

研究简报

二烷基氨基二苯基锗盐的合成及性质研究

张如芬 朱德中 尹汉东 马春林*

(聊城师范学院化学系, 聊城 252059)

关键词: 二苯基锗 氨基酸盐 合成 抗癌活性
分类号: O614.43+2

Synthesis and Properties of Diphenylgermanium Bis-Dithiocarbamates

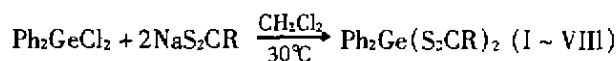
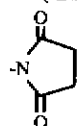
ZHANG Ru-Fen ZHU De-Zhong YIN Han-Dong MA Chun-Lin*

(Department of Chemistry, Liaocheng Teachers University, Liaocheng 252059)

The diphenylgermanium bis-dithiocarbamates $\text{Ph}_2\text{Ge}(\text{S}_2\text{CR})_2$ (I ~ VIII) have been synthesized by the reaction of Ph_2GeCl_2 with RCS_2Na in CH_2Cl_2 solvent. Their structures were characterized with IR, ^1H NMR, UV spectra and the in vitro antitumour activity are tested. In mentioned germanium complexes (I ~ VIII) the dithiocarbamatyl groups are monodentate ligands.

Keywords: diphenylgermanium dithiocarbamate synthesis antitumour activity

Organogermanium complexes containing coordination oxygen^[1], nitrogen^[2] or sulfur^[3, 4] have received a great deal of attention due to their antitumour activity. But the organogermanium dithiocarbamate complexes were reported very little^[5, 6]. Recently, we synthesis the triphenylgermanium dithiocarbamates by the reaction of triphenylgermanium chloride with sodium dithiocarbamate in dichloromethane solvent, these complexes all show up higher antitumour activity^[7]. In order to continue the study on properties of this kind of complexes, we synthesized bis-diphenylgermanium dithiocarbamates (I ~ VIII) by the reaction of diphenylgermanium dichloride with sodium dithiocarbamate. The procedure is as follows:

R = -N(CH₃)₂ (I); -N(CH₂CH₃)₂ (II);-N(CH₃)Ph (III); -NPh₂ (IV);-N(COCH₃)Ph (V); -N  (VI);(VII); -N(CH₂CH₂-OH)₂ (VIII)

1 Experimental

1.1 Measurement

Melting points were determined with Kofler micro melting point apparatus and the temperature was not corrected. IR spectra were recorded on a Nicolet-460

收稿日期: 2001-08-28。收修改稿日期: 2002-01-07。

高等学校骨干教师资助计划项目(No. 2050)和山东省自然科学基金资助项目(No. Y2000B08)。

*通讯联系人。E-mail: macl@lctu.edu.cn

第一作者: 张如芬, 女, 36岁, 高级实验师; 研究方向: 金属有机化学。

spectrophotometer in KBr. ^1H NMR spectra were measured on a JEOL-FX-90Q spectrometer using TMS as internal standard and CDCl_3 as solvent. The UV spectra were measured with a Shimadzu UV-365 ultraviolet-visible spectrophotometer in the $\lambda = 200 \sim 500\text{nm}$ region using CH_2Cl_2 as solvent. Elemental analyses were performed on a PE-2400II elemental analyzer.

1.2 Synthesis of complexes (I ~ VII)

The preparation of complexes (I ~ VIII) was carried out under nitrogen atmosphere, Ph_2GeCl_2 (1mmol) and excess of the anhydrous sodium dithiocarbamate (2.2mmol) were added to 20cm^3 of dry dichloromethane and stirred for 10h at 30°C . The precipitated salt was removed by filtration and the filtrate was concentrated to 5cm^3 under reduced pressure. Ether (5cm^3) and hexane (5cm^3) were added to this solution. A precipitate was immediately formed and collected as a raw product. It was then recrystallized from dichloromethane-ether-hexane to give a colorless crystal.

1.3 In Vitro Antitumour Activity Tests

The samples of antitumour activity tests were prepared by dissolving the complexes (I ~ VIII) in DMSO, and by diluting the solution with water to concentration $10\mu\text{g} \cdot \text{mL}^{-1}$, then according to literature method determining the inhibition rate of complexes (I ~ VIII) against culture cells of Ekrlich ascites carcinoma^[8].

2 Results and Discussion

The elemental analyses and physical properties of complexes (I ~ VIII) are shown in Table 1. The complexes (I ~ VIII) are stable to light and air, and are soluble in benzene, acetone, methylene dichloride, chloroform, tetrahydrofuran and dimethylsulfone, but insoluble in water, petroleum ether, hexane and cyclohexane.

The ^1H NMR spectra of complexes (I ~ VIII) are given in Table 2. It is shown that the chemical shift signals of the proton on the phenyl group (Ph-Ge) of the complexes (I ~ VIII) exhibit at $7.32 \sim 7.74\text{ppm}$ as multiplet, and shift higherfield than that of the diphenylgermanium chloride (Ph_2GeCl_2)^[9]. The proton signals of methylene (or methyl) connected directly with nitrogen in complexes (I, II, III and VI) appear at $3.67 \sim 3.86\text{ppm}$, they shift downfield about 0.52ppm than that of the salts of appropriate acid, this is due to the dithiocarbamatyl was coordinated to germanium atom, it is shown that electronegative of the coordinated dithiocarbamatyl group is stronger than that of no coordination one^[10].

The IR spectra of complexes (I ~ VIII) are shown in Table 3. The C-H stretching frequencies of phenyl and alkyl groups in complexes (I ~ VIII) are about $3022 \sim 2853\text{cm}^{-1}$. The characteristic stretching vibration of

Table 1 Physical and Elemental Analysis Data of the Complexes (I ~ VIII)

complex	formula	yield/%	M. P. / $^\circ\text{C}$	elemental analysis/% [*]		
				C	H	N
I	$\text{C}_{11}\text{H}_{12}\text{N}_2\text{S}_4\text{Ge}$	78	$92 \sim 94$	46.26(46.28)	4.75(4.79)	5.99(6.00)
II	$\text{C}_{11}\text{H}_{10}\text{N}_2\text{S}_4\text{Ge}$	76	$149 \sim 151$	50.48(50.50)	5.78(5.79)	5.32(5.35)
III	$\text{C}_{11}\text{H}_{12}\text{N}_2\text{S}_4\text{Ge}$	75	$87 \sim 89$	56.86(56.88)	4.43(4.47)	4.74(4.72)
IV	$\text{C}_{11}\text{H}_{12}\text{N}_2\text{S}_4\text{Ge}$	79	$84 \sim 86$	63.78(63.76)	4.23(4.25)	3.92(3.94)
V	$\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_2\text{S}_4\text{Ge}$	81	$90 \sim 92$	55.65(55.63)	4.05(4.07)	4.33(4.35)
VI	$\text{C}_{12}\text{H}_{14}\text{N}_2\text{S}_4\text{Ge}$	82	$126 \sim 128$	52.66(52.67)	5.52(5.55)	5.12(5.14)
VII	$\text{C}_{22}\text{H}_{14}\text{N}_2\text{O}_2\text{S}_4\text{Ge}$	80	$145 \sim 147$	45.93(45.95)	3.15(3.13)	4.87(4.89)
VIII	$\text{C}_{22}\text{H}_{16}\text{N}_2\text{O}_2\text{S}_4\text{Ge}$	74	$112 \sim 114$	45.93(45.95)	3.15(3.13)	4.87(4.89)

*Calculated values are given in parentheses

Table 2 ^1H NMR Spectra of Complexes (I ~ VIII) (δ/ppm)

complex	$\text{C}_6\text{H}_5\text{-Ge}$	$\text{N-CH}_2\text{-}$ or NCH_3	$\text{C}_6\text{H}_5\text{-N}$	other
I	7.32 ~ 7.70(10H, m)	3.55(12H, s)		
II	7.30 ~ 7.74(10H, m)	3.88(8H, q)		$-\text{CH}_3$, 1.26(12H, t)
III	7.35 ~ 7.64(10H, m)	3.65(6H, s)	7.21 ~ 7.37(10H, m)	
IV	7.35 ~ 7.67(10H, m)		7.23 ~ 7.35(20H, m)	
V	7.34 ~ 7.65(10H, m)		7.14 ~ 7.33(10H, m)	$-\text{COCH}_3$, 2.25(6H, s)
VI	7.32 ~ 7.70(10H, m)	3.67(8H, t)		$-\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-}$, 1.70(12H, m)
VII	7.24 ~ 7.68(10H, m)			$-\text{COCH}_2\text{CH}_2\text{-CO-}$, 2.83(8H, s)
VIII	7.32 ~ 7.69(10H, m)	3.54(8H, t)		$-\text{CH}_2\text{-O-}$, 3.78(8H, t), O-H, 4.6

s = singlet, t = triplet, q = quartet, m = multiplet

Table 3 IR Spectral Data (cm^{-1}) for Complexes (I ~ VIII)

complex	$\nu_{\text{Ph-H}}$	$\nu_{\text{C-H}}$	$\nu_{\text{C-N}}$	$\nu_{\text{C-S}}$	$\nu_{\text{Ge-S}}$	$\nu_{\text{Ge-C}}$	other
I	3022(w)	2962(m), 2853(m)	1487(s)	1258(s)	454(s)	1095(s)	
II	3023(w)	2978(m), 2868(m)	1489(s)	1257(s)	457(s)	1096(s)	
III	3025(w)	2985(m), 2872(m)	1486(s)	1256(s)	453(s)	1099(s)	
IV	3023(w)		1485(s)	1259(s)	461(s)	1098(s)	
V	3024(w)	2957(m), 2857(m)	1486(s)	1260(s)	458(s)	1097(s)	$\nu_{\text{C=O}}$, 1691(s)
VI	3023(w)	2947(m), 2848(m)	1488(s)	1255(s)	459(s)	1099(s)	
VII	3022(w)	2925(m), 2849(m)	1487(s)	1257(s)	457(s)	1095(s)	$\nu_{\text{C=O}}$, 1696(s)
VIII	3024(w)	2956(m), 2847(m)	1480(s)	1259(s)	458(s)	1093(s)	$\nu_{\text{C-H}}$, 3550(s)

germanium-carbon (Ge-C) is identified by a very strong absorption at 1097cm^{-1} , which is a little greater than that of the material Ph_2GeCl_2 (1089cm^{-1})^[11].

The C=O stretching vibration in complexes (V and VII) exhibits a strong absorption at 1693cm^{-1} . A new absorption at 450cm^{-1} is the characteristic vibration of Ge-S coordination bond^[6, 12]. The complexes (I ~ VIII) have a strong band of C-N vibration in the $1480 \sim 1489\text{cm}^{-1}$ region, this linkage is nearly normal single bond, the characteristic band of $\nu_{\text{C-S}}$ in complexes (I ~ VIII) appears one strong peak about 1257cm^{-1} ^[13].

UV spectra of complexes (I ~ VIII) are shown in Table 4. The band 1 at $223 \sim 226\text{nm}$ belongs to strong absorption K band from $\pi-\pi^*$ transition of dithiocarbamate N-C-S. The band 2 at $239 \sim 261\text{nm}$ from $\pi-\pi^*$ transition of S-C-S radical is a medium strength absorption, it is a hypsochromic shift about 18 nm than that of salt of the appropriate acid^[14]. The band 3 at $256 \sim 285\text{nm}$ which belongs to a weak absorption is attributed to electron-transfer transition $\pi-\pi^*$ in CS_2 radical, which exhibits a hypsochromic shift by $25 \sim 44\text{nm}$, as compared with the corresponding band of salt of dithiocarbamic acid.

Table 4 Selected UV Spectral Data of Complexes (I ~ VIII)

complex	band 1	band 2	band 3
I	223(215) ^a	256(280)	275(304)
II	225(216)	257(277)	276(306)
III	226(218)	255(283)	280(302)
IV	224(213)	260(280)	279(300)
V	225(220)	261(280)	285(310)
VI	223(217)	249(269)	256(301)
VII	225(220)	239(260)	259(302)
VIII	226(218)	248(254)	261(300)

^aThe values in parentheses are the absorption of sodium dithiocarbamate

The in vitro antitumour activity tests give that the inhibition rate(%) of complex (I ~ VIII) against culture cells of Ehrlich ascites carcinoma are 64, 67, 72, 74, 77, 68, 75 and 81 respectively, so the complex-

es (I ~ VIII) have higher antitumour activity to Ehrlich ascites carcinoma than that of *cis*- $[\text{Pt}(\text{NH}_3)_2\text{Cl}_2]$ (55)^[15].

Acknowledgement: We acknowledge the Financial Support of the Shandong Province Science Foundation, and the State Key Laboratory of Crystal Materials, Shandong University, P. R. China.

Reference

- [1] Gielen M., Khoulfi A. E., Biesemans M., Willem R. *Polyhedron*, **1992**, *11*, 1861.
- [2] Baz F. E., Riviere-Baudet M., Ahra M. *J. Organomet. Chem.*, **1997**, *548*, 123.
- [3] Kakimoto N. *Jpn. Kokai*, 85 ~ 16997, 85 ~ 12981.
- [4] Takeuchi Y., Tanaka K., Ohnishi-Kameyama M., Kaiman A., Rarkanyi L. *J. Chem. Soc., Chem. Commun.*, **1998**, 2289.
- [5] Chadha R. K., Drake J. E., Sarkar A. B. *Inorg. Chem.*, **1984**, *23*, 4769.
- [6] Chadha R. K., Drake J. E., Sarkar A. B. *Inorg. Chem.*, **1986**, *25*, 2201.
- [7] Yin H. D., Zhang R. F., Zhang L. Y., Ma C. L. *ACH-Model in Chemistry*, **2000**, *137*, 43.
- [8] Gielen M., EL Khoulfi A., Biesemans M., Willem R., Meunier-Piret J. *Polyhedron*, **1992**, *11*, 1861.
- [9] Ma Y., Ma C. L. *Chem. Papers*, **1989**, *43*, 761.
- [10] YIN Han-Dong (尹汉东), MA Chun-Lin (马春林), ZHANG Ru-Fen (张如芬) *Yingyong Huaxue (Chin. J. Appl. Chem.)*, **1998**, *15*, 76.
- [11] Cross R. J., Glockling F. *J. Organomet. Chem.*, **1965**, *3*, 146.
- [12] Molloy K. C., Hossain M. B., Helm D., Zuckerman J. J., Mallins F. P. *Inorg. Chem.*, **1981**, *20*, 2172.
- [13] Shinzi Kato, Kazuyasu Tani, Nobuyuki, Kohzaburoh Yamada, Hiroyuki Mifune *J. Organomet. Chem.*, **2000**, *611*, 190.
- [14] Antonio C. F. *Polyhedron*, **1986**, *5*, 871.
- [15] ZHANG Ru-Fen (张如芬), YIN Han-Dong (尹汉东), MA Chun-Lin (马春林), SHAO Xin (邵鑫) *Yong Huaxue (Chinese J. Org. Chem.)*, **2001**, *21*, 41.