b**

1–5 n = 2–5, 9

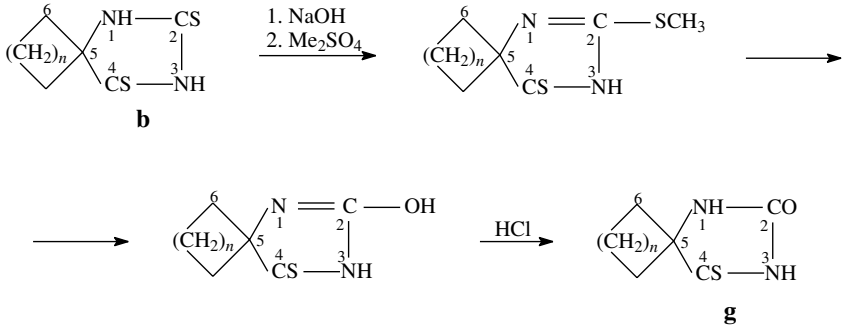
Scheme 1.



b **c** **d**

1–5 n = 2–5, 9

Scheme 2.



b **g**

1 and **2** n = 2, 3

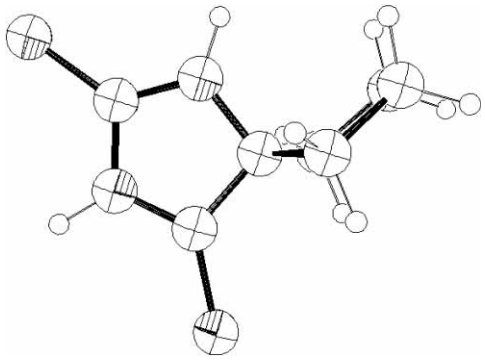
Scheme 3.

The 4-(2-hydroxyethyliminocycloalkanespiro-5-(2-thiohydantoins) **1c–5c** were obtained when the reaction mixture of 2,4-dithiohydantoin and aqueous solution of 2-aminoethanol was heated under reflux at 100 °C for 1½ hour. Then, the recrystallized product **c** was refluxed in 20 % HCl for an hour.

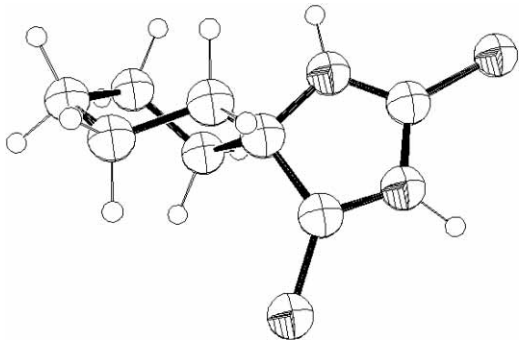
Synthesis of cycloalkanespiro-5-(4-thiohydantoins) **1g** and **2g** from cycloalkanespiro-5-(2,4-dithiohydantoins) is shown in Scheme 3.

The chemical structure of **1b–5b**, **1c–5c**, **1d–5d**, **1g** and **2g** was established by ^{1}H and ^{13}C NMR spectroscopy, employing the 1D and 2D (^{1}H/^{1}H and ^{1}H/^{13}C correlation spectra) NMR techniques. The ^{1}H and ^{13}C NMR data obtained are presented in Table II. The ^{1}H NMR spectra of **1b–5b**, **1c–5c**, **1d–5d**, **1g** and **2g** show resonance signals at 1.5–3.0 ppm (CH_2 protons of cycloalkane residue, multiplet) and two broad signals at 8.0–14.5 ppm characteristic of NH protons. The ^{1}H NMR spectra of **1c–5c** additionally contain three resonance signals at 3.3 ppm (N**C**$\mathbf{H}_2$), 3.5 ppm (**C**$\mathbf{H}_2$OH) and 4.8 ppm (O**H**). Analysis of the NOEs observed for **1b–5b** shows enhancement of the resonance of the alkyl protons from the cycle, when resonances at *ca.* 11.0 ppm were irradiated. The result was used to assign the signals at *ca.* 11.0 ppm to H1 and those at *ca.* 13.0 ppm to H3. The ^{13}C NMR chemical shifts assignment of the spectra was facilitated by analyses of the HMQC and HMBC spectra, which provide single and multiple bond ^{1}H/^{13}C connectivities. On the basis of the HMBC spectra it was possible to assign the resonance peaks of carbons C2 and C4. Resonance peaks of C2 and C4 of the dithioanalogues of spirohydantoins (**1b–5b**) appear at *ca.* 180 and 212 ppm, respectively. In the HMBC spectra of these compounds, cross peaks of C2 with H1 and H3, and C4 with H3 were observed. The ^{13}C NMR spectra of **1c–5c** show an up-field shift of the resonance signals of C4 as well as appearance of signals at 45.1 and 59.0 ppm characteristic of methylene protons of the –NCH_2CH_2OH group. The strong up-field shifts of the resonance signals of carbons C4 of cycloalkanespiro-5-(2-thiohydantoins) **1d–5d** confirm the presence of carbonyl group at C4 position. The ^{1}H and ^{13}C NMR data obtained confirm the structure of the compounds **1b–5b**, **1c–5c**, **1d–5d**, **1g** and **2g**.

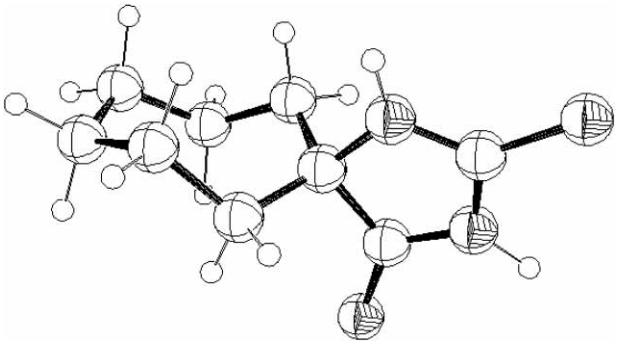
The *ab initio* HF/3-21G$^{(*)}$ calculated structures of cycloalkanespiro-5-(2,4-dithiohydantoins) **1b–4b** are shown in Figure 1. Conformations of cycloalkanes bound to the dithiohydantoin ring are »envelope«, »chair« and »saddle« for cyclopentane **1b**, cycloheptane **3b** and cyclooctane **4b**, respectively. The conformation of the cyclohexane ring in cyclohexanespiro-5-(2,4-dithiohydantoin), **2b**, is »twisted«, which is rarely observed. Similar results were obtained by us for the Cu complex of cyclohexanespirohydantoin[15] and Pt complexes of 3-amino-spirohydantoins.[16]



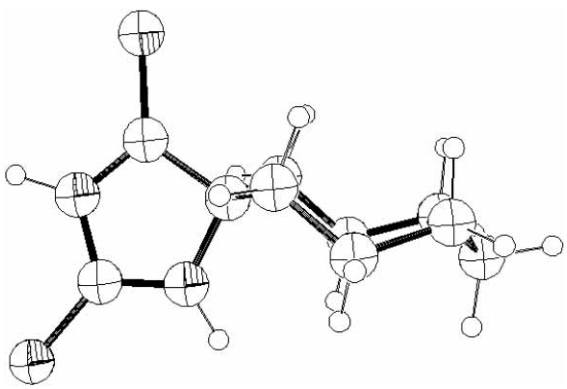
cyclopentanespiro-5-(2,4-dithiohydantoin) **1b**



cyclohexanespiro-5-(2,4-dithiohydantoin) **2b**



cycloheptanespiro-5-(2,4-dithiohydantoin) **3b**



cyclooctanespiro-5-(2,4-dithiohydantoin) **4b**

Figure 1. HF/3-21G$^{(*)}$ optimized geometries of compounds **1b–4b**.

TABLE II. Yields, melting points, IR, ^{1}H and ^{13}C NMR data of compounds **1b**–**5b**, **1c**–**5c**, **1d**–**5d** and **1g**–**2g** shown in Schemes 1–3

No.	Yield / %	M.p. / °C	IR (KBr) ν_{max} / cm^{-1}	^{1}H NMR (DMSO-d$_6$) δ / ppm	^{13}C NMR (DMSO-d$_6$) δ / ppm
1b	88	245–246	3184, 3125, 2947–2806, 1542, 1435, 1157–1133	2.00–2.49 (m, 8H), 10.9 (s, 1H), 13.11 (s, 1H)	25.3 (C7, C8), 41.8 (C6, C9), 83.3 (C5), 179.3 (C2), 212.5 (C4)
2b	91	269–270	3221, 3159, 2939–2856, 1538, 1427, 1378–1340, 1157–1117	1.54–1.74 (m, 10H), 11.07 (s, 1H), 13.06 (s, 1H)	20.8 (C7, C9), 24.4 (C8), 36.7 (C6, C10), 77.1 (C5), 180.0 (C2), 211.8 (C4)
3b	82	243–244	3145, 3055, 2933–2845, 1541, 1426, 1159–1126	1.54–2.50 (m, 12H), 10.89 (s, 1H), 13.03 (s, 1H)	22.1 (C7, C10), 29.1 (C8, C9), 40.1 (C6, C11), 79.1 (C5), 179.6 (C2), 213.5 (C4)
4b	86	255–256	3194, 3165, 2914–2861, 1546, 1428, 1197–1146	1.85–2.50 (m, 14H), 10.87 (s, 1H), 13.05 (s, 1H)	20.8 (C7, C11), 23.5 (C9), 27.3 (C8, C10), 34.9 (C6, C12), 78.4 (C5), 179.6 (C2), 212.7 (C4)
5b	96	239–240	3425, 3133, 2927–2856, 1557, 1438, 1467–1373, 1206–1153	3.28–3.52 (m, 22H), 12.55 (s, 1H), 14.51 (s, 1H)	19.1–34.1 (CH2), 78.5 (C5), 179.7 (C2), 211.2 (C4)
1c	69	254–255	3420–3250, 3180, 3130, 2980–2890, 1622, 1530, 1190, 1078	1.64–1.76 (m, 8H), 3.37 (s, 2H), 3.52 (s, 2H), 4.86 (s, 1H), 8.42 (s, 1H), 9.86 (s, 1H)	24.5 (C7, C8), 38.0 (C6, C9), 45.2 (C10), 59.1 (C11), 74.4 (C5), 182.1 (C2), 194.1 (C4)
2c	78	261–262	3410–3080, 2970–2880, 1620, 1525, 1195, 1065	1.01–1.59 (m, 10H), 3.36 (s, 2H), 3.48 (s, 2H), 4.85 (s, 1H), 8.39 (s, 1H), 10.02 (s, 1H)	21.5 (C7, C9), 24.4 (C8), 33.6 (C6, C10), 45.0 (C11), 59.1 (C12), 68.3 (C5), 182.7 (C2), 194.7 (C4)
3c	90	231–232	3239–3063, 2966–2859, 1616, 1546, 1179, 1071	1.46–1.84 (m, 12H), 3.32 (s, 2H), 3.51 (s, 2H), 4.83 (s, 1H), 8.29 (s, 1H), 9.90 (s, 1H)	21.8 (C7, C10), 27.0 (C8, C9), 36.9 (C6, C11), 45.1 (C12), 59.1 (C13), 71.4 (C5), 183.1 (C2), 195.2 (C4)
4c	95	233–234	3409–3065, 2968–2852, 1616, 1540, 1182, 1074	1.47–1.80 (m, 14H), 3.32 (s, 2H), 3.51 (s, 2H), 4.83 (s, 1H), 8.31 (s, 1H), 9.88 (s, 1H)	20.7 (C7, C11), 22.0 (C9), 27.3 (C8, C10), 32.8 (C6, C12), 45.1 (C13), 59.0 (C14), 70.8 (C5), 182.5 (C2), 195.3 (C4)
5c	96	243–244	3413–3228, 2974–2855, 1604, 1479, 1194, 1049	1.34–1.57 (m, 22H), 3.35 (s, 2H), 3.52 (s, 2H), 4.85 (s, 1H), 8.00 (s, 1H), 9.52 (s, 1H)	18.9–31.3 (CH2), 45.2 (C17), 59.0 (C18), 70.7 (C5), 182.4 (C2), 194.8 (C4)
1d	83	196–197	3330, 3124, 3000–2860, 1748, 1538, 1075	1.67–1.90 (m, 8H), 10.28 (s, 1H), 11.59 (s, 1H)	24.8 (C7, C8), 40.2 (C6, C9), 71.2 (C5), 179.7 (C2), 180.5 (C4)
2d	80	200–201	3520, 3140, 2990–2880, 1745, 1625, 1070	1.26–1.63 (m, 10H), 10.44 (s, 1H), 11.60 (s, 1H)	20.6 (C7, C9), 24.4 (C8), 32.6 (C6, C10), 65.3 (C5), 178.8 (C2), 180.9 (C4)
3d	92	210–211	3447, 3160, 2932–2852, 1739, 1533, 1035	1.53–1.82 (m, 12H), 10.36 (s, 1H), 11.52 (s, 1H)	21.9 (C7, C10), 29.2 (C8, C9), 36.1 (C6, C11), 67.7 (C5), 180.0 (C2), 180.5 (C4)
4d	88	203–204	3432, 3168, 2922–2851, 1737, 1536, 1069	1.49–1.83 (m, 14H), 10.30 (s, 1H), 11.54 (s, 1H)	20.9 (C7, C11), 23.9 (C9), 27.4 (C8, C10), 31.0 (C6, C12), 67.1 (C5), 179.3 (C2), 180.6 (C4)
5d	98	257–258	3141, 3103, 2945–2862, 1736, 1560	1.31–1.58 (m, 22H), 10.12 (s, 1H), 11.57 (s, 1H)	18.4–30.1 (CH2), 67.0 (C5), 178.5 (C2), 180.7 (C4)
1g	86	243–244		2.00–2.49 (m, 8H), 10.93 (s, 1H), 13.15 (s, 1H)	25.1 (C7, C8), 41.9 (C6, C9), 83.1 (C5), 179.1 (C2), 212.3 (C4)
2g	73	249–250		1.21–1.77 (m, 10H), 9.04 (s, 1H), 11.08 (s, 1H)	20.8 (C7, C9), 24.3 (C8), 36.6 (C6, C10), 70.9 (C5), 180.0 (C2), 212.7 (C4)

Conformations of the cycloalkane rings in compounds **1d**–**4d**, **1g**–**4g** were found to be the same and are not presented here.

Selected calculated bond lengths in cycloalkanespiro-5-(2,4-dithiohydantoins) **1b**–**4b**, cycloalkanespiro-5-(2--thiohydantoins) **1d**–**4d** and cycloalkanespiro-5-(4-thiohydantoins) **1g**–**4g** are listed in Table III. In the case of compounds **1b**–**4b**, it can be seen that on enlarging the cycloalkane ring, the N1–C5 and C4–C5 bonds become longer. Compared to the unsubstituted dithiohydantoin, the presence of a cycloalkane ring causes the N1–C2 bond to become shorter and the N1–C5 and C4–C5

TABLE III. *Ab initio* HF/3-21G(*) calculated bond lengths / Å in 2,4-dithiohydantoin, 2-thiohydantoin, 4-thiohydantoin, cycloalkane-5-spiro-2,4-dithiohydantoins **1b**–**4b**, cycloalkane-5-spiro-2-thiohydantoins **1d**–**4d** and cycloalkane-5-spiro-4-thiohydantoins **1g**–**4g**. For atom numbering see Schemes 1–3. Dipole moments / D and (hyper)polarizabilities / a.u. were calculated at the HF/6-31++G**//HF/3-21G(*) level

Parameter	Compound					
	2,4-dithiohydantoin	2,4-dithiohydantoin	**1b**	**2b**	**3b**	**4b**
Bonds						
C5–N1	1.450[a]	1.466	1.472	1.477	1.480	1.476
C5–C4	1.521[a]	1.529	1.526	1.535	1.539	1.542
C2–N1	1.354[a]	1.340	1.336	1.335	1.334	1.336
C2–N3	1.400[a]	1.391	1.390	1.390	1.389	1.389
C4–N3	1.365[a]	1.358	1.357	1.356	1.356	1.356
C2–S	1.639[a]	1.646	1.649	1.649	1.650	1.650
C4–S	1.629[a]	1.621	1.626	1.628	1.627	1.626
N1–H	1.006[a]	0.996	0.996	0.996	0.996	0.996
N3–H	1.010[a]	0.999	0.999	0.999	0.999	0.999
$\lvert\vec{\mu}\rvert$	2.91[b]	3.59	4.68	4.76	4.85	4.92
$\langle\alpha\rangle$	99[b]	89	130	140	151	162
β_{tot}	531[b]	1088	1004	972	948	877
$\langle\gamma\rangle$	29 641[b]	22 352	28 863	29 942	31 294	32 056
	2-thiohydantoin[a]	2-thiohydantoin	**1d**	**2d**	**3d**	**4d**
Bonds						
C5–N1	1.446[a] (1.448)[c]	1.460	1.463	1.469	1.472	1.468
C5–C4	1.528[a] (1.508)[c]	1.530	1.519	1.526	1.529	1.533
C2–N1	1.358[a] (1.322)[c]	1.345	1.342	1.341	1.341	1.342
C2–N3	1.393[a] (1.393)[c]	1.377	1.379	1.379	1.379	1.378
C4–N3	1.384[a] (1.349)[c]	1.377	1.380	1.379	1.379	1.379
C2–S	1.640[a] (1.642)[c]	1.650	1.653	1.653	1.653	1.653
C4–O	1.218[a] (1.225)[c]	1.201	1.204	1.206	1.206	1.204
N1–H	1.006[a]	0.995	0.996	0.996	0.996	0.996
N3–H	1.009[a]	0.997	0.997	0.997	0.997	0.997
$\lvert\vec{\mu}\rvert$	3.02[b]	3.74	4.68	4.70	4.78	4.90
$\langle\alpha\rangle$	76[b]	67	108	118	129	140
β_{tot}	67[b]	313	221	234	208	114
$\langle\gamma\rangle$	17 410[b]	12 914	18 358	19 597	20 903	21 661
	4-thiohydantoin[a]	4-thiohydantoin	**1g**	**2g**	**3g**	**4g**
Bonds						
C5–N1	1.447[a]	1.459	1.465	1.470	1.473	1.469
C5–C4	1.523[a]	1.532	1.529	1.539	1.543	1.546
C2–N1	1.366[a]	1.358	1.355	1.354	1.353	1.354
C2–N3	1.420[a]	1.412	1.411	1.410	1.410	1.409
C4–N3	1.360[a]	1.348	1.347	1.346	1.346	1.346
C2–O	1.218[a]	1.204	1.205	1.205	1.206	1.206
C4–S	1.630[a]	1.626	1.631	1.633	1.633	1.632
N1–H	1.005[a]	0.994	0.995	0.995	0.995	0.993
N3–H	1.010[a]	0.998	0.998	0.998	0.998	0.998
$\lvert\vec{\mu}\rvert$	2.63[b]	3.12	3.94	3.94	4.00	4.12
$\langle\alpha\rangle$	74[b]	67	107	117	127	138
β_{tot}	464[b]	586	627	580	586	663
$\langle\gamma\rangle$	15 510[b]	10 832	17 595	18 140	19465	20613

[a] Calculated at MP2/6-31G** level.[11]
[b] Calculated at MP2/6-31++G**//MP2/6-31G** level.[11]
[c] X-ray experimental data from Ref. 17

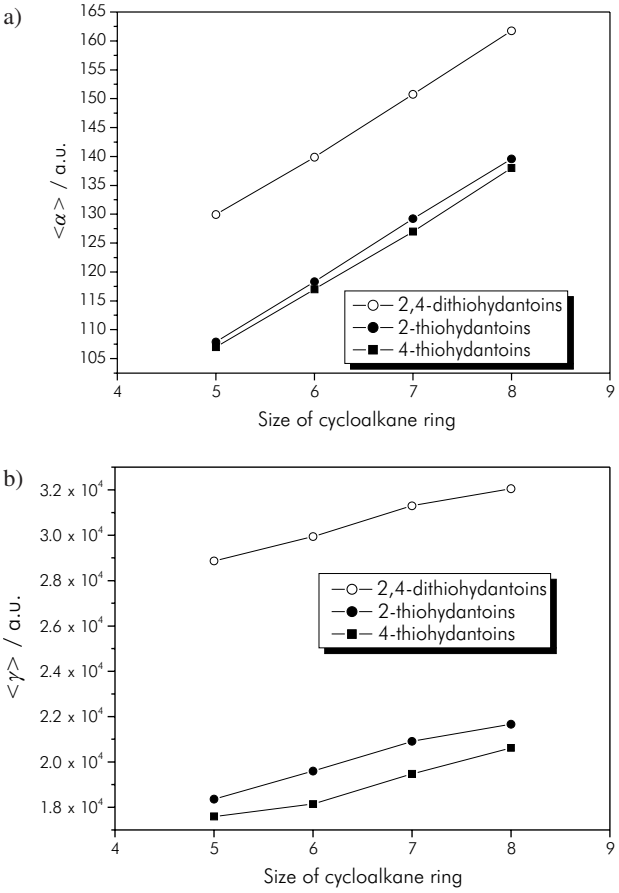


Figure 2. Dependence of the isotropic average polarizability $\langle\alpha\rangle$ and isotropic second hyperpolarizability $\langle\gamma\rangle$ on the size of the cycloalkane rings in compounds **1b**–**4b**, **1d**–**4d** and **1g**–**4g**.

bonds to become longer. Only in compound **1b**, where the cycloalkane ring is five-membered, the C4–C5 bond is shorter than that of the unsubstituted compound. The exocyclic C2–S and C4–S bonds in cycloalkanespiro-5-(2,4-dithiohydantoins) become longer by 0.004 Å and 0.006 Å, respectively. Similar changes were also observed for cycloalkanespiro-5-(2-thiohydantoins) **1d**–**4d**. The presence of the cycloalkane ring causes the N1–C5 and C4–C5 bonds to become longer and the change in the latter is more substantial.

The HF/6-31++G** calculations of the nonlinear optical properties of the compounds studied show a trend of increasing both the linear polarizability $\langle\alpha\rangle$ and the isotropic second hyperpolarizability $\langle\gamma\rangle$ with enlarging the cycloalkane ring (Figure 2). The $\langle\alpha\rangle$ values increase by 10 a.u. and the $\langle\gamma\rangle$ values by 1000 a.u. upon addition of a methylene group into the saturated ring. The opposite tendency was observed for the total first hyperpolarizability β_{tot} (Table III). The 2,4-dithiospirohydantoins **1b**–**4b** show higher values for $\langle\alpha\rangle$ (by 22 a.u.) and $\langle\gamma\rangle$ (by 10000–11000 a.u.) compared to the monothioanalogues **1d**–**4d** and **1g**–**4g** of spirohydantoin. Calculated $\langle\alpha\rangle$ values for compounds **1d**–**4d** and **1g**–**4g** are practically equal while the calculated $\langle\gamma\rangle$ values for cycloalkanespiro-5-(2-thiohydantoins) **1d**–**4d** are higher than the calculated ones for cycloalkanespiro-5-(4-thiohydantoins) **1g**–**4g**.

For comparison, the MP2/6-31G** optimized structures of 2-thiohydantoin, 4-thiohydantoin and 2,4-dithiohydantoin and their MP2/6-31++G** evaluated hyperpolarizabilities are presented in Table III. One can see that the electron correlation effects have a substantial impact on the molecular nonlinear properties.

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SAŽETAK

Sinteza, spektroskopska karakterizacija i *ab initio* istraživanje tioanaloga spirohidantoina

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Ditioanalozi cikloalkan-spiro-5-hidantoina pripravljeni su reakcijama odgovarajućih spirohidantoina i Lawesson-ovoga reagensa ili P_4S_{10}. Sintetizirani su i cikloalkan-spiro-5-(2-tiohidantoini) i cikloalkan-spiro-5--(4-tiohidantoini), uporabom različitih reakcijskih putova. Strukture dobivenih spojeva potvrđene su ^1H, ^{13}C NMR i IR spektroskopijom. Nelinearne molekularne karakteristike predviđene su kvantno-kemijskim računima na *ab initio* razini. U svim proučavanim strukturama, s povećanjem zasićenog prstena došlo je do porasta polarizabilnosti α i druge hiperpolarizabilnosti γ.