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Synthesis and Quantum Chemistry Study of Amide-type Acyclic Polyether

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Four kinds of amide-type acyclic polyether ligands were synthesized and the crystal structures of the ligands were determined by X-ray diffraction. The electronic structures of the amide-type acyclic polyether ligands have been studied by using the density functional theory of the quantum chemistry program package Gaussian 98. All the geometry of the ligands and the reactants have been optimized at the level of B3LYP/6-31G. The analysis of Mulliken populations and the main composition and proportion of the frontier orbitals indicated that these acyclic polyethers should have some capabilities to coordinate with metal ions and the active site of each ligand has been confirmed elementarily. Compound 4 was forecast as the ligand with a higher potency to coordinate with metal ions than others from the result of comparing the energy difference ($E_{LUMO} - E_{HOMO}$) of these compounds.

Key Words: **Synthesis, Quantum, Amide-type Acyclic polyether.**

INTRODUCTION

In the last two decades, there was increasing interest in acyclic polyethers. Simon *et al.*[1] exploited the studies of the amide-type acyclic polyethers and the aether-type acyclic polyethers separately. The amide-type acyclic polyethers coordinate with metal ion as a cyclic structure customarily which is the prevalent characteristic of the traditional crown polyethers. And the amide-type acyclic polyethers also have many special characteristics which are different from the traditional crown polyethers. In special conditions, these compounds easily release the metal ion that has coordinated with them[2]. Moreover, the hydrophilic and lipophilic characteristics of the amide-type acyclic polyethers are easily adjusted by changing substituent groups. Because of these advantages over the use of traditional crown ethers, the amide-type acyclic polyethers have wide application foreground in the fields of metal enrichment, extraction, ion-selection electrodes and bioinorganic chemistry etc[3, 4].

The interaction between the amide-type acyclic polyethers and the metal ions have some special characteristics and the theoretic study of these acyclic polyethers should be inverstigated further. The synthesis and the X-ray crystal structures of four novel amide-type acyclic polyethers have been reported previously[5–8]. However, the electronic structures of these compounds have not been investigated in detail. In this paper, the quantum chemistry study of these compounds based on the X-ray crystal structures has been reported. The electronic structures and the coordination capabilities of these compounds are investigated in detail according to the quantum chemistry calculations.

EXPERIMENTAL

Synthesis of N,N′-bis-(*p*-tolyl)-2,2′-(*m*-phenylenedioxy)diacetamide (1): N-(*p*-Tolyl)-2-chloroacetamide was prepared by the reaction of *p*-methylaniline and chloroacetyl chloride in the presence of triethyl-amine[9]. To a solution of N-(*p*-tolyl)-2-chloroacetamide (1.84 g, 10 mmol) in acetone (35 mL) was added 1,3-dihydroxybenzene (0.55 g, 5.0 mmol), K_2CO_3 (1.52 g, 11 mmol) and KI (0.5 g) and the mixture stirred at 328 K for 5 h. After cooling to room temperature, the mixture was washed three times with water and then filtered. The filtered solid was recrystallized from alcohol and water. The title compound was obtained after drying the yellow powder at room temperature for 48 h. Light-brown single crystals suitable for X-ray diffraction analysis were obtained by slow evaporation of a DMF-ethanol (1 : 20 v/v) solution over a period of one month.

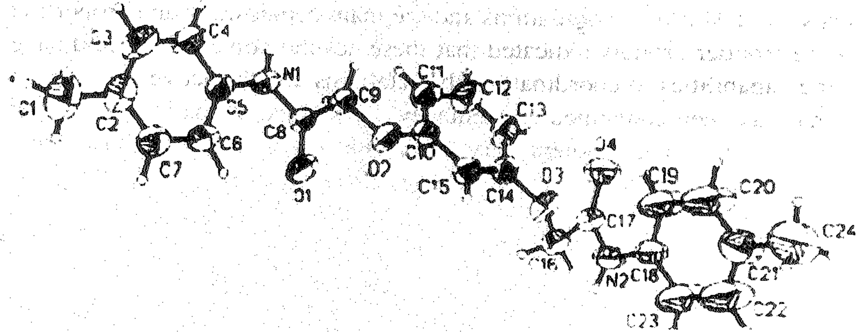

Fig. 1. The structure of **1**, showing 50% probability displacement ellipsoids and the atom-numbering

Synthesis of N,N′-bis-(*p*-methoxyphenyl)-2,2′-(*m*-phenylenedioxy)diacetamide (2): N-(*p*-Methoxyphenyl)chloroacetamide was prepared by the reaction of *p*-methoxyaniline and chloroacetyl chloride in the presence of triethylamine[9]. To a solution of N-(*p*-methoxyphenyl) chloroacetamide (2.0 g, 10 mmol) in acetone (35 mL) was added 1,3-dihydroxybenzene (0.55 g, 5.0 mmol), K_2CO_3 (1.52 g, 11 mmol) and KI (0.5 g) and the mixture was stirred at 328 K for 5 h. After cooling to room temperature, the mixture was washed three times with water and then filtered. The filtered solid was recrystallized from alcohol and water. The title compound was obtained after drying the light-grey powder at room temperature for 48 h. Colourless single crystals suitable for X-ray diffraction analysis were obtained by slow evaporation of a DMF-ethanol (1 : 20 v/v) solution over a period of one month.

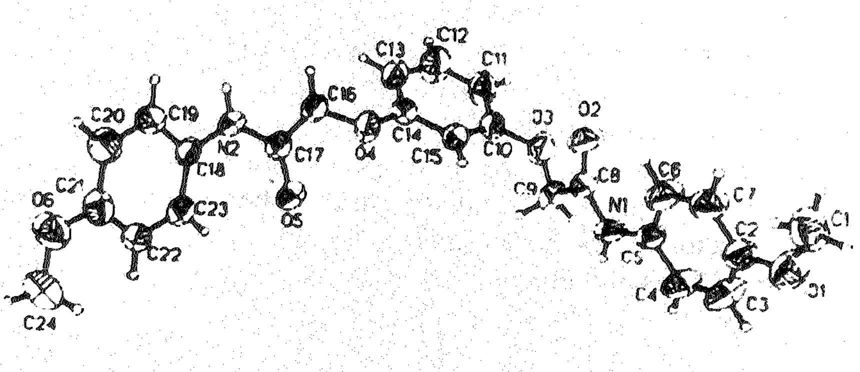

Fig. 2. The structure of **2**, showing 50% probability displacement ellipsoids and the atom-number

Synthesis of N,N′-bis-(*p*-methylphenyl)-2,2′-(*p*-phenylenedioxy)diacetamide (3): N-*p*-Methylphenyl chloroacetamide was prepared by the reaction of *p*-methylaniline and chloroacetyl chloride in the presence of triethylamine[9]. To a solution of N-*p*-methylphenyl chloroacetamide (1.84 g, 10 mmol) in acetone (35 mL) was added 1,4-dihydroxybenzene (0.55 g, 5.0 mmol), K_2CO_3 (1.52 g, 11 mmol) and KI (0.5 g). The mixture was stirred at 328 K for 5 h. After cooling to room temperature, the mixture was washed three times with water and then filtered. The residue was recrystallized from ethanol and water. The title compound was obtained after drying of the resulting yellow powder at room temperature for 48 h. Light brown single crystals suitable for X-ray diffraction study were obtained by slow evaporation of a DMF-CH_3CH_2OH (1 : 20, v/v) solution over a period of one month.

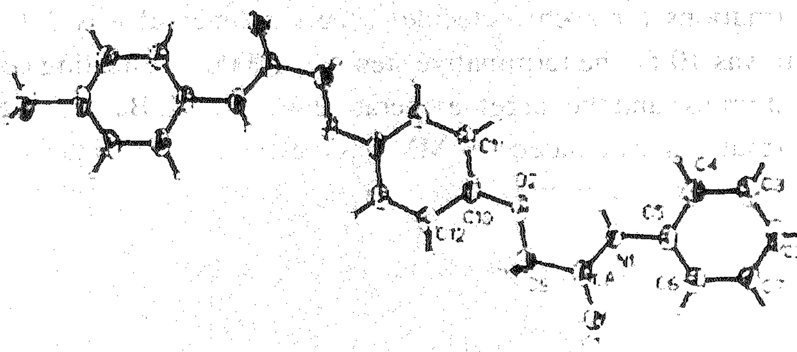

Fig. 3. The structure of 3, showing 50% probability displacement ellipsoids and the atom-numbering

Synthesis of N,N′-bis-(*p*-methoxyphenyl)-2,2′-(*p*-phenylenedioxy)diacetamide (4): To a solution of N-*p*-methoxyphenyl chloroacetamide (2.00 g, 10 mmol) in acetone (35 mL) were added 1,4-dihydroxybenzene (0.55 g, 5.0 mmol), K_2CO_3 (1.52 g, 11 mmol) and KI (0.5 g), and the mixture was stirred at 328 K for 5 h. After cooling to room temperature, the mixture was washed three times with water and then filtered. The filtered solid was recrystallized from ethanol and water. The title compound was obtained after drying the resulting yellow powder at room temperature for 48 h. Colourless single crystals for X-ray diffraction analysis were obtained by slow evaporation of a solution in dimethylformamide-ethanol (1 : 20, v/v) over a period of one month.

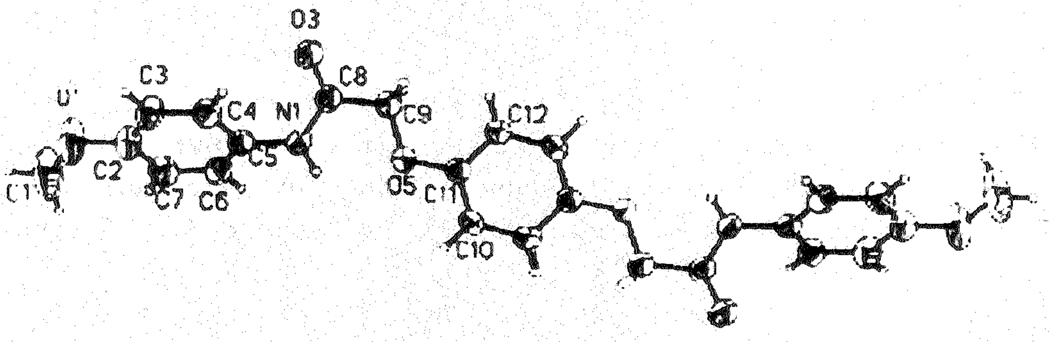

Fig. 4. The structure of 4, showing 50% probability displacement ellipsoids and the atom-number

Quantum Chemistry Calculation

Computational quantum chemistry may be used as an analytical instrument in structure analysis. It has predictive power to assist synthesis and characterization. The crystal structures of the compounds **1–4** had been determined by X-ray diffraction analysis[5-8]. So the original atomic coordinates of the compounds **1–4** were obtained from the X-ray analysis data. The structures of the compounds **1–4** were optimized at the density functional (DFT) level of theory using Beck 3 hybrid exchange (B3)[10] with Lee, Yang and Parr correlation[11] (B3LYP). The 6–31G* basis set was employed in this method.

Moreover, the three-dimensional structures of the reactants were built by the Chem3D package. And the MM2 force field was applied to search for the low energy conformations for each molecule[12], the step interval was 2.0 fs and the frame interval was 10 fs, the terminative step was 10000, the heating/cooling rate was 4.18 kJ (atom ps) and the target temperature was 300 K. Basing on the lowest energy conformations calculated by MM2 force field, the reactants geometry structures were optimized by means of DFT with 6–31G basis set.

RESULTS AND DISCUSSION

Optimized Structure Parameters

The finally optimized structure parameters of compounds **1–4** are partly summarized in Table-1.

As listed in Table-1, the bond lengths and angles of the compounds **1–4** calculated by using B3LYP/6-31G didn't differ substantially from those obtained with X-ray analysis. And the frequency calculations for each acyclic polyether molecule were carried out at 298.15 K and 1 atmosphere of pressure basing on the optimized geometries calculated by B3LYP/6-31G. There were no imaginary frequencies produced. So the calculation results should be reliable.

The energies and the main atomic electron density populations of the title compounds

To obtain a better understanding of the title compounds' stability, DFT calculations were used to examine the total energy of each acyclic polyether molecule and the reactant molecule. The calculation results were summarized in Table-2.

The energies of the acyclic polyethers were comparatively lower than those of the reactants (Table-2), so the molecules of the acyclic polyethers should be more stable than the reactants in the same condition. And the energies of **1** and **3** were lower than the energies of **2** and **3**, so the molecules of **1** and **3** would be more stable than those of **2** and **4**.

The analysis of Mulliken populations of the acyclic polyethers was based on the optimized geometry[13]. Main atomic electron density populations for the acyclic polyethers are given in Table-3.

TABLE-1
SELECTED BOND LENGTHS AND ANGLES FOR COMPOUNDS 1–4 BY CALCULATION AND X-RAY ANALYSIS

		Bond length (Å)			Bond angle (°)	
		Calculation	Crystal data		Calculation	Crystal data
Compound 1	O1-C8	1.219	1.225 (4)	O1-C8-C9	121.6	121.5
	O2-C10	1.369	1.368 (4)	O2-C9-C8	107.3	106.2
	O2-C9	1.409	1.413 (4)	O3-C16-C17	112.6	112.5
	O3-C14	1.370	1.375 (4)	O4-C17-C16	121.7	122.3
	N1-C8	1.374	1.347 (4)			
	N1-C5	1.414	1.411 (4)			
Compound 2	O2-C8	1.219	1.222 (2)	O2-C8-C9	121.8	122.6
	O3-C10	1.370	1.371 (2)	O3-C9-C8	112.7	112.3
	O3-C9	1.407	1.413 (3)	O4-C16-C17	107.1	106.5
	N1-C8	1.373	1.340 (3)	O5-C17-C16	121.2	120.6
	N1-C5	1.417	1.409 (3)			
	N2-C18	1.416	1.417 (3)			
Compound 3	O1-C8	1.224	1.220 (3)	N1-C8-O1	126.7	125.2
	O2-C10	1.375	1.392 (2)	O1-C8-C9	118.6	118.8
	O2-C9	1.421	1.411 (3)	O2-C9-C8	111.2	110.6
	N1-C8	1.363	1.343 (3)	C10-O2-C9	118.8	117.5
	N1-C5	1.412	1.434 (2)			
	C8-C9	1.532	1.527 (2)			
Compound 4	O1-C2	1.367	1.365 (3)	N1-C8-O3	126.7	124.0
	O1-C1	1.417	1.413 (4)	N1-C8-C9	114.7	117.5
	O3-C8	1.225	1.225 (2)	C8-C9-O5	111.2	110.6
	O5-C11	1.375	1.375 (2)	C9-O5-C11	117.4	118.8
	O5-C9	1.421	1.406 (2)			
	N1-C8	1.361	1.324 (3)			

TABLE-2
THE ENERGIES OF THE ACYCLIC POLYETHERS AND THE REACTANTS

Energies of the acyclic polyethers (A.U.)		Energies of the reactants (A.U.)	
Compound 1	−1339.4199	1,4-dihydroxybenzene	−382.6780
Compound 2	−1489.8275	1,3-dihydroxybenzene	−382.6816
Compound 3	−1339.4358	N-*p*-Methylphenyl chloroacetamide	−479.5831
Compound 4	−1489.8426	N-*p*-Methoxyphenyl chloroacetamide	−554.7869

TABLE-3
MAIN ATOMIC ELECTRON DENSITY POPULATION FOR THE ACYCLIC POLYETHERS

Compound 1		Compound 2		Compound 3		Compound 4	
Atom	Electric charge	Atom	Electric charge	Atom	Electric charge	Atom	Electric charge
O1	–0.4847	O1	–0.5108	O1	–0.5068	O1	–0.5068
O2	–0.5035	O2	–0.4850	N1	–0.7192	O3	–0.5104
O3	–0.5042	O3	–0.5044	O2	–0.5544	C2	0.3814
O4	–0.4808	C3	–0.1764	C10	0.3899	C3	–0.1905
N1	–0.7213	C7	–0.2108	C10A	0.3899	C4	–0.1625
N2	–0.7188	C4	–0.1977	O2A	–0.5544	C5	0.3566
C10	0.3795	C6	–0.1715	O1A	–0.5068	C6	–0.2046
C11	–0.2008	C5	0.3538	N1A	–0.7192	C7	–0.1994
C13	–0.1737	N1	–0.7198	C5A	0.3534	N1	–0.7208

There were mass negative electric charges on O1, O2, O3, O4, N1 and N2 of compound **1** as listed in Table-3. The charge of O1 was –0.4874 and the charge of O2 was –0.5035. And the steric location of O1 and O2 (Fig. 1) showed that they can coordinate with a metal ion to form a 5-member ring. So O1, O2 and O3, O4 would the active positions to donate electrons when the compound **1** coordinated with metal ions. The negative charges of compound **2** were mainly distributed on O1, O2, O3, O4, O5, O6, N1 and N2 which are partly listed in Table-3. Similarly, in compound **1**, O2, O3 and O4, O5 would also react with metal ions as the bidentate ligand.

Compounds **3** and **4** were centrosymmetric structures and the atomic electron density populations of **3** and **4** were also distributed symmetrically as listed in Table-3. For compound **3**, there were mass negative electric charges on O1, O1A, O2, O2A, N1 and N1A. So these atoms can support electrons to coordinate with metal ions. The atoms N1, N1A, O3 and O3A hold mass negative charges and strong nucleophilic characteristics of these atoms decided their capability to coordinate with metal ions.

Main composition and proportion of frontier orbitals in compounds 1–4

In order to investigate the relationship between the characteristics of the frontier orbital and the reactivity of the acyclic polyethers **1–4**, the atomic orbital populations were calculated based on the optimized geometries. The front molecular orbital energies (E_{HOMO} and E_{LUMO}) and DELH ($E_{LUMO} - E_{HOMO}$) are listed in Table-4. We use the sum of squares (SUMSQ) of each atomic orbital coefficient as the contribution of each atom to the molecular orbital and calculated by nomalization method[14]. Because the acyclic polyether ligand reacted with metal ions as an electron donor and the electron trasfer between the ligand and the metal ion mainly happened on the frontier orbital (HOMO) and the near occupied molecular obitals, so the main compositions and proportions of HOMO and the near occupied orbitals in each acyclic polyether molecule are listed in Table-4. The stereographs of the frontier molecular orbital HOMO of each acyclic polyether molecule are depicted in Fig. 5.

Compound 1 Compound 2

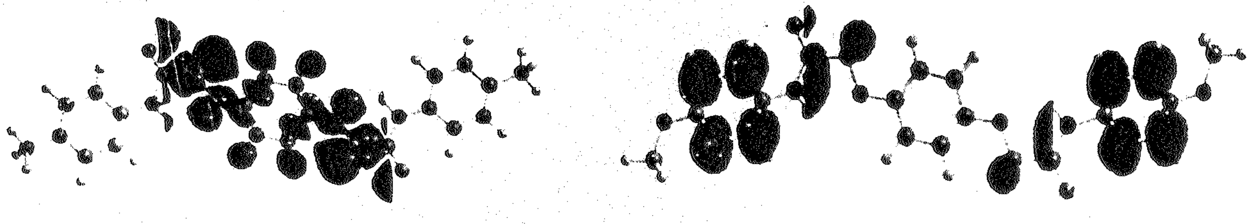

Fig. 5. The stereographs of the frontier molecular orbitals HOMO of the acyclic polyethers

TABLE-4
THE FRONT MOLECULAR ORBITAL ENERGIES AND THE ENERGY DIFFERENCE ($E_{LUMO} - E_{HOMO}$) OF COMPOUNDS 1–4

	Compound 1	Compound 2	Compound 3	Compound 4
E_{HOMO}/Hartree	–0.21499	–0.20175	–0.21410	–0.20173
E_{LUMO}/Hartree	–0.01165	–0.01196	–0.02295	–0.02156
DELH/Hartree	0.20334	0.18979	0.19115	0.18017

According to the molecular orbital theory, the frontier molecular orbitals (HOMO, LUMO) and near orbitals have great influence upon the biological activity of compounds$^{15-18}$. The reaction between the active molecules mainly happens on the frontier molecular orbitals and near orbitals. For the compound 1, the proportions of atoms O3, O4, C11 and C13 in HOMO (12.36, 13.14, 20.24 and 21.96%) were higher than other atoms as listed in Table-4 and these atoms all had negative charges (Table-3). So these atoms should be in a position to donate electrons as reacting with metal ions. Especially, O3 and O4 can form a didentate ligand to coordinate with metal ions. At the same time, although O1 and O2 had great negative charges (Table-3), but Fig. 5 shows that the atomic orbitals of these two atoms had little contribution to HOMO. Investigation found that O1 had 9.27% proportion in HOMO-2 has O2 and 8.33% proportion in

HOMO-1. So we can draw a conclusion that the coordination reaction between compound **1** and the metal ions should happen preferentially on O3 and O4.

The HOMO of compound **2** was mainly composed by the atoms of acetamide and *p*-methoxyphenyl (O1, O2, N1, C2, C3, C4, C5 and C7) as listed in Table-4. And O2 also had some contributions (6.27%) to HOMO. *p*-Methoxyphenyl is a strong electron-extract group. The dihedral angle C8-N1-C5-C6 is 11.3° basing on the X-ray analysis data. And the dihedral angle C17-N2-C18-C23 is –22°. So the atomic orbitals of N1, O2 and C8 can more easily conjugate with the π bond of *p*-methoxyphenyl and these atoms should be easier to coordinate with metal ions. N2 and O5 had proportions (15.81%, 6.79%) in HOMO-1; they should be able to coordinate with metal ions. But the coordinate capabilities of N2 and O5 would be lower than N1 and O2.

Compounds **3** and **4** were centrosymmetric (Figs. 3 and 4). And the stereographs showed that the frontier molecular orbitals (HOMO) of **3** and **4** were symmetrically distributed (Fig. 5). Most HOMO of compound **3** were symmetrically distributed on 1,4-dihydroxybenzene and O1, O1A, N1 and N1A (Table-5). And these were great negative charges on O1, O1A, O2, O2A, N1 and N1A. So these atoms should have the capabilities to coordinate with metal ions. N1, O2 and N1A, O2A may be chelated with metal ions as dident coordinate. Different from compound **3**, the HOMO of compound **4** was mainly composed of the atomic orbitals of the atoms on N-(*p*-methoxyphenyl)chloroacetamide (Fig. 5). *p*-Methoxyphenyl is a strong electron-extract group, it should have positive effect of increasing the electron cloud densities on the atoms O3, O3A, N1 and N1A. These atoms should be easier to coordinate with metal ions. So the coordination activity of compound **4** would be higher than compound **3**.

TABLE-5
MAIN COMPOSITIONS AND PROPORTIONS OF HOMO AND THE NEAR OCCUPIED ORBITALS IN 1–4 (%)

Compound 1				Compound 2				Compound 3				Compound 4			
	HOMO-2	HOMO-1	HOMO		HOMO-2	HOMO-1	HOMO		HOMO-2	HOMO-1	HOMO		HOMO-2	HOMO-1	HOMO
O3	0.03	1.11	12.36	O1	0.06	0	19.04	O1	0.25	5.04	4.69	O1	0.30	9.44	9.18
O4	0.64	1.30	13.14	O2	1.00	0	6.27	N1	1.19	11.63	10.15	C3	0.14	6.65	6.50
C10	0.06	0.96	9.70	C2	0.04	0	13.16	O2	16.71	0.04	3.22	C4	0.12	3.65	3.54
C11	0.02	1.58	20.41	C3	0.04	0	7.50	C10	13.60	0	2.16	C5	0.10	3.40	3.30
C13	0	1.86	21.96	C4	0.03	0	4.41	C10A	13.60	0	2.16	C9	0.01	2.06	2.04
C14	0.03	0.68	6.92	C5	0.12	0	16.50	O2A	16.71	0.04	3.22	C10	0.05	3.98	3.92
				C6	0.08	0	7.24	O1A	0.25	5.04	4.69	C13	0.26	8.06	7.80
				C7	0.04	0	6.68	N1A	1.19	11.63	10.15	N16	0.04	8.09	8.06
				N1	1.35	0	16.11	C5A	1.45	8.50	6.88	O19	0.01	3.67	3.72

Moreover, the front molecular orbital energies (E_{HOMO} and E_{LUMO}) and DELH ($E_{LUMO} - E_{HOMO}$) can also reflect the activities of the compounds. E_{HOMO} can be regarded as the measurement of the capability that the acyclic polyether ligand supports electrons to metal ions. Higher E_{HOMO} means that the electrons of the acyclic polyether are transferring to metal ions more easily. And DELH was correlated with the compound's stability. The energy difference of E_{HOMO} and E_{LUMO} is bigger and the compound is more stable. On the contrary, smaller energy difference means that the compound is instable. Accordingly, the activity of the compound is higher. As listed in Table-4, the E_{HOMO} of compound **4** (–0.20173) is the highest and DELH of compound **4** (0.18017) is the smallest coampared with others. The electrons transferring from compound **4** to metal ions should happen more easily than **1**, **2** and **3**, so compound **4** would be a better ligand to coordinate with metal ions.

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