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Elemento(III) Derivatives of N-(2-Hydroxy-3-Methyl Benzyl) Valine

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Elemento(III) *viz.* boron, aluminium, iron, arsenic and antimony derivatives of N-(2-hydroxy-3-methyl benzyl)valine have been prepared by the interaction of their corresponding isopropoxides with the latter, in appropriate stoichiometry in benzene medium.

INTRODUCTION

Preparation of the various metallo-organic/organometallic derivatives of N-(*o*-hydroxy substituted benzyl) glycines[1] and N-(*o*-hydroxy substituted benzyl) alanines[2] *via* the reactivity of the corresponding metal isopropoxide with the latter has recently been reported from these laboratories. The work described here deals with the preparation of several elemento(III) *viz*.. boron, aluminium, iron, arsenic and antimony derivatives of N-(2-hydroxy-3-methyl benzyl) valine (H_3hmbv-3) employing alcoholysis reactions involving the interaction of the corresponding elemento(III) isopropoxide and H_3hmbv-3 in appropriate stoichiometric ratios *viz.* 1:1, 1:2 and 1:3 in benzene medium.

The amount of isopropanol liberated during the course of reaction was fractionated out azeotropically and estimated to monitor the completion of reaction in each case[3, 4]. The compounds thus prepared were obtained as coloured solids and amongst them those containing isopropoxy group were observed to be hygroscopic. All these compounds were characterised by azeotrope and elemental analyses, as well as by IR and PMR spectral measurements.

EXPRIEMENTAL

The alcoholysis reactions were performed, as before[3, 4]. Benzene (BDH, AR), isopropanol (BDH, Glaxo, AnalaR) and solvent ether (E. Merck) were dried by already reproted methods[5]. The various elemento(III) isopropoxides were prepared and the corresponding amount of the trivalent element content in each case was estimated as earlier[3, 4]. Melting points were recorded on an electrothermal CAT No. IA 8103 digital m.p. apparatus and are uncorrected. The IR spectra were recorded on a Perkin-Elmer Model 983 Spectrometer in the region 4000–400 cm^{-1}, using KBr pellets, while the PMR spectral measurements were make in

DMSO-d_6 solution and recorded on a Varian E.M. 390, 90 MHz Spectrometer, using TMS as an internal standard.

Preparation of N-(2-hydroxy-3-methyl benzyl) valine

N-(2-Hydroxy-3-methyl benzyl) valine was prepared employing a procedure similar to those adopted for the preparation of the corresponding glycine/alanine derivatives[1,2]. To a mixture of equimolar amounts of *o*-cresol (E. Merck), valine (Loba) and sodium acetate trihydrate (Sarabhai, G.R.) in acetic acid (Sarabhai, G.R.) medium was added an equimolar amount of formaldehyde solution (Sarabhai, G.R.) and the contents were heated at 60–80°C till a viscous mass was obtained. The viscous mass was poured dropwise with brisk stirring in an excess of water, when the free acid precipitated which was filtered under suction and washed thoroughly with water. The crude product thus obtained was purified by dissolving it in a requisite quantity of sodium hydroxide solution, followed by its reprecipitation by 50% hydrochloric acid. The mother liquor was decanted and the precipitate was freed from chloride ions by washing it with water. Finally, it was filtered through a sintered funnel and air dried.

The analytical details of the compound, characteristic IR frequencies and PMR spectral data are recorded in Tables 1–3 respectively.

Preparation of elemento(III) derivatives of H_3hmbv-3

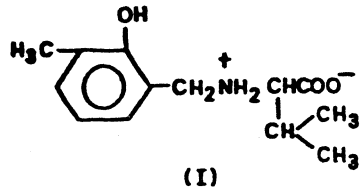
A mixture of elemento(III) isopropoxide and H_3hmbv-3 taken in appropriate stoichiometric ratio in dry benzene was refluxed on a wax bath (95–100°C). After several hours of reflux, the isopropanol-benzene azeotrope was fractionated out and the amount of isopropanol liberated was estimated oxidimetrically[3,4] to monitor the completion of the reaction. The excess of solvent from the reaction mixture was then removed *in vacuo* and the product was washed in dry benzene (3–4 times) followed by dry ether (2–3 times) to remove unreacted elemento(III) isopropoxide. The product was finally dried under vacuum which was found to be soluble in dimethyl formamide and dimethyl sulphoxide, sparingly soluble in chloroform but insoluble in other common organic solvents like ethanol, benzene, toluene and carbon tetrachloride etc.

It may be mentioned here that since the elemento(III) isopropoxides are soluble in benzene, while H_3hmbv-3 is insoluble, the latter was taken in slightly less than the required stoichiometric amount in order to avoid contamination of impurities likely to occur by unreacted H_3hmbv-3. The amount of isopropanol liberated was, therefore, calculated according to the amount of H_3hmbv-3 taken.

The relevant analytical detaills, characteristic IR frequencies and PMR spectral data are summarized in Tables 1–3, respectively.

RESULTS AND DISCUSSION

The analysis of IR and PMR spectra indicate that H_3hmbv-3 exists in zwitter ionic form [Structure (I)] similarly as the corresponding glycine/alanine derivatives[1,2]



(I)

TABLE-1
ANALYTICAL DETAILS OF N-(2-HYDROXY-3-METHYL BENZYL) VALINE AND ITS VARIOUS ELEMENTO(III) DERIVATIVES

Compound (molar ratio) (colour)	m.p. (°C)	Elemental analysis % Found (Calcd.)			
		C	H	N	M
H_3hmbv-3	130	65.65	7.96	5.88	—
(Light pink)		(65.85)	(8.01)	(5.90)	—
B(hmbv-3)	185	64.40	6.56	5.75	3.69
(1:1) (Brownish pink)		(64.19)	(6.58)	(5.76)	(3.70)
$B(OPr^i)(H_2hmbv\text{-}3)_2$	175	64.65	5.73	5.13	1.67
(1:2) (Brownish pink)		(64.44)	(5.76)	(5.16)	(1.67)
$B(H_2hmbv\text{-}3)_3$	180	65.45	7.55	5.85	1.26
(1:3) (Brownish pink)		(65.27)	(7.53)	(5.86)	(1.26)
Al(hmbv-3)	182	60.00	6.16	5.39	10.37
(1:1) (Brownish pink)		(59.77)	(6.13)	(5.36)	(10.34)
Al (Hhmbv-3)$(H_2hmbv\text{-}3)$	180	62.45	6.99	5.60	5.40
(1:2) (Brownish pink)		(62.65)	(7.02)	(5.62)	(5.42)
$Al(H_2hmbv\text{-}3)_3$	188	63.45	7.33	5.70	3.59
(1:3) (Brownish pink)		(63.67)	(7.35)	(5.71)	(3.61)
Fe(hmbv-3)	185	53.75	5.51	4.82	19.11
(1:1) (Dark brown)		(53.97)	(5.53)	(4.84)	(19.03)
Fe(Hhmbv-3)$(H_2hmbv\text{-}3)$	182	59.51	6.63	5.29	10.42
(1:2) (Brown)		(59.31)	(6.65)	(5.32)	(10.45)
$Fe(H_2hmbv\text{-}3)_3$	188	61.58	7.05	5.47	7.18
(1:3) (Dark brown)		(61.33)	(7.07)	(5.50)	(7.20)
$As(OPr^i)$(Hhmbv-3)	190	52.25	6.48	3.78	20.40
(1:1) (Brown)		(52.03)	(6.50)	(3.79)	(20.32)
$As(OPr^1)(H_2hmbv\text{-}3)_2$	185	57.65	7.06	4.60	12.33
(1:2) (Brownish pink)		(57.42)	(7.09)	(4.62)	(12.37)
$Sb(OPr^1)$(Hhmbv-3)	230	46.38	5.75	3.35	29.20
(1:1) (Light brownish pink)		(46.15)	(5.76)	(3.36)	(29.32)
$Sb(OPr^i)(H_2hmbv\text{-}3)_2$	225	53.50	6.56	4.26	18.61
(1:2) (Light brownish pink)		(53.29)	(6.58)	(4.28)	(18.68)
$Sb(H_2hmbv\text{-}3)_3$	245	56.65	6.48	5.04	14.68
(1:3) (Light brownish pink)		(56.38)	(6.50)	(5.06)	(14.69)

Abbreviations: $OPr^i = OC_3H_7$, $H_3hmbv\text{-}3 = CH_3C_6H_3(OH)CH_2\overset{+}{N}H_2CHCH(CH_3)_2COO^-$

TABLE-2
CHARACTERISTIC INFRARED FREQUENCIES (cm^{-1}) OF N-(2-HYDROXY-3-METHYL BENZYL) VALINE AND ITS VARIOUS ELEMENTO(III) DERIVATIVES

Compound	ν(OH)	ν(N—H) and aromatic νC—H	ν(C—H) of $—CH_3$ and $—CH_2—$ groups	ν(C=O) (ester)	ν_{asym}(COO)	ν_{sym}(COO)	Δν(COO)	ν(C—N)	ν(M—O)	ν(M—N)
H_3hmbv-3	3700–3000 (vb)	2320 (m)	2980 (m) 2860 (w)	—	1600 (vsb)	1405 (s)	—	1230 (s)	—	—
B(hmbv-3)	—	3400–3000 (b)	2980 (m) 2880 (w)	—	1610 (sb)	1360 (m)*	250	1230 (m)	1360 (m)	1500 (w)
B(OPr^i)(H_2hmbv-3)$_2$	3660–3400 (vb)	3400–3000 (vb)	2980 (s) 2880 (w)	1720 (mb)	1600 (sb)	1370 (m)	230	1230 (s)	1370 (m)	—
B(H_2hmbv-3)$_3$	3660–3400 (vb)	3400–3000 (b)	2980 (s) 2880 (w)	1720 (mb)	1600 (sb)	1370 (m)*	230	1230 (m)	1370 (m)	—
Al (hmbv-3)	—	3400–3000 (b)	2990 (m) 2880 (w)	—	1610 (sb)	1390 (m)	220	1280 (m)	650 (m)	470 (w)
Al(Hhmbv-3)(H_2hmbv-3)	3660–3400 (vb)	3400–3000 (b)	2980 (s) 2880 (w)	—	1580 (sb)	1370 (m)	210	1260 (s)	660 (m)	480 (w)
Al(H_2hmbv-3)$_3$	3660–3400 (vb)	3400–3000 (b)	2985 (s) 2880 (w)	—	1580 (sb)	1380 (m)	200	1270 (s)	620 (m)	485 (m) 565 (m)

Compound	ν(OH)	ν(N—H) and aromatic νC—H	ν(C—H) of —CH_3 and —CH_2— groups	ν(C=O) (ester)	ν_{asym}(COO)	ν_{sym}(COO)	Δν(COO)	ν(C—N)	ν(M—O)	ν(M—N)
Fe (hmbv-3)	—	3400–3000 (b)	2980 (s) 2880 (w)	—	1620 (sb)	1380 (m)	240	1260 (s)	450 (m)	425 (w)
Fe(Hhmbv-3)(H_2hmbv-3)	3670–3400 (vb)	3400–30000 (b)	2980 (s) 2880 (w)	—	1600 (sb)	1370 (m)	230	1260 (s)	485 (m)	425 (w)
Fe(H_2hmbv-3)$_3$	3670–3400 (vb)	3400–3000 (b)	2980 (m) 2880 (w)	—	1600 (sb)	1365 (m)	235	1280 (s)	480 (m)	420 (w)
As(OPr^i)(Hhmbv-3)	–	3400–3000 (b)	2980 (s) 2880 (w)	—	1610 (sb)	1370 (s)	240	1260 (s)	550 (m)	460 (s)
As(OPr^i)(H_2hmbv-3)$_2$	3670–3300 (vb)	3300–3000 (b)	2980 (s) 2870 (w)	—	1600 (sb)	1360 (s)	240	1265 (m)	570 (s)	460 (m)
Sb(OPr^i)(Hhmbv-3)	–	3390–3000 (b)	2960 (m) 2860 (w)	—	1620 (sb)	1370 (s)	250	1260 (m)	590 (s)	460 (m)
Sb(OPr^i)(H_2hmbv-3)$_2$	3690–3390 (vb)	3390–3000 (b)	2960 (s) 2860 (w)	—	1630 (sb)	1380 (m)	250	1270 (s)	540 (m)	460 (w)
Sb(H_2hmbv-3)$_2$	3690–3390 (vb)	3390–3000 (b)	2960 (s) 2860 (w)	—	1610 (sb)	1370 (m)	240	1265 (s)	570 (w)	465 (m)

*Overlapping of ν_{sym}(COO) and ν(B—O).

TABLE-3
PROTON MAGNETIC RESONANCE SPECTRAL DATA (δ VALUE) OF N-(2-HYDROXY-3-METHYL BENZYL) VALINE AND ITS VARIOUS ELEMENTO(III) DERIVATIVES (DMSO-d_6)

S. No.	Compound	Aromatic ring	Phenolic (—OH)	>CH-groups (of valine part)	>NH	—CH_3 (attached with the benzene ring)	—CH_2— (attached with the benzene rign)	*gem*-dimethyl
1.	H_3hmbv-3	6.60–6.70 (m)* 6.70–6.80 (d)* 6.90–7.10 (d)*	6.85	3.46–3.98 (s)	3.20–3.40 (h)	2.12–2.14 (d)	2.08 (s)	0.86–1.10 (d)
2.	B(OPr^i)(H_2hmbv-3)$_2$	6.30–7.20 (m)	6.85 (s)	3.30–4.00 (m)	3.10 (s)	2.20 (s)	2.10 (s)	0.70–1.10 (d)
3.	Al(H_2hmbv-3)$_3$	6.10–6.80 (m)	6.85 (s)	3.40–3.95 (m)	3.10 (s)	2.25 (s)	2.05 (s)	0.75–1.0 (d)
4.	Fe(hmbv-3)	6.10–7.30 (m)	—	3.20–3.96 (m)	—	2.05 (s)	1.95 (s)	0.40–1.30 (d)
5.	As(OPr^i)(Hhmbv-3)	6.05–6.80 (m)	—	3.30–4.00 (m)	3.18 (s)	2.15 (s)	2.00 (s)	0.75–1.25 (d)
6.	Sb(OPr^i)(Hhmbv-3)	6.10–7.00 (m)	—	3.35–3.85 (m)	3.00 (s)	2.30 (s)	2.00 (s)	0.60–1.10 (d)

Abbreviations: s = singlet, d = doublet, m = multiplet, h = hump.
*corresponds to the protons at positions 5, 6, 4 of a trisubstituted benzene ring.

The reaction between $B(OPr^i)_3$ and H_3hmbv-3 in 1:1 molar ratio may be illustrated as under

$$B(OPr^i)_3 + H_3hmbv\text{-}3 \rightarrow B(hmbve\text{-}3) + 3Pr^iOH$$

Identical reactions followed in case of iron(III) and aluminium(III). However, arsenic(III) and antimony(III) isopropoxides reacted differently as under:

$$As(OPr^i)_3 + H_3hmbv\text{-}3 \rightarrow As(OPr^i)(Hhmbv\text{-}3) + 2Pr^iOH$$

$$Sb(OPr^i)_3 + H_3hmbv\text{-}3 \rightarrow Sb(OPr^i)(Hhmbv\text{-}3) + 2Pr^iOH$$

In 1:2 molar ratio, the reaction between $B(OPr^i)_3$ and H_3hmbv-3 may be illustrated as under:

$$B(OPr^i)_3 + 2H_3hmbv\text{-}3 \rightarrow B(OPr^i)(H_2hmbv\text{-}3)_2 + 2Pr^iOH$$

Identical reactions followed in case of aresenic(III) and antimony(III). Here, aluminium(III) and iron(III) isopropoxides reacted differently as under:

$$Al(OPr^i)_3 + 2H_3hmbv\text{-}3 \rightarrow Al(Hhmbv\text{-}3)(H_2hmbv\text{-}3) + 3Pr^iOH$$

$$Fe(OPr^i)_3 + 2H_3hmbv\text{-}3 \rightarrow Fe(Hhmbv\text{-}3)(H_2hmbv\text{-}3) + 3Pr^iOH$$

The reaction between $B(OPr^i)_3$ and H_3hmbv-3 in 1:3 molar ratio may be illustrated as under.

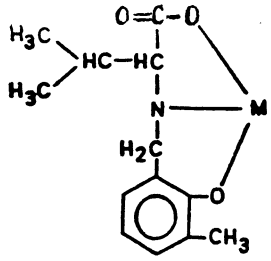
$$B(OPr^i)_3 + 3H_3hmbv\text{-}3 \rightarrow B(H_2hmbv\text{-}3)_3 + 3Pr^iOH$$

Identical reactions followed in case of aluminium(III), iron(III) and antimony(III). However, 1:3 reaction in case of arsenic(III) did not proceed at all even after prolonged reflux and fractionation.

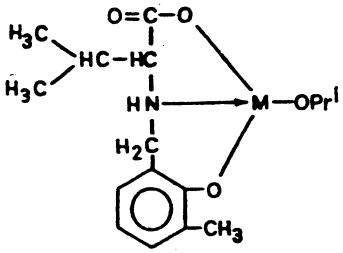
Based on azeotrope and elemental analysis, as well as the spectral data[6–14] in respect of the various derivatives prepared, the main findings relating to their structures are as under:

The boron, aluminium or iron atom in B(hmbv-3), Al(hmbv-3) and Fe(hmbv-3) [Structure (II)] exhibits trivalency in the corresponding case as a result of bonding with one of the oxygens from the carboxylate group, the nitrogen from the deprotonated imino group and the oxygen from the phenolate group. However, the arsenic or antimony atom in $As(OPr^i)$ (Hhmbv-3) and $Sb(OPr^i)$ (Hhmbv-3) [Structure (III)] displays tetra-coordination in the corresponding case as a result of bonding with one of the oxygens from the carboxylate group, the nitrogen from the imino group and the oxygen from the phenolate group, along with an isopropoxy group.

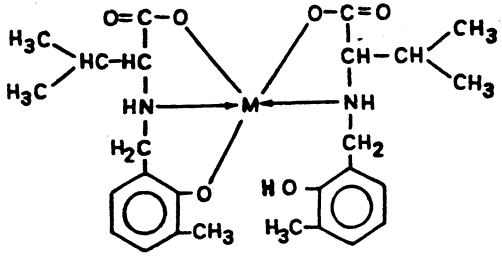
The aluminium or iron atom in Al(Hhmbv-3), (H_2hmbv-3) and Fe(Hhmbv-3) (H_2hmbv-3) [Structure (IV)] shows penta-coordination in the corresponding case as a result of bonding with one of the oxygens from the carboxylate group, the nitrogen from the imino group, as well as the oxygen from the phenolate group from the first mole of H_3hmbv-3 and the oxygen from the carboxylate group, the nitrogen from the imino group from the second mole of the H_3hmbv-3. However, the derivatives $As(OPr^i)(H_2hmbv\text{-}3)_2$ and $Sb(OPr^i)(H_2hmbv\text{-}3)_2$ [Structure (V)] possess a penta-coordinated arsenic or antimony atom in the corresponding case



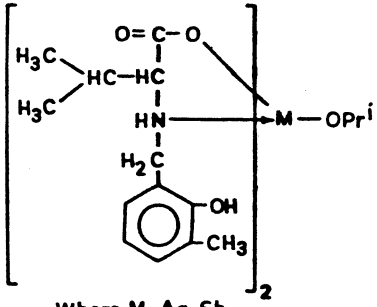
Where M=B, Al, Fe
(II)



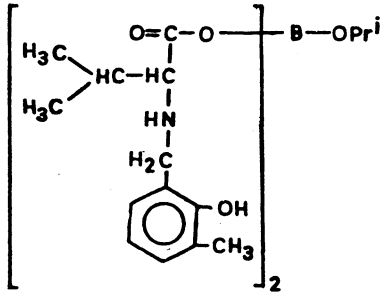
Where M=As, Sb
(III)



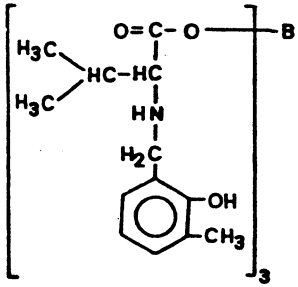
Where M=Al, Fe
(IV)



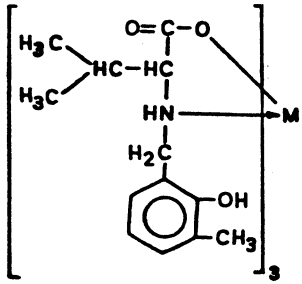
Where M=As, Sb
(V)



(VI)



(VII)



Where M=Al, Fe, Sb
(VIII)

by way of bonding with one of the oxygens from each of the two carboxylate groups and the nitrogen from each of the two imino groups available from two moles of H_3hmbv-3, along with an isopropoxy group. The boron atom in $B(OPr^i)(H_2hmbv\text{-}3)_2$ [Structure (VI)] displays trivalency as a result of bonding with one of the oxygens from each of the two carboxylate groups available from two moles of H_3hmbv-3 through a normal ester type of linkage along with an isopropoxy group.

The boron atom in $B(H_2hmbv\text{-}3)_3$ [Structure (VIII)] also shows trivalency by way of bonding with one of the oxygens from each of the three carboxylate groups available from three moles of H_3hmbv-6 through a normal ester type of linkage. However, the aluminium, iron or antimony atom in $Al(H_2hmbv\text{-}3)_3$, $Fe(H_2hmbv\text{-}3)_3$ and $Sb(H_2hmbv\text{-}3)_3$ [Structure (VIII)] exhibits hexa-coordination in the corresponding case, as a consequence of bonding with one of the oxygens from each of the three carboxylate groups and the nitrogen from each of the three imino groups, available from three moles of H_3hmbv-3.

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