Heteroatom Chemistry
Volume 14, Number 5, 2003

1,3,2-Oxazastibinanes: Novel Six-Membered Heterocycles

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Received 17 August 2000; revised 2 January 2003

ABSTRACT: *The hitherto unreported oxazastibinanes* **3** *have been synthesized by the sodium borohydride reduction of 3-phenyl-1-arylamino-3-oxopropane (***1***) and subsequent cyclization of the disodium salt of 3-phenyl-1-arylamino-3-hydroxypropane (***2***) with R_3SbBr_2 (R = Ph,* p*-tolyl, or mesityl). These compounds have been characterized by elemental analyses, molecular weight determination, and by IR, far IR, ^1H, and ^{13}C NMR spectral studies.*
 Heteroatom Chem 14:417–420, 2003; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10155

INTRODUCTION

Although the majority of published reports on group 15 heterocycles are concerned with those derived from nitrogen, a wide range of analogous ring systems containing the heavier group 15 heteroatoms are also known [1]. Some of these heterocycles, e.g., 1,3-oxazines, have gained importance because of their biological and pharmacological activity [2–7]. Introduction of phosphorus in the oxazine ring at the 2-position yields compounds that find applications in cancer research [8–13]. Some heterocycles containing N, As, and O are also known [14,15]. Regarding the heterocycles containing N, Sb, and O, only a few five-membered rings have been reported [16,17]. Recently, we have synthesized six-membered benzoxazastibinines [18,19]. However, we have found no report on oxazastibinanes in literature. Thus, we thought it worthwhile to synthesize these heterocyclic compounds.

RESULTS AND DISCUSSION

Six-membered heterocyclic compounds containing N, Sb, and O, viz., oxazastibinanes, have been synthesized by the reaction of the disodium salt of aminocarbinol **2** (3-phenyl-1-arylamino-3-hydroxypropane) with R_3SbBr_2 (R = Ph, *p*-tolyl, or mesityl) in dry THF, as shown in Scheme 1. The stoichiometry of the reaction has been confirmed by the amount of precipitated sodium bromide. These compounds are soluble in organic solvents such as chloroform, THF, benzene, and diethyl ether and are stable toward atmospheric oxygen and moisture. The elemental analyses of these compounds correspond to the assigned formulas, and vapor pressure osmometry measurements indicate that these compounds are monomeric in chloroform (Table 1).

The IR spectrum of 3-phenyl-1-arylamino-3-oxopropane (**1**) shows strong absorption band for N—H at 3390 cm^{-1} and C=O absorption at 1680 cm^{-1}. The O—H and N—H bands of **2** appear as strong bands at 3550 and 3380 cm^{-1}, respectively. These bands are absent in the IR spectra of heterocyclic compounds indicating N—Sb—O bond formation (Table 2).

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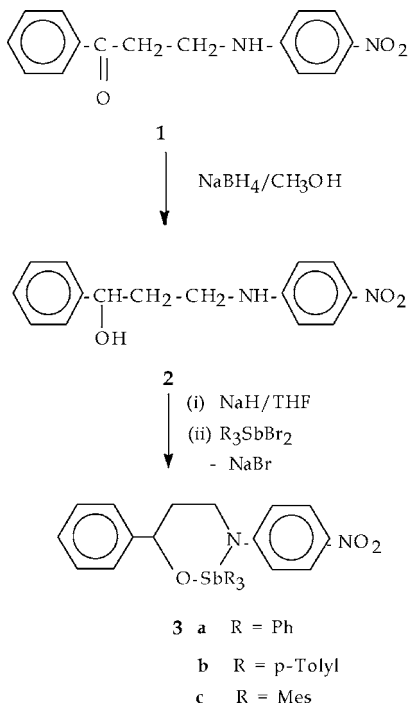
Contract grant sponsor: Indian Institute of Technology, New Delhi.



SCHEME 1

The C—O stretching vibration in **2** appears at 1126 cm^{-1}, which undergoes a shift toward higher frequency in the oxazastibinanes, which further confirms the participation of oxygen in C—O—Sb bonding [20,21]. Similar trend has been observed for the C—N stretching vibration in these heterocyclic compounds indicating C—N—Sb bonding. Apart from these vibrations, the spectra are further marked by the presence of aromatic nitro group absorptions, viz., asymmetric, symmetric, and C—N stretching at about 1520, 1345, and 850 cm^{-1}, respectively [22].

In the far IR region of **3** there are some additional peaks that are not present in the reactants. A new band present in the region 410–416 cm^{-1} may be attributed to Sb—O stretching vibration [23–25]. Another band observed at 250–260 cm^{-1} may be assigned to Sb—N stretching [25]. However, Sb—Ar absorption (X-sensitive t-vibration) also appears in the same region and indeed these bands are stronger in the heterocycles compared to those in triarylantimony dibromides. The y-mode of the Sb—Ar group appears in the region 464–480 cm^{-1} in these heterocycles.

In the ^1H NMR spectrum of **1** (Table 3) the N—H proton appears as a broad signal at δ 2.04 while in that of **2** the N—H and O—H signals are observed at δ 1.59 and 5.05. The presence of these protons was confirmed by deuterium exchange with D_2O. The spectra of oxazastibinanes **3** do not exhibit the signals due to N—H and O—H protons, implying the bonding of antimony to nitrogen and oxygen. The ^1H signals due to the two types of methylene protons and the benzylic proton appear at almost the same positions as in the aminocarbinol **2**. The methyl protons in **3b** appear at the same position as in $(p\text{-tolyl})_3SbBr_2$. The two methyl groups are observed at δ 2.31 and 2.69 in Mes_3SbBr_2, whereas these groups are found at δ 2.31 and 2.54 in **3c**.

The spectra of **3** show the benzylic proton as double doublet (tending to be a triplet). The methylene protons adjacent to nitrogen appear as multiplet, whereas analogous methylene protons in aminocarbinol are observed as triplet. The methylene protons adjacent to benzylic proton appear as multiplet (overlapping triplets) in these heterocycles. The ^{13}C NMR signals (Table 4) were assigned using standard correlations [22].

EXPERIMENTAL

The triarylantimony dibromides were prepared and purified by the methods reported in the literature [26–29]. The Mannich base was synthesized and was subjected to sodium borohydride reduction as per literature methods [30–32]. Solvents and other materials were dried and purified before use. The purity of the sample was checked by TLC. Elemental analyses were carried out on a Perkin-Elemer 240C elemental analyzer. Antimony was determined volumetrically by a reported method [33]. Molecular weights of the

TABLE 1 Elemental Analyses and Physical Properties

				Found (Calculated)				
	Formula	*Yield (%)*	*m.p. (°C)*	*C*	*H*	*N*	*Sb*	*Mol. Wt.*
1	$C_{15}H_{14}N_2O_3$	52	170	66.23 (66.67)	5.46 (5.19)	9.88 (10.37)	–	263 (270)
2	$C_{15}H_{16}N_2O_3$	75	93	65.93 (66.18)	5.72 (5.88)	10.06 (10.29)	–	266 (272)
3a	$C_{33}H_{29}N_2O_3Sb$	56	138(d)	63.10 (63.59)	4.48 (4.66)	3.82 (4.50)	20.06 (19.55)	592 (622.8)
3b	$C_{36}H_{35}N_2O_3Sb$	50	153(d)	64.48 (64.99)	4.98 (5.27)	4.04 (4.21)	19.06 (18.32)	634 (664.8)
3c	$C_{42}H_{47}N_2O_3Sb$	60	142-4	67.65 (67.31)	6.04 (6.28)	3.38 (3.74)	16.62 (16.26)	727 (748.8)

TABLE 2 Important IR and Far IR Bands (cm^{-1})

	ν_{O-H}	ν_{N-H}	ν_{C-H}	ν_{C-N}	ν_{C-O}	ν_{Sb-O}	ν_{Sb-Ar} *(Y-mode)*	ν_{Sb-N} + *ts (Sb–Ar)*
1	–	3390 (s)	3090 (w)	1330 (s) 1136 (w)	–	–	–	–
2	3550 (s)	3380 (s)	3100 (w) 3060 (w)	1334 (s) 1144 (w)	1126 (s)	–	–	–
3a	–	–	3100 (w)	1340 (s) 1152 (w)	1130 (s)	410 (m)	464 (s)	250 (m)
3b	–	–	3054 (w)	1340 (s) 1152 (w)	1130 (s)	410 (m)	480 (s)	260 (s)
3c	–	–	3050 (w)	1342 (s) 1154 (w)	1132 (s)	416 (m)	466 (s)	250 (vs)

TABLE 3 Chemical Shift δ ^{1}H in $CDCl_3$ (ppm)

	NH/OH	*1-CH_2*	*2-CH_2*	*CH*	*CH_3*	*ArH*
1	2.04 (1H, br)	3.72 (2H, t)	3.31 (2H, t)	–	–	6.51–8.13 (9H, m)
2	1.59 (1H, br) 5.05 (1H, br)	3.36 (2H, t)	2.09 (2H, q)	4.90 (1H, t)	–	6.44–8.14 (9H, m)
3a	–	3.32–3.35 (2H, m)	2.06 (2H, m[a], $J = 6.7, 6.1$ Hz)	4.83 (1H, dd[b] $J = 6.7, 5.7$ Hz)	–	6.44–8.14 (24H, m)
3b	–	3.33–3.36 (2H, m)	2.07 (2H, m[a], $J = 6.7, 6.1$ Hz)	4.87 (1H, dd [b] $J = 6.7, 5.7$ Hz)	2.35 (9H, s)	6.42–8.09 (21H, m)
3c	–	3.32–3.36 (2H, m)	2.06 (2H, m[a], $J = 6.7, 6.1$ Hz)	4.87 (1H, dd[b] $J = 6.8, 5.7$ Hz)	2.31 (9H, s) 2.54 (18H, s)	6.42–8.09 (15H, m)

[a]Overlapping triplets.
[b]Tending to be a triplet.

compounds were determined in chloroform using a Knauer vapor pressure osmometer.

IR spectra in the range 4000–400 cm^{-1} were recorded as KBr pellets on a Nicolet (5DX) FT IR spectrophotometer. Far IR spectra were recorded in polyethylene in the range of 700–50 cm^{-1} on a Perkin-Elmer 1700X Far IR FT spectrophotometer. The ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Jeol JNM FX-100 FT-NMR spectrometer using TMS as an internal standard.

Preparation of **3**

R_3SbBr_2(5 mmol in 50 ml THF) was added dropwise to a stirred solution of the disodium salt of **2** prepared from **2** (5 mmol) and NaH (10 mmol) in THF under nitrogen atmosphere. The mixture was refluxed for 2 h. The resultant solution was then taken to dryness under vacuum at 40–50°C, and 30 ml of benzene was added to the residue. Sodium bromide separated and was filtered off and weighed. The filtrate was concentrated to obtain compound **3**, which was recrystallized from a benzene–hexane mixture.

TABLE 4 Chemical Shift δ ^{13}C in $CDCl_3$ (ppm)

	CH	*2-CH_2*	*1-CH_2*	*CH_3*	*ArC*
2	73.15	37.29	40.65	–	110.82–153.46
3a	72.89	33.78	37.38	–	110.87–135.09
3b	72.22	36.89	40.31	21.35	110.38–144.98
3c	72.61	33.53	40.55	20.90, 24.37	110.77–142.25

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