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INTRODUCTION OF A NEW CONCEPT: "*d*-ORBITAL PARTICIPATION IN ASYMMETRIC RECOGNITION" (DOPAR) FOR USE WITH CD ABSORPTION DATA OF DITHIOLANE DERIVATIVES[1]

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Abstract - An empirical correlation between the signs of circular dichroism (cd) absorption (at 237 and 252 nm) and the absolute configuration of two asymmetric carbons in a compound containing a dithiolane ring was elucidated by use of two types of molecular orbital calculation (MOC) (CNDO/2 and *ab initio* with STO-3G* set). These used the atom coordinates from X-ray crystallography of α-tetrahydro-ℓ-α-santonin ethylene dithioacetal. The contributions of both the 3*d*-orbital of sulfur atom and the 2*p*-orbitals of asymmetric carbons in LUMO (excited state) in the results of MOC were shown to be relatively large. These results suggested that "*d*-orbital participation in asymmetric recognition" (DOPAR) would help explain the cd absorption data of the compound. The calculated/observed ratios (c/o ratio) of two transition energy differences in the CD absorption were 2.7 in CNDO/2 and 3.5 in the *ab initio*, respectively.

Does the 3*d*-orbital of a sulfur atom participate in chemical reactions or in the uv absorption[2] of a compound containing divalent sulfur? This question has been an interesting one though there is so far no suitable model for obtaining an answer.

It is presumed, in general, that the excitation in uv region from ground state to excited state should be a better model than an organic reaction for analysing the components of individual atomic orbitals[3] in the case of molecular orbitals which play important roles for the energy transfer.

Dithiolane (or ethylene dithioacetal) rings containing two divalent sulfurs in the five membered ring are readily made by condensing carbonyls with dimercaptoethane (or ethane dithiol) in the presence of some Lewis acid.[4,5]

The dithioacetal has so far been an important protective group for carbonyl group and a key intermediate to make methylene residue by reducing with Raney nickel.[6] Taking account of the fact that the reactivity of sulfhydryl group to carbonyl is higher than that of hydroxyl group,[7] we recently reported the comparison of reactivity of *1,3-peri* repulsion with those of *1,3-diaxial* interactions using the dithiolane formation at low temperature (below -10°C) without acetic acid.[5]

Because we used tetrahydro-ℓ-α-santonin (THS) group which contains two asymmetric carbons in ring A, four stereoisomers of the THSs could be collected as ethylene dithioacetals derivatives (THS-EDT). These were reducible at γ-lactone to give the four diols of ethylene dithioacetals (3-oxo-eudesman-6,12-diol ethylene dithioacetals; THS-diol-EDT). Cd spectra of these eight dithioacetals showed originally two peaks in the region near 250 nm (210-300 nm). A new empirical correlation was found between the sign of cd absorption of the two original peaks at 237 and 252 nm and the absolute configurations at C4 and C5 in both THS-EDT and THS-diol-EDT series. For example, rectus (R) and sinister (S) forms of the absolute configuration at asymmetric carbons corresponded to plus (+) and minus(-) signs of the cd peaks, respectively, as shown in Table 1.[8] This correlation also can be applied to another reported set of cd data of steroidal dithioacetals.[9] Of course, there is no cd peak in the series of synthetic (racemic) tetralone ethylene dithioacetals.[8]

The purpose of this study is to assign the two cd absorption bands near 250 nm to the excitation energies of the molecular orbitals calculated with or without 3*d*-orbitals of sulfur atom in dithiolane ring. We used two types of molecular orbital calculations[10] (MOC): CNDO/2 and *ab initio* with *STO-3G or STO-3G* basis sets in Gaussian H* program. The atomic coordinates of X-ray crystallography of α-tetrahydro-ℓ-α-santonin ethylene dithioacetal (α-THS-EDT) were determined and transformed to those for the two types of MOCs. The MOC results gave us the transition energy from ground state (HOMO) to excited state (LUMO) including 3*d*-orbital of divalent sulfur atoms in the dithiolan ring *and also gave us the participation ratios of s, p and d-orbitals from two sulfurs* and two asymmetric carbon atoms as shown below.

RESULTS

X-ray crystallography of α-tetrahydro-ℓ-α-santonin ethylene dithioacetal (α-THS-EDT)

α-Tetrahydro-ℓ-α-santonin ethylene dithioacetal (α-THS-EDT) was synthesized[5] from THS and recrystallized twice from ethyl acetate to give colorless plates (a single crystal: 1.2 x 1.5 x 1.2 mm). A direct X-ray crystallographic analysis was carried out by a Philips four circle diffractometer with graphite-monochromated Cu-Kα radiation to elucidate the stereostructure. The space group of the crystal belongs to $P2_1$.

We measured 1674 reflections and used 1520 of these for the structure determination.

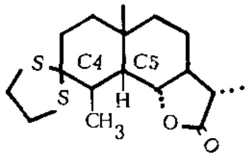
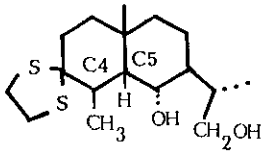
Table 1

a. Empirical correlation between absolute configurations and signs of CD absorption

Compounds	Absolute config.		CD absorption at 237 nm		at 252 nm	
	C_4	C_5	sign	amplitude ($\theta \times 10^{-3}$)	sign	amplitude ($\theta \times 10^{-3}$)
α-THS-EDT	S	S	-	2.9	-	2.8
β-THS-EDT	R	S	+	3.5	-	1.4
γ-THS-EDT	R	R	+	6.3	+	6.1
δ-THS-EDT	S	R	-	2.4	+	1.7
α-THS-diol-EDT	S	S	-	18.2	-	18.9
β-THS-diol-EDT	R	S	+	2.9	-	2.7
γ-THS-diol-EDT	R	R	+	7.5	+	9.0
δ-THS-diol-EDT	S	R	-	4.0	+	0.9

Abbreviations: CD, circular dichroism; THS, tetrahydro-ℓ-α-santonin; EDT, ethylene dithioacetal; THS-diol, 3-oxo-eudesman-6,12-diol; R, rectus; S, sinister

b. Structure of eight ethylene dithioacetals

Tetrahydro-ℓ-α-santonin ethylene dithioacetal (THS-EDT)	*3-Oxo-eudesman-6,12-diol* ethylene dithioacetal (THS-diol-EDT)
	

	Relative (and absolute) configuration at C_4	at C_5	
α-THS-EDT	$\cdots\mathrm{CH_3}$ (S)	$\cdots$H (S)	α-THS-diol-EDT
β-THS-EDT	—$\mathrm{CH_3}$ (R)	$\cdots$H (S)	β-THS-diol-EDT
γ-THS-EDT	—$\mathrm{CH_3}$ (R)	—H (R)	γ-THS-diol-EDT
δ-THS-EDT	$\cdots\mathrm{CH_3}$ (S)	—H (R)	δ-THS-diol-EDT

Table 2 Crystal Data of α-tetrahydro-ℓ-α-santonin ethylene dithioacetal

1. $C_{17}H_{26}O_2S_2$ mw 326.51
2. rhombic form; $P2_1$
3. a = 15.2200(2) α = 90.000
   b = 6.7620(6) β = 102.533
   c = 8.2760(5) γ = 90.000
4. V = 832.30/A
5. Z = 2
6 d = 1.307 calcd/g cm^{-3}

The crystal structure was solved by the direct method using MULTAN.[11] Refinement by the block-matrix least-squares method without hydrogen atoms yielded the final R value of 0.074. Other data are shown in Table 2. Atomic co-ordinates are shown in Table 3, with the standard deviations indicated in the parentheses.

The stereoview of the molecular structure of α-THS-EDT drawn by the ORTEP program is illustrated in Figure 1. The bond lengths are shown in Figure 2; the distances between two sulfurs and two asymmetric carbons were in the range from 2.8 to 4.2 A.

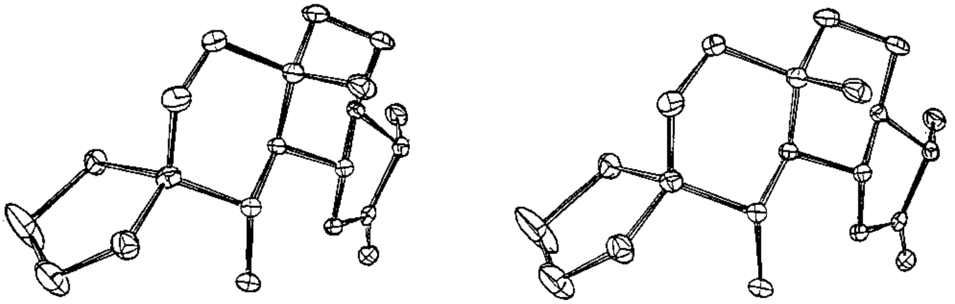


Figure 1 Stereoview of α-tetrahydro-ℓ-α-santonin ethylene dithioacetal

Table 3 Atomic position coordinates of α-tetrahydro-ℓ-α-santonin ethylene dithioacetal

Atom name	Peak height	X	Y	Z
C1	1.0	0.8008(1)	0.5410(2)	1.0672(1)
C2	1.0	0.8884(1)	0.5237(3)	1.0005(1)
C3	1.0	0.8643(0)	0.5332(1)	0.8064(1)
C4	1.0	0.7921(0)	0.3772(1)	0.7318(1)
C5	1.0	0.7067(0)	0.4157(1)	0.8012(1)
C6	1.0	0.6243(0)	0.2905(1)	0.7311(1)
C7	1.0	0.5439(0)	0.3579(1)	0.8007(1)
C8	1.0	0.5607(1)	0.3093(2)	0.9860(1)
C9	1.0	0.6435(1)	0.4280(2)	1.0668(1)
C10	1.0	0.7288(0)	0.3858(2)	0.9967(1)
C11	1.0	0.4643(0)	0.2735(1)	0.6788(1)
C12	1.0	0.4984(0)	0.3024(1)	0.5169(1)
C13	1.0	0.3938(0)	0.3788(2)	0.6671(2)
C14	1.0	0.7714(1)	0.3681(3)	0.5385(1)
C15	1.0	0.7633(1)	0.1690(2)	1.0484(1)
O1	3.0	0.5895(0)	0.3209(1)	0.5528(1)
O2	3.0	0.4543(1)	0.3139(2)	0.3768(1)
Sa	4.0	0.9713(0)	0.5011(2)	0.7426(2)
Sb	4.0	0.8238(1)	0.7871(1)	0.7351(2)
C1'	1.0	0.9619(1)	0.6969(3)	0.5919(3)
C2'	1.0	0.9102(1)	0.8593(3)	0.6325(6)

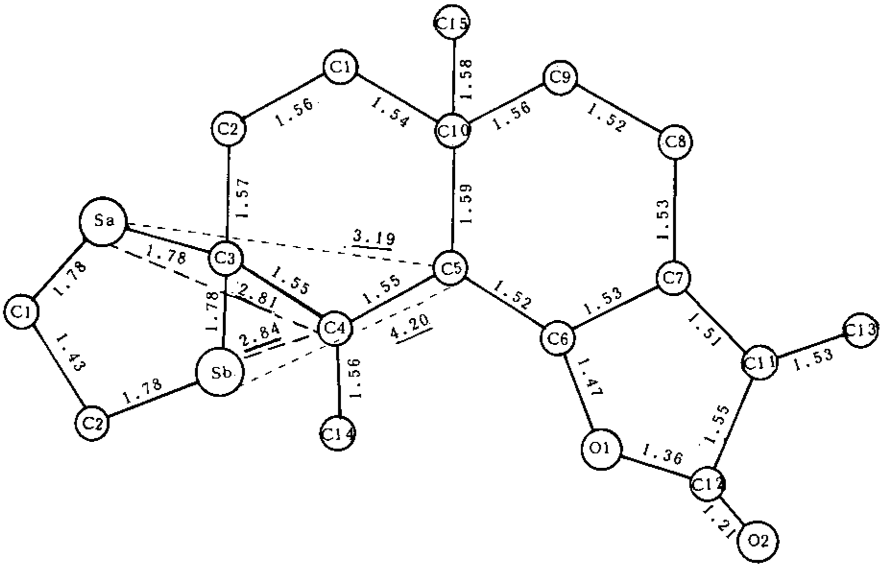


Figure 2 Bond length in α-tetrahydro-ℓ-α-santonin ethylene dithioacetal (A unit)

It is impossible to explain such a long distance interaction between the two sulfurs and the two asymmetric carbons with only their *s*- and *p*-orbitals.

We would like to interpret this empirical correlation by use of the molecular orbital calculations with *d*-orbitals using the atom coordinates obtained by X-ray crystallography.

CNDO/2 CALCULATION

The atom coordinate for CNDO/2 calculation was derived from the coordinates of X-ray crystallography. As the z-axis of the new rectangle coordinate is perpendicular to the plane of the dithiolane ring at C3 of the THS-EDT, the xy-plane of the coordinate has two *d*-orbitals out of the ordinary five *d*-orbitals (Figure 3).

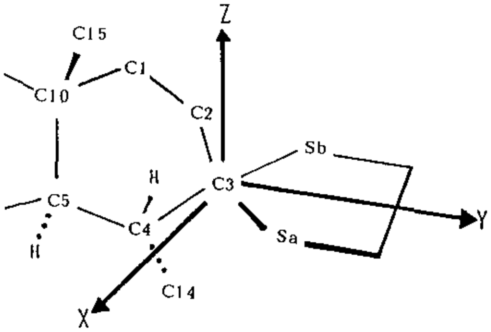


Figure 3 Right coordinate for CNDO/2 calculation of α-THS-EDT

Energy diagram of α-THS-EDT			Main atomic orbitals which contribute to MOs	
LUMO-2 Calcd / Obsbd	14.38 eV / 5.232 eV	= 2.75	S_a: (a=-0.982) $3p_y$ (A_1) $3d_{x^2-y^2}$ (A_1) (19.8%)	C_5: (a=-0.027)
2nd excitation (237 nm)				
LUMO-1 Calcd / Obsbd	13.55 eV / 4.921 eV	= 2.75	S_a: (a=1.4873) $3p_x$ (B_2) $3d_{z^2}$ (A_1) (27.9%)	C_4: (a=0.107)
1st excitation (252 nm)				
HOMO-1 HOMO-2			S_b: $3p_z$ (B_1) S_a: $3p_x$	

Figure 4 Calculation results of CNDO/2 in α-THS-EDT

In the calculated energy levels (Figure 4), there is little difference between the 1st highest occupied molecular orbital ($HOMO_1$) and the 2nd one ($HOMO_2$), from which an electron should be excited to the lowest unoccupied molecular orbital(LUMO). Both $HOMO_1$

and HOMO$_2$, containing mainly p_z of sulfur b (S$_b$) and p_x of sulfur a (S$_a$), should be ground states of molecular orbitals from which electrons can be activated by uv (or cd) absorption to excited states: the lowest LUMO would be LUMO$_1$ and the 2nd one LUMO$_2$, including atom orbital d_z2 (27.9%) of S$_a$ and $d_x2{-}_y2$ (19.8%) orbital of S$_b$, respectively, as shown in Figure 4. The number inside the parentheses is the contribution ratio.

It is most interesting that LUMO$_1$ and LUMO$_2$ are getting a large contribution from d-orbitals and a somewhat smaller contribution from asymmetric carbons; C4 (a = 0.107) and C5 (a = -0.027), respectively.

In other words, 3d-orbital clouds of sulfurs in the dithiolane ring are extending to the asymmetric carbons to hybridize with p-orbitals of the carbons. The calculated energy differences from HOMO$_1$ to LUMO$_1$ or LUMO$_2$ (13.55 or 14.38 eV, respectively) are closely proportional to the observed cd absorption energy at the two peak tops (252 or 237 nm corresponding to 4.921 or 5.232 eV, respectively), in the ratio of 2.75. This shows the good agreement between the absorption energy and the calculated energy differences.

The important d-orbitals in the LUMOs are: 3d_{xy}, 3d_{yz} and 3$d_x2{-}_y2$ (4.61%, 4.01% and 2.01%, respectively) of S$_a$ atom and 3d_xz (1.23%) of S$_b$ atom in LUMO$_2$, and 3d_{xz}, 3d_{xy}, 3$d_x2{-}_y2$ (12.92, 12.24% and 3.33%, respectively) of S$_a$ in LUMO$_3$.

We used 0.39 as the polarization exponent factor[12] for d-like orbital and exponent (coefficient) of three GTO (3a1; 0.5229 (0.16866); 3a2, 0.1636 (0.58480); and 3a3, 0.06387 (0.405678), respectively) to 3d-orbitals of sulfur atoms. The GTO of 3d orbitals of sulfur atoms should obviously be more important than the polarization factor of d-like orbitals for the long distance interaction.

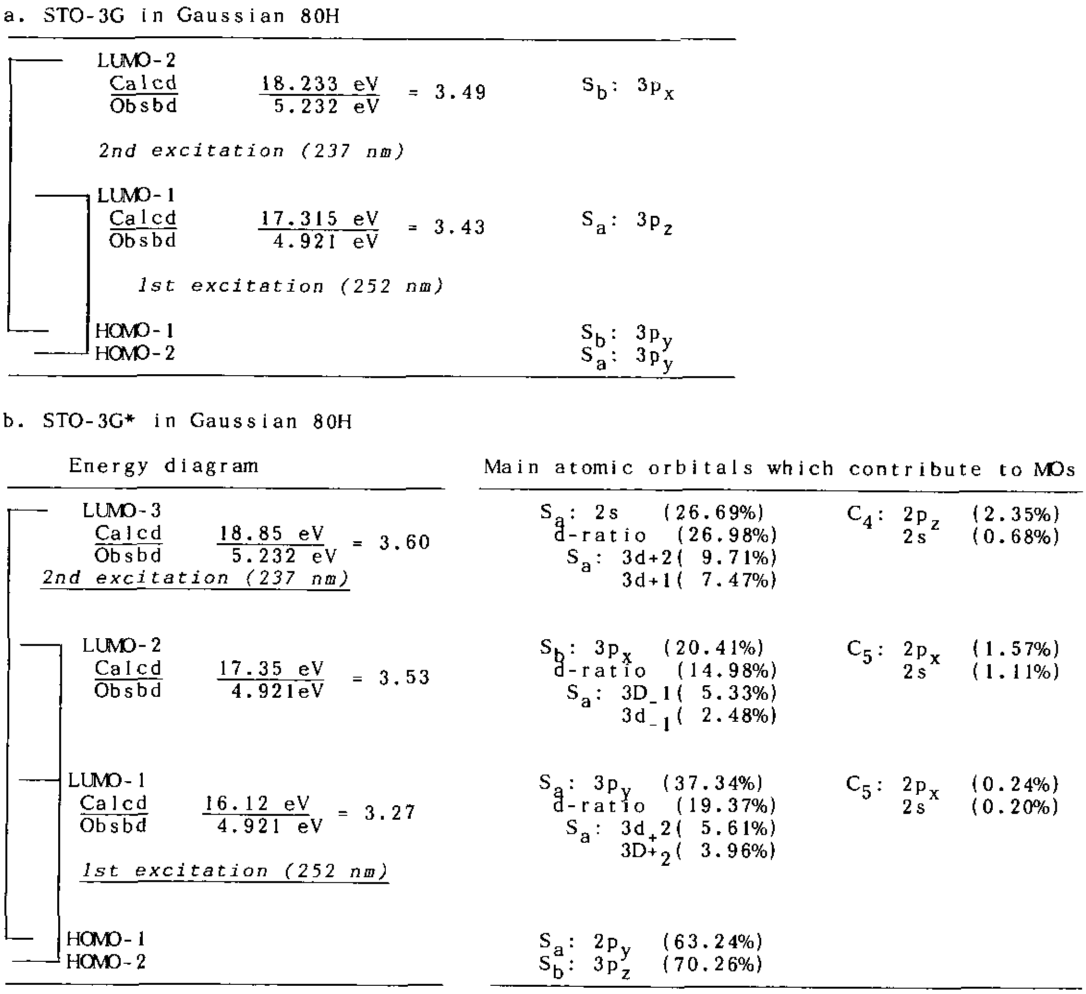
"ab initio" CALCULATION

(1) Without d-orbitals, using STO-3G basis set of Gaussian 80H

There is also little energy difference between HOMO$_1$ and HOMO$_2$ results, which include mainly 3p_y orbitals of S$_b$ and S$_a$, respectively, in 2,4-dimethylcyclohexanone ethylene dithioacetal. This is a model molecule for a partial and functional structure of α-THS-EDT molecule. Although two excited states, LUMO$_2$ and LUMO$_3$, include mainly p_z and p_x of sulfur atoms, p-orbital contributions of the asymmetric carbons were negligible.

(2) With d-orbitals, using STO-3G* basis set of Gaussian 80H

There is also little difference between HOMO$_1$ and HOMO$_2$ results, which include 2p_y electron (63%) of S$_a$ and 2p_z electron (70%) of S$_b$. The total contributions from d-orbital participations (d-ratio in Figure 5b) in the excited states are as the same



a. STO-3G in Gaussian 80H

LUMO-2	Calcd / Obsbd	18.233 eV / 5.232 eV = 3.49	S_b: $3p_x$
2nd excitation (237 nm)			
LUMO-1	Calcd / Obsbd	17.315 eV / 4.921 eV = 3.43	S_a: $3p_z$
1st excitation (252 nm)			
HOMO-1			S_b: $3p_y$
HOMO-2			S_a: $3p_y$

b. STO-3G* in Gaussian 80H

Energy diagram		Main atomic orbitals which contribute to MOs	
LUMO-3	Calcd / Obsbd: 18.85 eV / 5.232 eV = 3.60 *2nd excitation (237 nm)*	S_a: 2s (26.69%) d-ratio (26.98%) S_a: 3d+2(9.71%) 3d+1(7.47%)	C_4: $2p_z$ (2.35%) 2s (0.68%)
LUMO-2	Calcd / Obsbd: 17.35 eV / 4.921eV = 3.53	S_b: $3p_x$ (20.41%) d-ratio (14.98%) S_a: 3D_1(5.33%) $3d_{-1}$(2.48%)	C_5: $2p_x$ (1.57%) 2s (1.11%)
LUMO-1	Calcd / Obsbd: 16.12 eV / 4.921 eV = 3.27 *1st excitation (252 nm)*	S_a: $3p_y$ (37.34%) d-ratio (19.37%) S_a: $3d_{+}2$(5.61%) $3D+_2$(3.96%)	C_5: $2p_x$ (0.24%) 2s (0.20%)
HOMO-1 HOMO-2		S_a: $2p_y$ (63.24%) S_b: $3p_z$ (70.26%)	

Figure 5 Calculation results of "ab initio" (Gaussian 80H) calculation of 2,3-dimethylcyclohexanone ethylene dithioacetal
a: without d-orbitals of sulfur atoms (with STO-3G basis set).
b: with d-orbitals of sulfur atoms (with STO-3G* basis set).

as that of CNDO/2 [$LUMO_1$(19.4%), $LUMO_2$ (15.0%) and $LUMO_3$ (27.0%)]. But the participation ratios from individual *d*-orbitals of sulfurs are less than that of CNDO/2: 5.6% for $3d_{+2}$ of S_a atom in $LUMO_1$, 2.48% for $3d_{-1}$ of S_a atom and 9.72% for $3d_{+2}$ of S_a atom. The *p*-orbital participation ratios of asymmetric carbons are 1.57% for $2p_x$ of C5 in $LUMO_2$ and 2.35 for $2p_z$ of C4 in $LUMO_3$.

DISCUSSION

3*d*-Orbitals have been considered to contribute to uv (or cd) excitation[2] and also to participate in chemical reactions,[7] because the radius of 3*d*-orbital is large and diffuse. However, it was reported that a wide energy gap was needed to account the *d*-orbitals for the excited state in relevant organic reactions.

Williams reported[13] that the 1st transition energy (longest wave length) calculated by considering *d*-orbital participation was lower than the observed one.

In our study, a lone pair electron of the sulfurs in a 3*p*-orbital seems to be excited to a LUMO_I withup to 36% of 3*d*-character and 44-66% of C-S contribution in case of STO -3G* of Gaussian 80H, though such CNDO/2 calculation data have been criticized for the overestimation of *d*-orbital participation. We expected that the wave shape of uv or cd absorption should show us the electronic structure of the excited state (LUMO in MOC). LUMO should be formed from three types (*s*, *p* and *d*) of individual atom orbitals, mainly from asymmetric carbon atoms and two divalent sulfur atoms and these diffuse 3*d*- and asymmetric 2*p*-orbitals of the sulfurs should play important roles for cd absorption. Besides, these four isomers of THSs and THS-diols seem to be suitable model compounds which would retain their rigid stereostructure fastened by the γ-lactone in the former series and which would be without rigidity in the latter one.

The single crystal of α-THS-EDT was prepared and its X-ray crystallography was measured to elucidate its stereostructure. The atom coordinates of solid state were changed to new atom coordinates along a rectanglar coordinate for the two types of MOC [CNDO/2 and *ab initio* (with STO-3G or STO-3G* set of Gausian 80H)] of α-THS-EDT and 2,3-dimethyl-cyclohexanone ethylene dithioacetal as model compounds. More than 20% of individual *d*-orbital should contribute to the LUMOs of two MOC (CNDO/2 and *ab initio* with STO-3G*), which indicate recognition of the absolute configuration of asymmetric carbon.

We could not define or identify which two *d*-orbitals mainly contribute to the cd absorption in these two series of calculations: $3d_z2$ and $3d_x2\text{-}_y2$ for CNDO/2 and $3d_{xz}$, $3d_{xy}$ and $3d_x2\text{-}_y2$ for STO-3G*.

Nevertheless, the combination of 3*d*-orbital participation of sulfur and of *p*-orbital of asymmetric carbon to form the LUMO should be the mechanism of "*d*-orbital participation in asymmetric recognition" (DOPAR), a new conception. *Thus, this empirical correlation in cd absorption of the dithiolane adjacent to the asymmetric carbons should be explained by the participation of 3d-orbitals of divalent sulfur in determining the bond lengths between the two sulfurs and the two asymmetric carbons.*

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