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ORIGINAL ARTICLE

Synthesis and pharmacological activity of diorganoantimony(III) and triorganoantimony(V) derivatives of Schiff bases derived from amino acids

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Abstract Some new diorganoantimony(III) and triorganoantimony(V) compounds of Schiff bases derived from amino acids having the general formula $Ph_2Sb[OC(R)CHC(R')NC(Y)\ COOH]$ [where R = CH_3, R′ = C_6H_5, Y = $-H_2CH_2$(1), $-HCH_2C_6H_5$(2); R = R′ = C_6H_5, Y = $-H_2CH_2$(3), $-HCH_2C_6H_5$(4)] have been synthesized by the reaction of Ph_3Sb with RC (O) CHC(R′) NHC(Y) COOH in 1:1 M ratio. Whereas $Ph_3Sb[OC(R)CHC(R')NC(Y)\ COOH]_2$ (where R = CH_3, R′ = C_6H_5, Y = $-H_2CH_2$(5), R = R′ = C_6H_5, Y = $-HCH_2C_6H_5$(6)) have been synthesized by the reactions of Ph_3SbBr_2 with Na [OC(R) CHC(R′)NC(Y) COOH] in 1:2 M ratio, respectively in anhydrous benzene. All these compounds have been characterized by elemental analyses and molecular weight measurement. Probable structures of these compounds have been proposed on the basis of spectral studies (I.R. ^1H and ^{13}C NMR). Schiff base (R = CH_3 R′ = C_6H_5, Y = $-H_2CH_2$) and its corresponding organoantimony(III) and -antimony(V) compounds have been screened for antimicrobial, antioxidant and antiplatelet activities. These synthesized compounds can be used as new class of antimicrobial, antioxidant and antiplatelet agents with potential for clinical development.

1. Introduction

Bioorganometallic chemistry is dedicated to the study of biological applications of organometallic compounds with a view to design new drugs offering better performance than those already known. In recent years, the chemistry of organoantimony derivatives continues to attract the attention due to wide structural diversities [1–4]. In addition to this organoantimony compounds have shown a number of biological

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activities such as antitumor [5,6], antimicrobial [7,8] and antispermatogenic [9–10]. Schiff bases derived from amino acid behave as unidentate [11], bidentate [12] or bridging ligands [13] in their metal complexes. These ligands demonstrate not only a remarkable diversity in their structure, but also exhibit interesting biocidal activities [14–16]. We have reported organoantimony complexes in +3 and +5 oxidation state of Schiff bases [17,18] derived from amino alcohols, but organoantimony(III) and -antimony(V) derivatives of Schiff bases derived from amino acids have not been reported so far. In the present investigation we report the synthesis, spectroscopic analysis, and antimicrobial, antioxidant and antiplatelet activities of organoantimony(III) and -antimony(V) compounds of Schiff base derived from amino acids. Blood platelets are involved in hemostasis. The normal hemostatic system limits blood loss by precisely regulating interactions between components of vessel wall, circulating blood platelets and plasma proteins. Platelets can adhere to the walls of the blood vessels, release bioreactive compounds and then aggregate to each other. These properties increase to a well established level under conditions of arterial thrombosis and atherogenesis that may cause life-threatening disorders such as unstable angina, heart attack and reclusions after angioplasty [19]. Therefore, inhibition of platelet aggregation is important in the prevention and treatment of cardiovascular diseases [20].

2. Experimental

2.1. Materials

Solvents were dried by standard methods [21] before use. Ph_3Sb(Aldrich) has been used as supplied. Ph_3SbBr_2 [22] and Schiff bases [12] have been prepared by literature methods. Antimony was estimated by iodometric method [23].

2.2. Physical measurements

^1H and ^{13}C NMR spectra in $CDCl_3$ solution were recorded with a JEOL-FT Al 300 MHz Spectrometer using TMS an internal reference. IR spectra were recorded on an 8400 s Shimadzu FT-IR Spectrophotometer as Nujol mull on KBr cells in the range 4000–400 cm^{-1}. Elements (C, H and N) were recorded on a Perkin Elmer-2400 C, H, N analyzer. Molecular weights were determined cryoscopically in freezing benzene solution using a Beckmann's thermometer. Since diorganoantimony(III) and triorganoantimony(V) derivatives have been synthesized by different methods we have given here the synthesis of one compound of each series in detail. The synthetic and analytical data of analogous have been summarized in Table 1.

2.3. Synthesis of diphenylantimony(III) derivatives $Ph_2Sb[OC(CH_3)CHC(C_6H_5)\ NCH_2CH_2\ COOH]$

A benzene solution of Schiff base [$CH_3C(O)$ CHC (C_6H_5) $NHCH_2CH_2COOH$] [0.95 g 4.07 mM] was added to benzene solution of Ph_3Sb [1.43 g 4.05 mM] in 1:1 M ratio. The reaction mixture was refluxed for ~4 h. After the completion of reaction, the excess solvent was removed under reduced pressure to yield colored viscous product (yield 82%). It was purified by benzene/n-hexane mixture. The analytical results are presented in Table 1.

2.4. Synthesis of triphenylantimony(V) derivatives $Ph_3Sb[OC(CH_3)CHC(C_6H_5)\ NCH_2CH_2COOH]_2$

A benzene solution of Schiff base[$CH_3C(O)$ CHC (C_6H_5) $NHCH_2CH_2COOH$] (1.01 g 4.33 mM) was added to the sodium methoxide solution obtained by the interaction of sodium (0.11 g, 4.78 mM) with methanol, and the reaction

Table 1 Synthetic and analytical data of diphenylantimony(III) and triphenylantimony(V) complexes of Schiff base derived from amino acids.

S.No	Na	Reactants (g) RC (O) CHC(R′) NHC(Y) COOH	Ph_3Sb	Ph_3SbBr_2	Product % yield	Elemental analyses found (Calcd.)				Mol. Wt. Found (Calcd.)
						C	H	N	Sb	
1	–	R = CH_3, R′ = C_6H_5, Y = $-H_2CH_2$ 0.95	1.43	–	$C_{25}H_{24}O_3NSb$ 82%	59.00 (59.08)	4.12 (4.72)	2.12 (2.75)	20.00 (23.97)	490 (507.75)
2	–	R = CH_3, R′ = C_6H_5, Y = $-HCH_2C_6H_5$ 1.02	1.16	–	$C_{31}H_{28}O_3NSb$ 85%	63.12 (63.72)	4.72 (4.71)	2.00 (2.39)	19.23 (20.85)	570.00 (583.75)
3	–	R = R′ = C_6H_5, Y = $-H_2CH_2$ 1.12	1.34	–	$C_{30}H_{26}O_3NSb$ 88%	62.90 (63.18)	4.00 (4.56)	2.12 (2.45)	19.82 (21.36)	550.00 (569.75)
4	–	R = R′ = C_6H_5, Y = $-HCH_2C_6H_5$ 1.10	1.04		$C_{36}H_{30}O_3NSb$ 80%	66.12 (66.89)	4.23 (4.64)	1.92 (2.16)	17.92 (18.85)	600.00 (645.75)
5	0.11	R = CH_3, R′ = C_6H_5, Y = $-H_2CH_2$ 1.01	–	1.22	$C_{44}H_{43}O_6N_2Sb$ 80%	64.00 (64.64)	5.18 (5.26)	3.12 (3.42)	14.18 (14.90)	790.00 (816.81)
6	0.12	R = R′ = C_6H_5, Y = $-HCH_2C_6H_5$ 1.21	–	1.33	$C_{56}H_{51}O_6N_2Sb$ 83%	68.96 (69.36)	5.20 (5.26)	2.13 (2.89)	12.00 (12.56)	920.00 (968.75)