

Synthesis of sterically hindered cyclohexyl Bismuth(V) carboxylates, amides and oximes

SHAILJA PANDEY¹, *S.K.NAMAN² and SHRADHA SINHA¹

¹Chemistry Department, Babu Banarasi Das Northern India Institute of Technology, Lucknow (INDIA)

²*Saraswati Institute of Technology and Management, Lucknow (INDIA)

(Acceptance Date 18th December, 2012)

Abstract

Several new sterically hindered cationic complexes of tricyclohexylbismuth (V) carboxylates, amides and oximes have been synthesized by the reaction of substituted carboxylic acids, substituted amides and ketoximes with tricyclohexylbismuth dichloride, which in turn was obtained from cyclohexylbromide magnesium and bismuth trichloride. New compounds were characterized by melting point, elemental analysis and infrared spectroscopy. The antimicrobial activity of these compounds are under study.

Key words: Organometallic compounds, Bismuth, Carboxylates, Amides, Oximes.

Introduction

In the past two decades, despite the toxicity of group 15 elements, arsenic, antimony and bismuth possessed considerable importance from industrial point of view and as biocides and chemotherapeutic agents¹⁻³. Several workers reported the anti microbial activity of organobismuth compounds⁴⁻⁶. Finet *et.al.*⁷ reported the synthesis and reactivity of chiral pentavalent bismuth derivatives. Bismuth is a rare element in terms of its low levels of toxicity and noncarcinogenic nature inspite of its heavy metal status. Kotars⁸ and his coworkers reported the antibacterial properties of some cyclic organo-

bismuth (III) compounds. Anti proliferative activity against ehrlich ascites tumor growing as fluid tumor in the peritoneal cavity of mice of organobismuth(III) bis thiolates was also reported⁹. Singhal *et. al.*¹⁰⁻¹² reported the synthesis of triaryl bismuth diamides and dioximates. Synthesis of organobismuth(III) derivatives of sterically hindered bifunctional tetradentate schiff bases were reported¹³. Moreover recent studies have shown that bismuth compounds especially thiolates and other nitrogen containing derivatives are better antitumor agents and even in certain cases can supersede known platinum based drugs¹⁴⁻¹⁵.

In view of the above facts we initiated a systematic study of sterically hindered organobismuth compounds containing Bi-O and Bi-N bonds by incorporating the substructural unit carboxylates, which have been found increasing importance as antitumor agents. In the present paper we have synthesized tricyclohexylbismuth dicarboxylates, tricyclohexylbismuth diamides and tricyclohexylbismuth dioximates and study their antimicrobial activity.

Material and Methods

The melting points of the compounds were determined in a Toshniwal Electric melting point bath and are uncorrected. IR spectra were recorded on Perkin-Elmer 577 spectrophotometer in the range 4000-400 cm^{-1} using KBr. Special precautions were taken to exclude moisture. Anhydrous benzene (Aldrich) was used as the solvent.

Synthesis of tricyclohexylbismuth dichloride (Cy-C₆H₁₁)₃BiCl₂ :

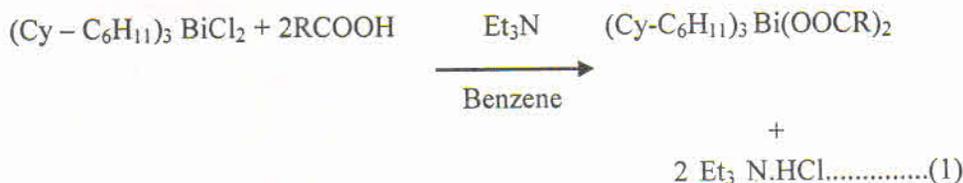
A Grignard solution was prepared from cyclohexyl bromide (0.50 mol) and magnesium (0.50 mol) in dry ether in the Nitrogen atmosphere with exclusion of light in

ether (150 ml). A solution of BiCl₃ (0.16 mol) in benzene solvent was added dropwise, the reaction mixture was stirred vigorously after complete addition of BiCl₃ it refluxed for 2 hours. This gave Tri cyclohexyl bismuth was bubbled with chlorine for half an hour. The reaction mixture was hydrolysed by addition of 10% HCl in cold water. The organic layer was separated and dried over sodium sulphate. Removal of solvent followed by crystallization of white solid from absolute alcohol.

Melting Point: 124°C

Synthesis of tricyclohexylbismuth dicarboxylates (Fig 1) :

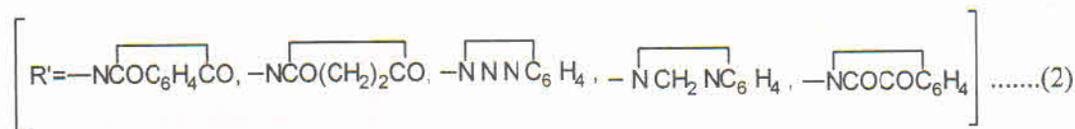
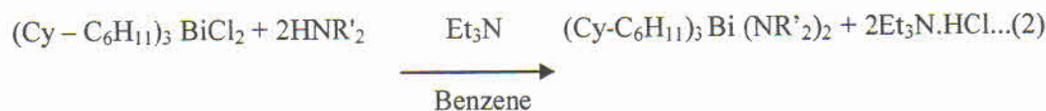
Tricyclohexylbismuth dichloride (1 mol), substituted carboxylic acid (2 mole) and triethylamine (1 ml) were stirred in benzene (30 ml) at room temperature for 2 hrs. The reaction mixture was then refluxed for one hr to ensure completion of the reaction. The precipitated triethylamine hydrogen chloride was filtered off (m.p. > 240°C) and the filtrate on concentration in vacuum, afforded the corresponding product which was precipitated out by adding petroleum ether (40-60°) to concentrated mixture. (Table 1)



[RCOO=C₆H₅ COO⁻, *m*-OH C₆H₄COO⁻, *p*-NH₂ C₆H₄COO⁻, *p*-NO₂ C₆H₄COO⁻, *p*-Cl C₆H₄COO⁻]

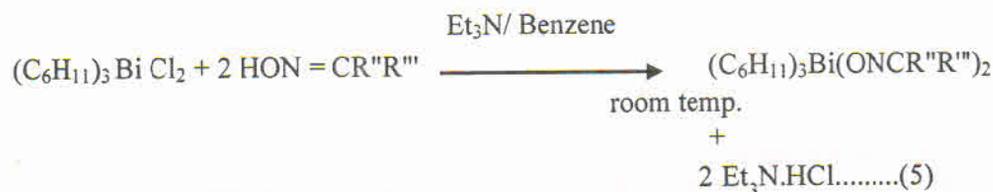
Synthesis of tricyclohexylbismuth diamides (Fig 2) :

To a stirred solution of tricyclohexylbismuth dichloride (1 mol) in solvent benzene (40 ml), substituted amide (2 mol) and triethylamine in the same solvent was added at room temperature. The reaction mixture



Synthesis of tricyclohexylbismuth dioximates (Fig. 3) :

To a stirred solution of tricyclohexylbismuth dichloride (1 mol) in solvent benzene (50 ml), ketoxime (2 mol) and triethylamine (1 ml) in the same solvent was added at room temperature. The reaction mixture was stirred



(R'', R''' = Me, Me; Me, Ph)

SUGGESTED STRUCTURES OF TRI(CYCLOHEXYL)BISMUTH(V) DERIVATIVES

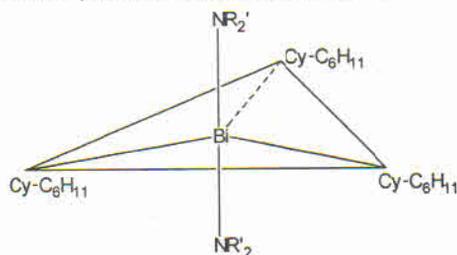
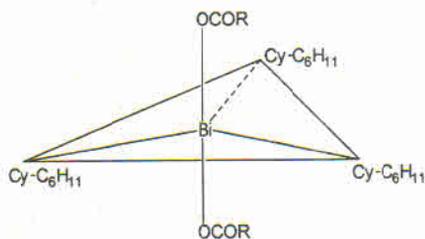


FIG. 1: TRICYCLOHEXYLBISMUTH DICARBOXYLATES
($(\text{Cy}-\text{C}_6\text{H}_{11})_3\text{Bi}(\text{OOCR})_2$)

FIG. 2: TRICYCLOHEXYLBISMUTH DIAMIDES.
($(\text{Cy}-\text{C}_6\text{H}_{11})_3\text{Bi}(\text{NR}_2)_2$)

was stirred for 3 hrs then it was refluxed for one hr to ensure completion of the reaction. The precipitated triethylamine hydrogen chloride was filtered off and the filtrate was distilled off followed by addition of petroleum ether (40-60°) to obtain the desired compound. (Table 2)

for 3 hrs then refluxed for one hr to ensure completion of the reaction. The precipitated triethylamine hydrogen chloride was filtered off and then filtrate was distilled off followed by addition of petroleum ether (40-60) to obtain the desired oxime derivative which is stable and do not decompose on storage. (Table 3)

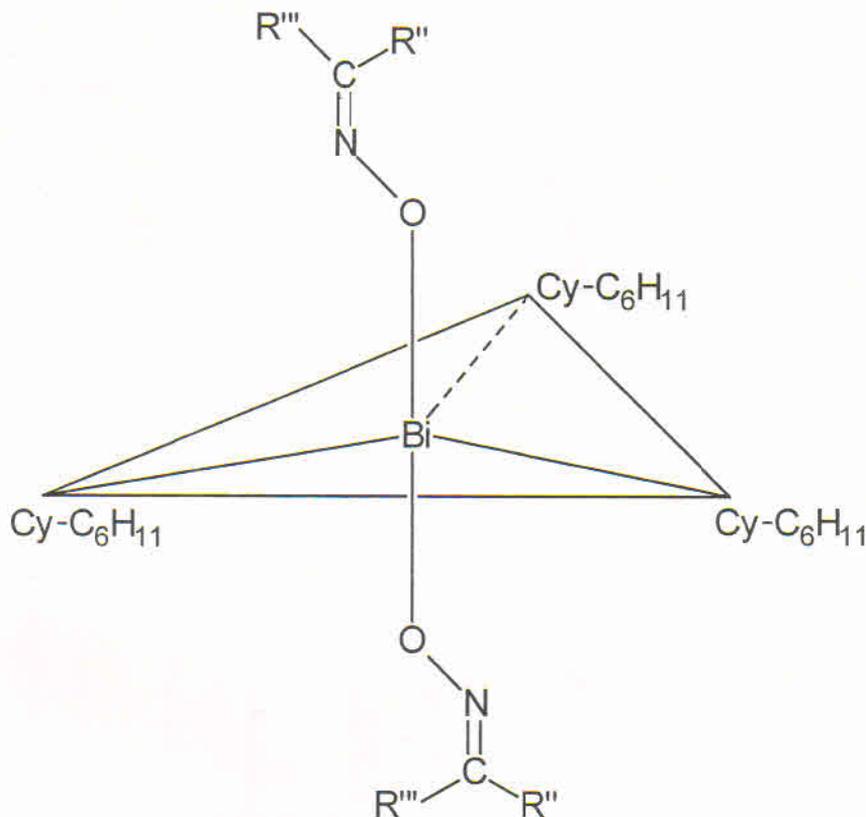


FIG. 3: TRICYCLOHEXYLBISMUTH DIOXIMATES
 $(\text{Cy-C}_6\text{H}_{11})_3\text{Bi}(\text{ONCR}''\text{R}''')_2$

Where,

OCOR = C₆H₅COO⁻, *m*-OHC₆H₄COO⁻, *p*-NH₂ C₆H₄COO⁻, *p*-NO₂ C₆H₄COO⁻, *p*-Cl C₆H₄COO⁻

R' = $\text{--NCOC}_6\text{H}_4\text{CO}$, $\text{--NCO}(\text{CH}_2)_2\text{CO}$, $\text{--N NN C}_6\text{H}_4$,

$\text{--NCH}_2\text{NC}_6\text{H}_4$, $\text{--NCOCOC}_6\text{H}_4$

R'', R''' = Me, Me; Me, Ph

Table I. Analytical data of tricyclohexylbismuth (V) dicarboxylates.

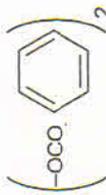
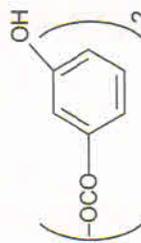
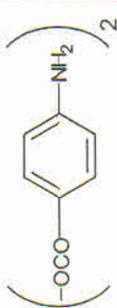
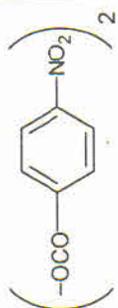
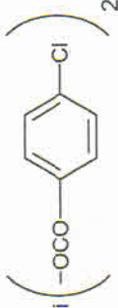
S. No.	Compound	Molecular Formula* (Molecular Weight)	Solvent	M.P.	Analysis Found (Calcd.) %		
					C%	H%	N%
1.	(Cyclo-C ₆ H ₁₁) ₃ Bi 	C ₃₂ H ₄₃ O ₄ Bi (700.3)	Benzene	134 ⁰ C	54.82 (54.88)	6.13 (6.14)	
2.	(Cyclo-C ₆ H ₁₁) ₃ Bi 	C ₃₂ H ₄₃ O ₆ Bi (732.3)	Benzene	139 ⁰ C	52.42 (52.48)	5.86 (5.87)	
3.	(Cyclo-C ₆ H ₁₁) ₃ Bi 	C ₃₂ H ₄₅ O ₄ N ₂ Bi (730.3)	Benzene	121 ⁰ C	52.56 (52.62)	6.14 (6.16)	3.81 (3.83)
4.	(Cyclo-C ₆ H ₁₁) ₃ Bi 	C ₃₂ H ₄₁ O ₈ N ₂ Bi (790.3)	Benzene	141 ⁰ C	48.57 (48.63)	5.18 (5.19)	3.53 (3.54)
5.	(Cyclo-C ₆ H ₁₁) ₃ Bi 	C ₃₂ H ₄₁ O ₄ Cl ₂ Bi (769.3)	Benzene	154 ⁰ C	49.90 (49.96)	5.32 (5.33)	

Table 2. Analytical data of tricyclohexylbismuth (V) diamides.

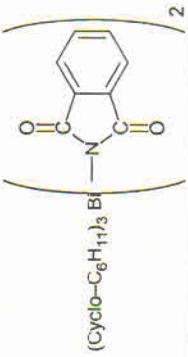
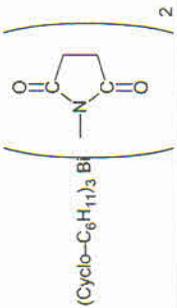
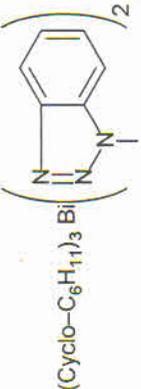
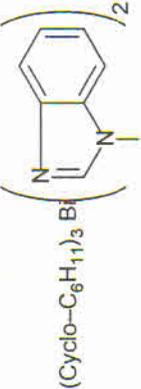
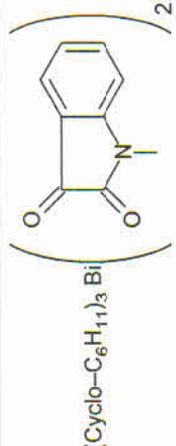
S. No.	Compound	Molecular Formula (Molecular Weight)	Solvent	M.P.	Analysis Found (Calcd.) %		
					C%	H%	N%
6.		C ₃₄ H ₄₁ O ₄ Bi (750.32)	Benzene	110 ⁰ C	54.36 (54.42)	5.45 (5.46)	3.71 (3.73)
7.		C ₂₆ H ₄₁ O ₄ N ₂ Bi (654.24)	Benzene	152 ⁰ C	47.67 (47.73)	6.25 (6.26)	4.27 (4.28)
8.		C ₃₀ H ₄₁ N ₆ Bi (694.28)	Benzene	142 ⁰ C	51.83 (51.89)	5.89 (5.90)	12.08 (12.09)
9.		C ₃₀ H ₄₃ N ₄ Bi (668.28)	Benzene	150 ⁰ C	53.85 (53.91)	6.42 (6.43)	8.37 (8.38)
10.		C ₃₄ H ₄₁ O ₄ N ₂ Bi (750.32)	Benzene	132 ⁰ C	54.36 (54.42)	5.45 (5.46)	3.72 (3.73)

Table 3. Analytical data of tricyclohexylbismuth (V) dioximates.

S. No.	Compound	Molecular Formula (Molecular Weight)	Solvent	M.P.	Analysis Found (Calcd.) %		
					C%	H%	N%
11.	$\left(\text{Cyclo-C}_6\text{H}_{11} \right)_3 \text{Bi} \left(\begin{array}{c} \text{CH}_3 \\ \diagup \quad \diagdown \\ \text{---ONC---} \\ \diagdown \quad \diagup \\ \text{C}_6\text{H}_5 \end{array} \right)_2$	$\text{C}_{34}\text{H}_{49}\text{O}_2\text{N}_2\text{Bi}$ (726.32)	Benzene	88°C	56.16 (56.22)	6.73 (6.74)	3.84 (3.85)
12.	$\left(\text{Cyclo-C}_6\text{H}_{11} \right)_3 \text{Bi} \left(\begin{array}{c} \text{C}_6\text{H}_5 \\ \diagup \quad \diagdown \\ \text{---ONC---} \\ \diagdown \quad \diagup \\ \text{C}_6\text{H}_5 \end{array} \right)_2$	$\text{C}_{44}\text{H}_{53}\text{O}_2\text{N}_2\text{Bi}$ (850.42)	Benzene	96°C	62.08 (62.14)	6.22 (6.23)	3.27 (3.29)

*Molecular weight and conductance of 10^{-3} M solution ($\text{ohm}^{-1} \text{cm}^2 \text{mole}^{-1}$) was found in satisfactory range.

Result and Discussion

The compounds reported herein were characterized by elemental analysis, melting points and spectroscopic data. Infrared spectra of all the compounds were run in the solid state in the region $4000\text{--}400 \text{ cm}^{-1}$ in KBr Infrared absorption due to cyclohexyl group ($\text{Cy-C}_6\text{H}_{11}$) bonded to bismuth do not differ significantly from those reported in the literature and hence not discussed here^{16,17}.

IR Spectra of Tricyclohexyl bismuth(V) dicarboxylates (Table IV):

In the solid-state vibrational spectra of tricyclohexyl-bismuth dicarboxylates, the peaks due to $\nu_{\text{asy}}(\text{OCO})$ stretching mode appear in the range $1600\text{--}1655 \text{ cm}^{-1}$ and $\nu_{\text{sym}}(\text{OCO})$ appear in the range $1311\text{--}1340 \text{ cm}^{-1}$ as a medium strong bond. Since the difference $\Delta\nu$ between $\nu_{\text{asy}}(\text{OCO})$ and $\nu_{\text{sym}}(\text{OCO})$ is quite larger [$\Delta\nu \{ \nu_{\text{asy}}(\text{OCO}) - \nu_{\text{sym}}(\text{OCO}) \} > 250 \text{ cm}^{-1}$] in all the cases, it seems reasonable to conclude that the carboxylate moiety behaves as unidentate, ester type-OCO group.

Infrared Spectra of Tricyclohexylbismuth(V) diamides (Table V):

One of the important features of the spectra of the ureido derivatives is the presence of a strong band in the region $1710\text{--}1740 \text{ cm}^{-1}$ indicating the presence of 'ester like' co-groups(s). The symmetric stretching mode was found to appear between $1310\text{--}1325 \text{ cm}^{-1}$ which correspond well to earlier reported values on phenyl.

Infrared Spectra of Tricyclohexyl bismuth(V)

dioximates (Table V):

In case of the free oximes a weak but broad band appears in the 3000-4000 cm^{-1} region and has been assigned to the intramolecularly hydrogen-bonded OH group¹⁸. However, this band is absent in the spectra of the dioximate derivatives of bismuth. Another diagnostic band is related to the $\nu\text{C}=\text{N}$ stretching vibration. This band in the dioximates appears in the 1570-1610 cm^{-1} region which is considerably lower than is observed in the free oximes (1668 cm^{-1}). This 60-90 cm^{-1} downfield shift may be ascribed to a mass effect as has been reported earlier for analogous group 14

compounds¹⁹. It could also be related to the stabilization of C=N bond by resonance.

The N-O stretching vibration of weak intensity was observed as 910-930 cm^{-1} , while a medium band appearing in the region 445-460 cm^{-1} may be assigned to the Bi-C Y-mode¹⁷. No assignments could be made for the Bi-O bond owing to the complexity of the spectra in the 600-400 cm^{-1} region.

Biological Activity:

The antimicrobial activity of synthesized compounds are under study.

Table 4. Important IR data of tricyclohexylbismuth (V) dicarboxylates (Cm^{-1})

S. No.	Compounds	ν_{asym} (OCO)	ν_{sym} (OCO)
1.	$\text{C}_{32}\text{H}_{43}\text{O}_4\text{Bi}$	1650	1334
2.	$\text{C}_{32}\text{H}_{43}\text{O}_6\text{Bi}$	1635	1312
3.	$\text{C}_{32}\text{H}_{45}\text{O}_4\text{N}_2\text{Bi}$	1640	1335
4.	$\text{C}_{32}\text{H}_{41}\text{O}_8\text{N}_2\text{Bi}$	1636	1320
5.	$\text{C}_{32}\text{H}_{41}\text{O}_4\text{Cl}_2\text{Bi}$	1600	1313

Table 5. Important IR data of tricyclohexylbismuth (V) dicarboxylates (Cm^{-1})

S.No.	Compounds	$\nu(\text{C}=\text{N})$	$\nu(\text{N}-\text{O})$	$\nu(\text{Bi}-\text{C})$
1.	$\text{C}_{34}\text{H}_{41}\text{O}_4\text{Bi}$	1725		
2.	$\text{C}_{26}\text{H}_{41}\text{O}_4\text{N}_2\text{Bi}$	1740		
3.	$\text{C}_{34}\text{H}_{41}\text{O}_4\text{N}_2\text{Bi}$	1720		
4.	$\text{C}_{34}\text{H}_{49}\text{O}_2\text{N}_2\text{Bi}$	1570	920	445
5.	$\text{C}_{44}\text{H}_{53}\text{O}_2\text{N}_2\text{Bi}$	1610	915	458

References

1. R. Asato, K. Kamamuta, Y. Akamine, T. Fukami, R. Nukada, M. Mikuriya, S. Deguchi, Y. Yokota. *Bull. Chem. Soc. Japan*, **70**, 639-648 (1997).
2. R. Diemer, B.K. Keppler, U. Dittes, B. Nuber, V. Seifried, W. Opferkuch, *Chem. Ber.*, **128**, 335-342 (1995).
3. U. Dittes, E. Vogel, B.K. Keppler, *Coord. Chem. Rev.*, **163**, 345-364 (1997).
4. P. Pergo, G.S. Jimenez, L. Gatti, S.B. Howell, F. Zunnino, *Pharmacol. Rev.*, **52**, 4770491 (2000).
5. T. Klapotke, *Monatsh. Chem.* **119**, 1317 (1998).
6. H. Suzuki, T. Ogawa, N. Komatsu, Y. Motano, T. Murafuji, T. Ikegami, *Organobismuth Chem.*, 247-278 (2001).
7. J.P. Finet and A. Yu. Fedorov; *Russian Chemical Bulletin*, Vol. **53**, 1488-1495 (2004).
8. T. Kotani, D. Nagai, K. Asshi, H. Suzuki, F. Yamao, N. Kataoka and T. Yagura; Antibacterial properties of some cyclic organobismuth (III) compounds *Antimicrob. Agents Chemother.* **49**, 2729-2734 (2005).
9. P.K. Kopf-Maier; *Inorg. Chim. Acta* **152**, 49-52 (1988).
10. K. Singhal, P. Raj F. Jee, *Synth. React. Inorg. Met. Org. Chem.* **16**, 343 (1986).
11. P. Raj, A.K. Saxena, K. Singhal and A. Ranjan, **4**, 251 (1985).
12. P. Raj, A. Ranjan, K. Singhal and R. Rastogi, *Synth. React. Inorg. Met. Org. Chem.* **14**, 269 (1984).
13. R. K. Sharma, A. K. Rai, Y. P. Singh, Vol. **178**, 1727-1732 (2003). Organobismuth (III) derivatives of sterically hindered bifunctional tetradentate Schiff bases: Synthesis and spectroscopic characterization, Publisher: Gordon and Breach / Horwood Academic publishing.
14. B. Rosenberg, L. Vamcamp, T. Krigas, *Nature* **205**, 698-699 (1965).
15. L.R. Keltand G. Abel, M.J. Meckeage *et al. Cancer Res.*, **53**, 2581-2586 (1993).
16. R. Silverstein, G. Claylon Bassler and Terence C. Morrill "Spectrometric Identification of Organic Compounds", 3rd Ed. John. Wiley and Sons, New York (1974).
17. E. Maslowsky (Jr.), *J. Organometal. Chem.* **70**, 153 (1974).
18. R.E. Rundle and M. Porsole, *J. Chem. Phys.* **20**, 1487 (1952).
19. P.G. Harrison and J.J. Zuckerman, *Inorg. Chem.* **9**, 175 (1970).