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

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Several elemento(III) *viz.* boron, aluminium, iron, arsenic and antimony derivatives of N-(2-hydroxy-3-methyl benzyl) alanine have been prepared by the interaction of the corresponding elemento (III) isopropoxide with the latter in 1 : 1, 1 : 2 and 1 : 3 molar ratios in benzene medium. The compounds thus prepared were generally obtained as coloured solids, with some of them being hygroscopic. All these compounds have been characterized by azeotrope and elemental analyses, as well as by IR and PMR spectral measurements.

INTRODUCTION

Preparation of several organotin derivatives of N-(*o*-hydroxy substituted benzyl) alanines *via* the reactivity of the corresponding organotin isopropoxide with the latter has recently been reported from these laboratories[1]. The work described here relates to the preparation of elemento(III) *viz.* boron, aluminium, iron, arsenic and antimony derivatives of N-(2-hydroxy-3-methyl benzyl) alanine (H_3hmba-3) on similar lines adopting alcoholysis reactions involving the interaction of the corresponding elemento(III) isopropoxide with H_3hmba-3 in appropriate stoichiometric ratios *viz.* 1 : 1, 1 : 2 and 1 : 3 in benzene as a reaction 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. 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 characterized by azeotrope and elemental analyses, as well as by IR and PMR spectral measurements.

EXPERIMENTAL

Stringent precautions were taken to exclude moisture throughout the experiments, as before[1].

Benzene (BDH, AR), isopropanol (BDH, Glaxo, AnalaR) and solvent ether (E. Merck) were dried by standard procedures[2]. Before use, boric acid (S. Merck,

GR) was dried under vacuum, aluminium foil (E. Merck) was degreased, ferric chloride (S. Merck GR) was dried in an atmosphere of chlorine, and arsenic trichloride (Riedel) and antimony trichloride (E. Merck) were purified by distillation at 130°C and 223°C, respectively. N-(2-hydroxy-3-methyl benzyl) alanine was prepared and purified by already reported methods[1] (Fig. 1). The various elemento(III) isoproxides were also prepared by known methods[3–7]. Boron(III) was estimated by Thomas method[8], while aluminium(III) as aluminium oxinate[2]. Iron was estimated as ferric oxide[2], while arsenic(III) and antimony (III) were first oxidized respectively to arsenic(V) and antimony(V) and then estimated iodometrically[9].

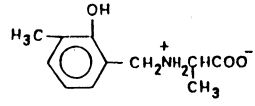


Fig. 1

Reaction between boron tri-isopropoxide and H_3hmba-3; 1:3 moalar ratio

A mixture of $B(OPr^i)_3$ (0.2818 g; 1.50 mmole) and H_3hmba-3 (1.402 g; 4.49 mmole) suspended in dry benzene (60 mL) taken in a R.B. flask was refluxed on a wax bath (95–100°C), using a fractionating column 30 cm. long. After *ca.* 10 h of reflux, the isopropanol liberated during the course of reaction was fractionated out azeotropically and estimated by an oxidimetric method, as before[1]. On completion of the reaction, the excess of solvent from the reaction mixture was removed *in vacuo* when the product, $B(H_2hmba\text{-}3)_3$ isolated as a brownish white solid, which was washed with dry benzene (3–4 times) followed by dry ether (2–3 times) to remove excess of $B(OPr^i)_3$ and then dried under suction. The product was found to be soluble in dimethylformamide and dimethylsulphoxide but insoluble in other common organic solvents like ethanol, benzene, toluene, carbon tetrachloride and chloroform etc.

It may be mentioned here that since $B(OPr^i)_3$ is soluble in benzene, while H_3hmba-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_3hmba-3. The amount of isopropanol liberated was, therefore, calculated according to the amount of H_3hmba-3 taken.

Identical procedure was adopted for the preparation and purification of other derivatives. The relevant analytical details, characteristic IR frequencies and PMR data are summarized in Tables 1–3 respectively.

TABLE-1
ANALYTICAL DETAILS OF THE VARIOUS ELEMENTO(III) DERIVATIVES OF N-(2-HYDROXY-3-METHYL BENZYL) ALANINE

Compound (molar ratio)/colour	m.p. °C	Azeotropic analysis Pr^iOH(g) found (calcd.)	Analysis % Found (Calcd.)			
			C	H	N	M
$B(OPr^i)(Hhmba\text{-}3)$ (1:1) (brownish white)	167	0.70 (0.72)	60.50 (60.67)	7.22 (7.27)	5.00 (5.05)	3.85 (3.90)
$B(OPr^i)(H_2hmba\text{-}3)_2$ (1:2) (brownish white)	175	1.16 (1.18)	61.67 (61.73)	7.20 (7.25)	5.70 (5.76)	2.16 (2.22)
$B(H_2hmba\text{-}3)_3$ (1:3) (brownish white)	175	0.46 (0.48)	62.50 (62.56)	6.62 (6.68)	6.56 (6.65)	1.64 (1.71)
Al(hmba-3) (1:1) (light brown)	197	0.25 (0.26)	56.46 (56.65)	5.10 (5.19)	5.90 (6.01)	11.45 (11.57)
$Al(H_2hmba\text{-}3)(Hhmba\text{-}3)$ (1:2) (light brown)	175	0.29 (0.30)	59.62 (59.72)	6.80 (6.83)	6.28 (6.33)	6.05 (6.10)
$Al(H_2hmba\text{-}3)_3$ (1:3) (light brown)	164	0.70 (0.71)	60.53 (60.82)	6.32 (6.50)	6.23 (6.45)	4.00 (4.14)
$Fe(OPr^i)(Hhmba\text{-}3)$ (1:1) (light brown)	143	0.40 (0.41)	52.00 (52.19)	6.20 (6.26)	4.25 (4.35)	17.28 (17.34)
$Fe(OPr^i)(H_2hmba\text{-}3)_2$ (1:2) (light brown)	137	0.42 (0.43)	56.38 (56.50)	6.50 (6.64)	5.15 (5.27)	10.35 (10.51)
$Fe(H_2hmba\text{-}3)_3$ (1:3) (light brown)	148	0.48 (0.49)	58.20 (58.24)	6.18 (6.22)	6.12 (6.17)	8.14 (8.21)
$As(OPr^i)(Hhmba\text{-}3)$ (1:1) (light brown)	157	0.49 (0.51)	49.20 (49.27)	5.82 (5.91)	4.00 (4.11)	21.82 (21.95)
$As(OPr^i)(H_2hmba\text{-}3)_2$ (1:2) (light brown)	152	0.98 (0.99)	54.42 (54.55)	6.35 (6.41)	4.90 (5.09)	13.50 (13.61)
$Sb(OPr^i)(Hhmba\text{-}3)$ (1:1) (brown)	174	0.64 (0.65)	43.28 (43.33)	5.12 (5.19)	3.55 (3.61)	31.32 (31.37)
$Sb(OPr^i)(H_2hmba\text{-}3)_2$ (1:2) (brown)	155	0.41 (0.44)	50.18 (50.27)	5.85 (5.91)	4.62 (4.69)	20.32 (20.38)
$Sb(Hhmba\text{-}3)_3$ (1:3) (brown)	168	0.48 (0.49)	53.05 (53.10)	5.62 (5.67)	5.58 (5.63)	16.25 (16.31)

Abbreviations: $OPr^i = OC_3H_7$, $H_3hmba\text{-}3 = CH_3C_6H_3(OH)CH_2\overset{+}{N}H_2CH(CH_3)COO^-$

RESULT AND DISCUSSION

The various reactions occurring between boron tri-isopropoxide and $H_3hmba\text{-}3$ may be illustrated as:

$$B(OPr^i)_3 + H_3hmba\text{-}3 \rightarrow B(OPr^i)(Hhmba\text{-}3) + 2Pr^iOH \quad (1)$$

$$B(OPr^i)_3 + 2H_3hmba\text{-}3 \rightarrow B(OPr^i)(H_2hmba\text{-}3)_2 + 2Pr^iOH \quad (2)$$

$$B(OPr^i)_3 + 3H_3hmba\text{-}3 \rightarrow B(H_2hmba\text{-}3)_3 + 3Pr^iOH \quad (3)$$

TABLE-2
CHARACTERISTIC INFRARED FREQUENCY (cm^{-1}) OF THE VARIOUS ELEMENTO(III) DERIVATIVES OF N-(2-HYDROXY-3-METHYL BENZYL) ALANINE

S. No.	Compound	ν(OH)	ν(N—H) and aromatic ν(C—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)
1.	B(OPr^i)(Hhmba-3)	—	3300–3100 (b)	2980 (wb) 2940 (wb)	—	1630 (sb)	1390 (w)	240	1265 (mb)	1375 (w)	1520 (mb)
2.	B(OPr^i)(H$_2$hmba-3)$_2$	3500–3300 (vb)	3250–3000 (mb)	2940 (wb) 2845 (wb)	1720 (s)	1600 (vs)	1380 (mb)*	220	1235 (m)	—	—
3.	B(H$_2$hmba-3)$_3$	3500–3300 (b)	3265–3000 (b)	2910 (m) 2810 (m)	1680 (b)	1600 (s)	1370 (s)*	230	1235 (w)	—	—
4.	Al(hmba-3)	—	3250–3000 (b)	2910 (m) 2845 (m)	—	1610 (b)	1380 (b)	230	1260 (m)	680 (m) 600 (mb)	470 (w) 450 (m)
5.	Al(H$_2$hmba-3)$_3$(Hhmba-3)	3600–3300 (b)	3250–3000 (mb)	2920 (w) 2910 (w) 2885 (m)	—	1620 (s)	1390 (s)	230	1260 (w)	640 (m) 620 (m)	490 (m) 450 (m)
6.	Al(H$_2$hmba-3)$_3$	3500–3300 (b)	3200–3000 (mb)	2925 (m) 2910 (m)	—	1610 (sb)	1400 (m)	210	1255 (b)	680 (m) 610 (w)	450 (w)
7.	Fe(OPr^i)(Hhmba-3)	—	3200–3000 (b)	2950 (m) 2910 (m)	—	1630 (sh)	1375 (m)	255	1250 (m)	490 (m) 450 (m)	480 (w) 450 (m)

S. No.	Compound	ν(OH)	ν(N—H) and aromatic ν(C—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)
8.	$Fe(OPr^i)(H_2hmba\text{-}3)_2$	3450–3000 (vb)	3200–3000 (m)	2930 (w) 2900 (m)	1680 (s)	1600 (s)	1380 (m)	220	1235 (s)	545 (s) 440 (b)	—
9.	$Fe(H_2hmba\text{-}3)_3$	3400–3300 (b)	3200–3000 (m)	2930 (m) 2850 (w)	—	1615 (vs)	1370 (mb)	245	1250 (w)	540 (s)	430 (m) 410 (m)
10.	$As(OPr^i)(Hhmba\text{-}3)$	—	3140–3000 (m)	2950 (m) 2925 (w)	—	1610 (s)	1390 (w)	220	1265 (b)	590 (w)	495 (w)
11.	$As(OPr^i)(H_2hmba\text{-}3)_2$	3500–3280 (vb)	3200–3000 (m)	2940 (m)	1700 (s)	1625 (s)	1375 (b)	250	1235 (b)	580 (w)	—
12.	$Sb(OPr^i)(Hhmba\text{-}3)$	—	3300–3060 (b)	2950 (m) 2890 (mb)	—	1610 (s)	1380 (sh)	230	1260 (m)	580 (m)	430 (s)
13.	$Sb(OPr^i)(H_2hmba\text{-}3)_2$	3500–3300 (b)	3200–3000 (m)	2980 (m) 2920 (m)	—	1610 (b)	1400 (s)	210	1255 (b)	670 (m) 580 (m)	490 (m) 430 (m)
14.	$Sb(H_2hmba\text{-}3)_3$	3500–3300 (vb)	3140–3000 (b)	2940 (m) 2860 (m)	—	1630 (sb)	1390 (sb)	240	1265 (m)	670 (s) 590 (s)	495 (s) 420 (w)

Abbreviations: b = broad, m = medium, mb = medium broad, s = strong, sh = shoulder, vb = very broad, vs = very strong, vw = very weak, w = weak.

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

TABLE-3
PROTON MAGNETIC RESONANCE SPECTRAL DATA (δ VALUE) OF SEVERAL ELEMENTO(III) DERIVATIVES OF N-(2-HYDROXY-3-METHYL BENZYL) ALANINE

S. No.	Compound	Aromatic ring	Phenolic —(OH)	>CH—	>NH—	CH_3 attached with the benzene ring	$—CH_2—$	$—CH_3$ of the alanine part	*Gem*-di-methyl
1.	$B(H_2hmba\text{-}3)_3$	6.60–7.20 (m)	6.30 (s)	3.60–4.00 (m)	3.10 (h)	2.15 (s)	2.00 (d)	1.20 (d)	—
2.	$Al(H_2hmba\text{-}3)_3$	6.45–7.10 (m)	6.25 (s)	3.75–4.00 (m)	3.10 (h)	2.05 (s)	1.95 (d)	1.10 (d)	—
3.	$Fe(OPr^i)$ (Hhmba-3)	6.35–7.00 (m)	—	3.20–3.85 (m)	3.10 (h)	2.10 (s)	2.00 (d)	1.20 (d)	1.00 (d)
4.	$As(OPr^i)$ (Hhmba-3)	6.80–7.50 (m)	6.75 (s)	3.50–4.00 (m)	3.10 (s)	2.40 (s)	2.20 (d)	1.35 (d)	1.15 (d)
5.	$Sb(OPr^i)$ $(H_2hmba\text{-}3)_2$	6.50–7.00 (m)	6.25 (s)	3.50–4.00 (m)	3.10 (s)	2.15 (s)	2.00 (d)	1.25 (d)	0.90 (d)

Abbreviations: s = singlet, d = doublet, m = multiplet, h = hump.

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

The various reactions occurring between aluminium tri-isopropoxide and H_3hmba-3 may be illustrated as under:

$$Al(OPr^i)_3 + H_3hmba\text{-}3 \rightarrow Al(hmba\text{-}3) + 3Pr^iOH \quad (4)$$

$$Al(OPr^i)_3 + 2H_3hmba\text{-}3 \rightarrow Al(H_2hmba\text{-}3)(Hhmba\text{-}3) + 3Pr^iOH \quad (5)$$

$$Al(OPr^i)_3 + 3H_3hmba\text{-}3 \rightarrow Al(H_2hmba\text{-}3)_3 + 3Pr^iOH \quad (6)$$

Infrared Spectra

The derivative, $B(H_2hmba\text{-}3)_3$ displays a broad band in the region 3500–3300 cm^{-1} which may be assigned to ν(OH) of the unbonded phenolic group, while another broad band between 3265-3000 cm^{-1} corresponds to the overlapping of unbonded ν(N—H) and aromatic ν(C—H)[10, 11]. The medium absorptions at 2910 cm^{-1} and 2810 cm^{-1} may be assigned to ν(C—H) of the —CH_2— and —CH_3 groups. A broad band at 1680 cm^{-1} occurs due to ν(C=O) expected of a normal ester type of linkage between the carboxylate oxygen and boron[12]. The overlaping of ν_{asym}(COO), aromatic ν(C=C) and N—H deformation[13, 14] is identified by the appearance of a strong band at 1600 cm^{-1}. A broad band between 1450–1400 cm^{-1} shows the overlapping of aromatic skeletal vibrations[11, 15] and C—H bending of the —CH_2— and —CH_3 groups. A strong band at 1370 cm^{-1} may be assigned to the overlapping of ν_{sym}(COO) and ν(B—O)[16, 17]. The separation value, Δν(COO) of 230 cm^{-1}, as observed here, indicates the absence of bridged or coordinated carboxylate groups. The weak band at 1235 cm^{-1} corresponding to ν(C—N) as observed in H_3hmba-3, remains unchanged. A broad band at 1205 cm^{-1} occurs due to ν(C—O) while medium bands at 1150 cm^{-1}, 1100 cm^{-1} and 1025 cm^{-1} indicate the aromatic C—H-in-plane bending[11, 18]. The absorptions due to the characteristic C—H out-of-plane-bending expected of a trisubstituted benzene ring[17] are identified by the bands at 920 cm^{-1}, 865 cm^{-1}, 800 cm^{-1} and 755 cm^{-1}. It is thus evident that the boron atom in $B(H_2hmba\text{-}3)_3$ [Structure (II)] shows trivalency by way of bonding with one of the oxygens from each of the three carboxylate groups available from three moles H_3hmba-3 through a normal ester type of linkage.

Proton Magnetic Resonance Spectra

The presence of the aromatic ring protons in $B(H_2hmba\text{-}3)_3$ is identified by a multiplet in region δ 6.60–7.20, while the singlet at δ 6.30 corresponds to the unbonded penolic group proton. The hump in the region δ 3.20–3.40 due to the $>\overset{+}{N}H_2$ protons, as observed in H_3hmba-3, is found to be absent here, while a new hump at δ 3.10 may be assigned to the proton of the >NH group obtained as a result of deprotonation of the $>\overset{+}{N}H_2$ group. The broad multiplet between δ 3.60–4.00 shows the >CH— group proton of the alanine part of H_3hmba-3, while the singlet due to the protons of the —CH_3 and —CH_2— groups attached

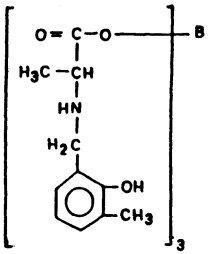
with the benzene ring appear in the form of a singlet at δ 2.15 and doublet at δ 2.00, respectively. The doublet at δ1.20 corresponds to the —CH_3 group protons of the alanine part of H_3hmba-3. Hence the conclusions drawn here are in conformity to those inferred from the IR measurements earlier.

The IR and PMR spectral data were similarly interpreted for the other derivatives and the main findings in the context of their structures are as under:

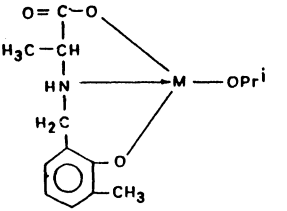
The boron, iron, arsenic or antimony atom in B(OPr^i)(Hhmba-3), Fe(OPr^i)(Hhmba-3), As(OPr^i)(Hhmba-3) and Sb(OPr^i)(Hhmba-3) [Structure (III)] displays tetra-coordination in the corresponding case as a result of bonding with one of the oxygens from the carboxylate group, the nitrogen from the imino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

The boron, iron or arsenic atom in B(OPr^i)(H_2hmba-3)$_2$, Fe(OPr^i)(H_2hmba-3)$_2$ and As(OPr^i)(H_2hmba-3)$_2$ [Structure (V)] shows trivalency in the corresponding case, as a consequence of bonding with one of the oxygens from each of the two carboxylate groups available from two moles of H_3hmba-3 through a normal ester type of linkage, along with an isopropoxy group. However, the derivative, Sb(OPr^i)(H_2hmba-3)$_2$ [Structure (VI)] possesses a penta-coordinated antimony atom 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_3hmba-3, along with an isopropoxy group. Again, the aluminium atom in Al(H_2hmba-3)(Hhmba-3), [Structure (VII)] displays penta-coordination 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_3hmba-3 and one of the oxygens from the carboxylate group, and the nitrogen from the imino group from the second mole of H_3hmba-3.

The aluminium, iron or antimony atom in Al(H_2hmba-3)$_3$, Fe(H_2hmba-3)$_3$ and Sb(H_2hmba-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_3hmba-3.

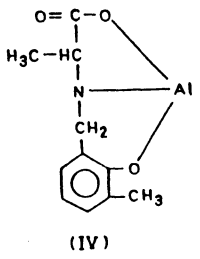


(II)



Where M= B Fe As Sb

(III)



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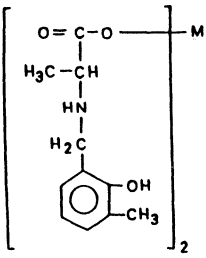

Where M = B As Fe

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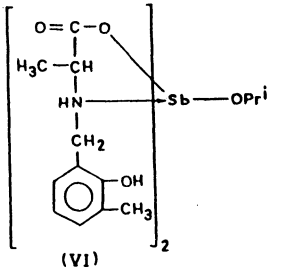

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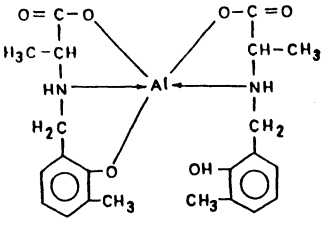

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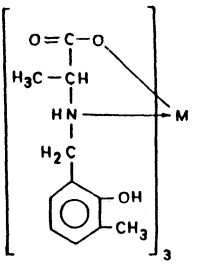

Where M = Al Fe Sb

(VIII)

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