Chiroptical Spectra of 1,2-Cyclopropanedicarboxylic Monothioimides[1]

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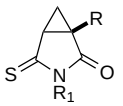
Received September 9, 1996

The structure, electronic absorption spectra, and chiroptical properties of imides have been a subject of considerable interest in recent years.[2,3] These compounds show two weak n−π* absorption bands followed by a moderately intense π−π* transition in the region of 270−200 nm as predicted by semiempirical MO calculations.[2a,c] It is well known that the substitution of sulfur for oxygen in the carbonyl group shifts absorption maxima to much longer wavelengths.[4] This allows observation of the lowest energy excited states of thiocarbonyls at the visible or near-UV region. There are some reports on the electronic and circular dichroism (CD) spectra of dithioimides,[5,6] but much less is known on the spectroscopic properties of monothioimides.[6]

In this paper, we describe the electronic and chiroptical spectra of *cis*-1,2-cyclopropanedicarboxylic monothioimides **1**−**4**. Their bicyclic skeleton is relatively rigid due to steric constraints imposed by the cyclopropane ring, and thus, the influence of conformational effects on the CD spectra should be negligible. By analogy with the parent imides, the geometries of which are known from the X-ray structures,[3,7] the 3-azabicyclo[3.1.0]hexane moiety in **1**−**4** is expected to adopt a sofa-like (half-boat) conformation with the β-carbon atom being out of the plane formed by the remaining ring atoms. For comparison, we prepared and measured the CD of the related monocyclic thioimide **5**, for which much more conformational freedom was expected. Its geometry in the solid state was established by X-ray crystallography.



1, R = R_1 = H
2, R = Me, R_1 = H
3, R = Pr^i, R_1 = H
4a, R = Ph, R_1 = H
4b, R = Ph, R_1 = Me

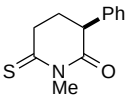


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Table 1. Electronic Absorption (UV−vis) and Circular Dichroism (CD) Data of Compounds 1−5

compd	solv[a]	UV λ, nm (ϵ)	CD λ, nm ([θ] × 10^{-3})
1	C	408 (46)	415 (12.7)
	M	400 (38)[b]	410 (9.2)
2	C	414 (33)	418 (11.7)
	M	405 (33)	412 (9.7)
3	C	414 (44)	413 (12.5)
	M	406sh (39)[b]	410 (9.3)
4a	C	418 (42)	414 (12.3)
	M	*c*	413 (10.2)
4b	C	412 (56)	414 (12.6)
	M	*c*	409 (10.3)
5	C	425 (35)	434 (1.39), 383 (−0.04)
	M	414 (32)	460 (0.02), 405 (−0.73)
	KBr[d]		398 (−0.76)[e]

[a] M = methanol, C = cyclohexane. [b] Shoulder. [c] No observable maximum of absorption. [d] KBr pellet. [e] The approximate value determined from a w/w concentration using a KBr density of 2.75 g cm^{-3}.

Results and Discussion

The synthesis of the compound **1** with chirality solely due to the sulfur substitution has been described earlier.[8] Thioimides **2**−**5** were obtained by thionation of corresponding imides of the known absolute configuration[3] with Lawesson's reagent.[9] Owing to a steric effect of the α-substituent, the reaction occurs at the less hindered carbonyl to give single isomers **3**−**5**. Only in the case of **2** was the reaction product contaminated with a small amount of the second isomer and purified by fractional crystallization. Small quantities of the corresponding dithioimides formed during the thionation can be readily separated by column chromatography in the workup procedure.

The UV−vis spectrum of the thioimide **1** in cyclohexane contains two weak absorption bands appearing as a maximum at 408 nm (ϵ 46) and a shoulder at 326 nm (97), in addition to a strong absorption at 274 nm (18 000), shifting in methanol to 400, 320, and 276 nm, respectively. In the six-membered ring compound **5** the analogous UV bands are shifted to slightly longer wavelengths (Table 1). A similar observation concerning the electronic spectra of thiosuccinimide and thioglutarimide has been described by Berg and Sandström.[6] The intensity of the observed absorptions and the solvent effects suggest the n−π* character of two lowest energy transitions and the π−π* nature of the strong absorption at the shorter wavelengths. The shape of the molecular orbitals involved in these transitions was established by the CNDO/S-CI[10] calculations for **1**. According to this method, the major components of the initial n orbitals, for the first and the second n−π* excitations, are the sulfur 3p and oxygen 2p functions, respectively, whereas the lowest energy π* orbital is delocalized over both thioimide and cyclopropane moieties. Thus, the thioimide group can be considered as "conjugated" with the three-membered ring,[11] and together they form an inherently chiral (dissymmetric) chromophore.

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(1) Presented in part at the XIth European Symposium of Organic Chemistry, Warsaw, June 1995.

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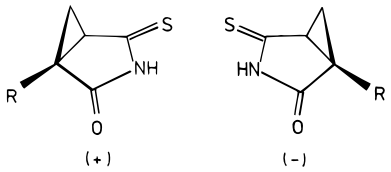
S0022-3263(96)01724-0 CCC: $14.00

Chart 1



The CD spectra of the bicyclic thioimides **1**−**4** are characterized by a strong positive Cotton effect (CE), about 415 nm corresponding to the long-wavelength n−π* transition. A relatively high value of the dissymmetry factor ($g = \Delta\epsilon/\epsilon$ of 0.08) indicates magnetic character of this transition.[12] In contrast to the parent imides[3] and related dithioimides,[13] the CE magnitude remains almost unaffected by substituents and is only weakly influenced by solvent changes. Moreover, both imides and dithioimides show a CD considerably weaker than those of **1**−**4**. Apparently, the inherent chirality of the chromophore (chiral first sphere according to Snatzke doctrine of spheres)[14] is responsible for the strong CEs of the title compounds, and its contribution to the CE outweighs that made by the ring substituents (chiral third sphere). Thus, the CE sign associated with the first n−π* excitation is determined by the helicity of the chromophore (Chart 1). The above situation closely resembles that encountered in cyclopropyl ketones, where the "conjugation" of the carbonyl group with the three-membered ring results in strong CEs.[15] There are also some analogies with the 1,2-cyclopropanedicarboximides, however, in that case contribution from the cyclopropane moiety to the CE may arise only upon distortion of the imide chromophore from the C_s symmetry, i.e., deviation of the imide group from planarity induced by substituents or solvation effects.[3]

The CD curves of the monocyclic compound **5** are strikingly different (Figure 1). They exhibit bisignate CEs within the first n−π* band; their magnitudes are much weaker than that of the related thioimide **4b**, and moreover, they are extremely sensitive to solvent changes. There are two reasons for a relatively low intensity of the overlapping CEs: the symmetric character of the chromophore "restricted" to the thioimide group, which gains optical activity only from the perturbation caused by chiral environment and a conformational flexibility of the six-membered ring in **5**. This compound may adopt two possible sofa conformers: one with the equatorial and the second with the axial phenyl substituent, contributing with the opposite signs to the CE. A conformational equillibrium between these forms can rationalize the bisignate CD curve with low CE magnitudes. The semiempirical AM1 calculations[16] revealed nearly the same heats of formation for both conformers, and thus, their populations in solution may not differ significantly. The X-ray structure of **5**[17] (Figure 2) shows that the equatorial conformer is preferred in the crystal state. The

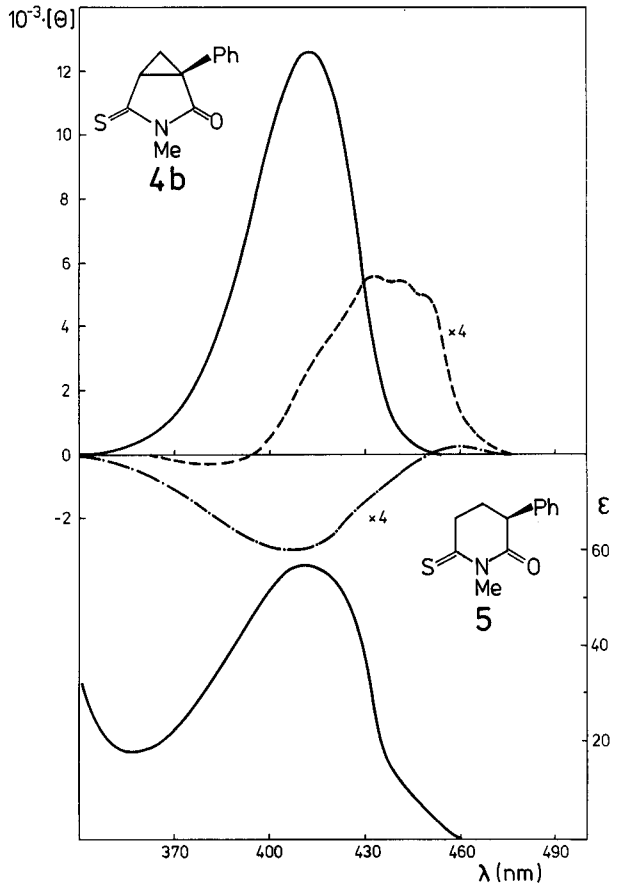


Figure 1. CD and UV spectra of **4b** in cyclohexane (—) and CD of **5** in cyclohexane (---) and methanol (—·—).

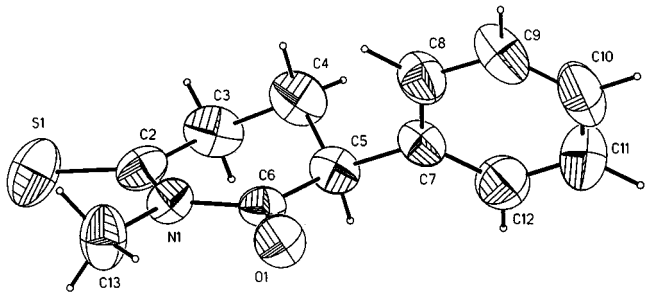


Figure 2. X-ray structure of thioimide **5**.

CD spectrum measured in the solid state (KBr pellet) exhibits the negative and monosignate CE in the n−π* region, and therefore, the negative CE should be associated with equatorial conformer and the positive one probably with the axial form. According to the solution spectra the first one dominates in polar media and the second one in hydrocarbon solvents. In this case, as well as in the case of other monothioglutarimides, the ring chirality (chiral second sphere) is expected to play an important role in determination of the CE sign. However, predictions based solely on the ring geometry might be risky for these compounds since other factors like inherent chirality of the chromophore and vicinal effects of substituents may also contribute to the CE; e.g., the

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crystal structure of **5** exhibited slight deviation of the thioimide group from planarity reflected by the C−N−C=S and C−N−C=O torsional angles [174.3(3)° and −175.7(4)°, respectively].

Surprisingly, the compounds **1**−**5** do not show measurable CEs corresponding to the second n−π* transition, probably due to the overlap with much stronger π−π* band. The CE associated with the π−π* absorption exhibits sign opposite to that observed for the long-wavelength n−π* excitation; e.g., **1** shows [θ] −65 000 at 280 nm in cyclohexane. However, measurements in this region are less reliable due to the low dissymmetic factor (g of 0.001) for the electric dipole allowed π−π* transition.

Experimental Section

All spectroscopic measurements were carried out as described previously.[2b] The synthesis of compound **1** has been published elsewhere.[8]

(1*S*,5*R*)-1-Methyl-4-thioxo-3-azabicyclo[3.1.0]hexan-2-one (2). A mixture of (1*S*,2*R*)-1-methyl-1,2-cyclopropanedicarboximide[3] (0.345 g, 3 mmol) and Lawesson's reagent (0.606 g, 1.5 mmol) was refluxed in benzene (15 mL) for 1 h. The reaction mixture was chromatographed on silica gel with chloroform as eluent. A small orange-red fraction of the dithioimide was collected first followed by a yellow fraction of the title product. After evaporation of the solvent the residue (0.21 g) was crystallized from toluene−hexane: yield 0.105 g (26%); mp 69 °C; $[\alpha]^{22}_{D}$ +166 (*c* 0.44, C_6H_6); IR (KBr) ν 1725, 1450, 1210, 1175 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.73 (br s, 1 H), 2.84 (ddd, J = 1.8, 3.2, 8.0 Hz, 1 H), 1.68 (dd, J = 3.2, 4.6 Hz, 1 H), 1.53 (dd, J = 4.6, 8.0 Hz, 1 H), 1.48 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 209.3, 178.8, 37.8, 30.7, 12.8; UV (cyclohexane) λ_{max} 414 (ϵ 33), 273 nm (16 400).

Anal. Calcd for C_6H_7NOS (141): C, 51.04; H, 5.00; N, 9.92; S, 22.71. Found: C, 51.12; H, 4.91; N, 9.88; S, 22.82.

(1*R*,5*R*)-1-Isopropyl-4-thioxo-3-azabicyclo[3.1.0]hexan-2-one (3) was obtained from (1*R*,2*R*)-1-isopropyl-1,2-cyclopropanedicarboximide[3] in a manner similar to that for compound **2**: mp 84 °C (from hexane); $[\alpha]^{20}_{D}$ +147.5 (*c* 2, C_6H_6); IR (CCl_4) ν 3415, 1755, 1430, 1150, 1025 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.16 (br s, 1 H), 2.81 (ddd, J = 1.8, 4.0, 7.4 Hz, 1 H), 2.12 (sep, J = 6.9 Hz, 1 H), 1.57 (m, 2 H), 1.04 (d, J = 6.9 Hz, 3 H), 0.98 (d, J = 6.9 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 209.6, 178.5, 40.7, 35.3, 27.7, 26.1, 19.6, 18.9; UV (cyclohexane) λ_{max} 414 (ϵ 44), 275 nm (13 200).

Anal. Calcd for $C_8H_{11}NOS$ (169): C, 56.80; H, 6.55; N, 8.28; S, 18.93. Found: C, 56.75; H, 6.77; N, 8.44; S, 18.73.

(1*S*,5*R*)-1-Phenyl-4-thioxo-3-azabicyclo[3.1.0]hexan-2-one (4a) was obtained from (1*S*,2*R*)-1-phenyl-1,2-cyclopropanedicarboximide[3] in a manner similar to that for compound **2**: mp 115−116 °C; $[\alpha]^{21}_{D}$ +139 (*c* 1, C_6H_6); IR (CCl_4) ν 3410, 1760, 1430, 1150, 1020 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.76 (br s, 1 H), 7.26 (s, 5 H), 3.28 (m, 1 H), 2.02 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 208.0, 176.9, 131.5, 128.8, 128.7, 128.4, 39.1, 38.5, 30.5; UV (cyclohexane) λ_{max} 418 (ϵ 60), 332 (136), 277 nm (19 700).

Anal. Calcd for $C_{11}H_9NOS$ (203): C, 65.02; H, 4.46; N, 6.89; S, 15.76. Found: C, 65.05; H, 4.15, N, 6.72; S, 15.73.

(1*S*,5*R*)-3-Methyl-1-phenyl-4-thioxo-3-azabicyclo[3.1,0]-hexan-2-one (4b) was obtained from (1*S*,2*R*)-*N*-methyl-1-phenyl-1,2-cyclopropanedicarboximide[3] in a manner similar to that for compound **2**: mp 136−137 °C (from heptane); $[\alpha]^{20}_{D}$ +45 (*c* 1, C_6H_6); $[\alpha]^{20}_{546}$ +107 (*c* 1, C_6H_6); IR (KBr) ν 1730, 1355, 1175, 1020 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.38 (m, 5 H), 3.35 (dd, J = 3.5, 8.0 Hz, 1 H), 3.23 (s, 3 H), 1.97 (dd, J = 4.6, 8.0 Hz, 1 H), 1.86 (dd, J = 3.5 and 4.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 207.9, 176.4, 132.1, 128.8, 128.7, 128.3, 37.4, 37.1, 31.3, 28.6; UV (cyclohexane) λ_{max} 412 (ϵ 56), 332 (82), 280 nm (19 800).

Anal. Calcd for $C_{12}H_{11}NOS$ (217): C, 66.35; H, 5.10; N, 6.45; S, 14.72. Found: C, 66.38; H, 4.90; N, 6.38; S, 14.44.

(*S*)-*N*-Methyl-2-phenylglutarimide. (S)-2-Phenylglutaric acid[18] (1.0 g, 5 mmol) was refluxed with acetyl chloride (5 mL) for 20 min and evaporated to dryness. The residue was treated with a 30% ethanolic solution of methylamine (3 mL) with cooling of the reaction mixture in an ice bath. After evaporation of the solvent, 5% hydrochloric acid (5 mL) was added, and the solution was extracted with chloroform. The organic layer was dried ($MgSO_4$), the solvent was evaporated, and the result *N*-methylamide was refluxed with acetyl chloride (5 mL) for 30 min. After evaporation to dryness, the title product was crystallized from toluene: yield 0.62 g (60%); mp 129−130 °C; $[\alpha]^{22}_{546}$ −10.7 (*c* 2.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.4−7.2 (complex m, 5 H), 3.84 (dd, J = 5.5 and 9.0 Hz, 1 H), 3.23 (s, 3 H), 2.73 (m, 2 H), 2.22 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 173.4, 172.4, 138.0, 128.8, 127.9, 127.5, 48.5, 31.3, 26.8, 25.2.

Anal. Calcd for $C_{12}H_{13}NO_2$ (203): C, 70.92; H, 6.45; N, 6.89. Found: C, 70.85; H, 6.31; N, 7.00.

(*S*)-1-Methyl-3-phenyl-6-thioxo-2-piperidinone (5) was obtained from the above imide in a manner similar to that for compound **2**: mp 84−85 °C (toluene−heptane); $[\alpha]^{20}_{D}$ +109 (1.9, C_6H_6); IR (KBr) ν 1695, 1360, 1275, 1120 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.4−7−2 (complex m, 5 H), 3.94 (t, J = 7.5, Hz, 1 H), 3.67 (s, 3 H), 3.42 (dt, J = 7.0 and 18.1 Hz, 1 H), 2.24 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 209.1, 171.0, 138.0, 128.8, 127.9, 127.6, 127.4, 127.2, 49.2, 42.1, 34.2, 26.8.

Anal. Calcd for $C_{12}H_{13}NOS$ (219): C, 65.72; H, 5.97; N, 6.39; S, 14.62. Found: C, 65.67; H, 5.84; N, 6.35; S, 14.57.

X-ray Diffraction Analysis. Crystal structure analysis was carried out for the racemic thioimide **5**.

Crystal data for $C_{12}H_{13}NOS$ (**5**): orthorhombic, space group *Pbca*, a = 16.721(8) Å, b = 6.343(4) Å, c = 22.012(8) Å, V = 2335(1) $Å^3$, Z = 8, D_{calcd} = 1.248 g cm^{-3}, λ(Mo Kα) = 0.710 73 A, T = 292 K, R_1 = 0.044, wR_2 = 0.109 for 1842 independent reflections with $I > 2\sigma(I)$.

Acknowledgment. This work was supported in part by the Committee of Scientific Research.

JO961724P

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