

Studies on the Synthesis of Heterocyclic Compounds.
Synthesis of 1,3,2-Benzoxathia- and 1,3,2-Benzodioxastibole Derivatives

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The preparation of 1,3,2-benzoxathia- and 1,3,2-benzodioxachlorostiboles (IIa-b) by reaction of antimony trichloride with 2-hydroxythiophenol (Ia) or 1,2-benzodiol (Ib) is described. The halogen was easily removed. Thus a Wurtz-like reaction gave the distibole compounds (IVa-b), which were also produced by organolithium compounds or pyridine. The compounds Va-b were obtained with sodium hydroxide, ethoxide and phenoxide, but spiran derivatives VIIa-b, of antimony, were obtained by treating IIa-b with 2-hydroxythiophenol or 1,2-benzodiol in the presence of triethylamine. The structure of the prepared compounds was determined by spectroscopic methods.

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The chemistry of the heterocyclic compounds with oxygen-antimony-oxygen and oxygen-antimony-sulphur bonds has not been sufficiently studied. A few examples of 1,3,2-benzodioxastibole derivatives have been reported (Ia-d), but there is only one example of 1,3,2-benzoxathia-stibole derivatives (Ia).

Following our studies on five-membered heterocyclic compounds with O-M-O and O-M-S groups (2a-b), we synthesized and investigated the properties of 1,3,2-benzoxathia- and 1,3,2-benzodioxastibole compounds.

The structures of compounds Va-b have been determined by the elemental analysis and by ir, nmr and mass spectroscopy. The ir spectra show at 790 cm^{-1} the characteristic band of the Sb-O-Sb bond (7), while the mass spectra gave for both compounds the molecular ion peak; elemental analysis agrees with the proposed structure.

The structure of VI has been unambiguously determined by spectroscopic data: the mass spectrum shows the peak of the molecular ion, and the nmr spectrum shows three signals centered at δ 6.90, δ 3.50 and δ 1.35 ppm, attributable to the aromatic, methylenic and methylic protons, respectively.

The reaction of IIa-b with Ia or Ib, in triethylamine, gave VIIa-c where the antimony is bonded with two cyclic systems and coordinated with the amine nitrogen. These compounds were obtained as crystalline solids and their structures were determined by elemental analyses and

spectroscopic data. The ir spectra, besides the =C-O and disubstituted benzene bands, show bands attributable to the Sb-N bond (8), at $595\text{-}560$ and $370\text{-}335\text{ cm}^{-1}$. The mass spectrum shows the molecular ion corresponding to the deaminated molecule and that corresponding to the amine. The nmr spectrum besides the aromatic resonances indicates the presence of aminic hydrogens.

The reaction of IIa-b with triethylamine alone gave a mixture of IVa-b and VIIa-b. The formation of IVa-b agrees with the aforementioned reactions with pyridine, while the presence of VIIa-b can be explained by an initial partial cleavage of the Sb-O and Sb-Y bonds. Traces of Ia or Ib support this hypothesis.

Analogous reactions of IIa-b with phenol in the presence of triethylamine always gave mixtures of IVa-b, Va-b, VIIa-b, and this agrees with previous considerations.

EXPERIMENTAL

The infrared spectra were recorded on a Perkin-Elmer model 325 spectrophotometer; compounds were examined in the range $4000\text{-}600\text{ cm}^{-1}$ using the pressed potassium bromide disk and in the range $1000\text{-}200\text{ cm}^{-1}$ using Nujol mulls between cesium iodide plates. The nmr spectra were recorded on a Varian A-60 instrument in DMSO- d_6 and compared with hexamethyldisiloxane as an internal standard. Mass spectra were measured with an "Hitachi" Perkin-Elmer RMU-6D spectrometer at 70 eV. Microanalyses for CHN were carried out on a Perkin-Elmer model 240 Elemental

Analyzer; analyses for C, S and Sb were performed by the literature procedures (9). Melting points were uncorrected and obtained on a Tottoli apparatus.

2-Hydroxythiophenol (Ia).

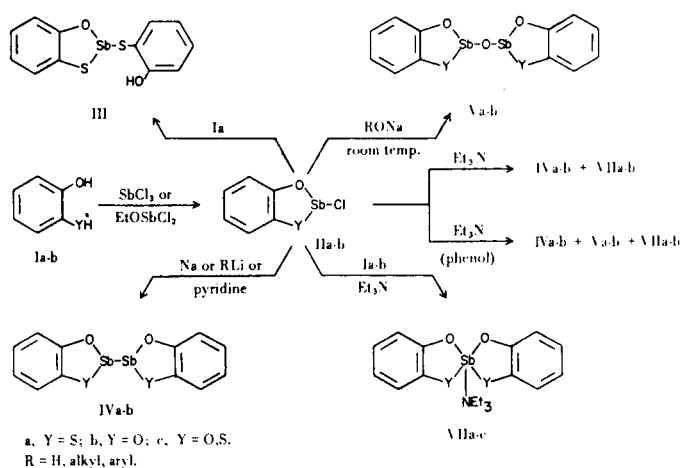
This compound was obtained by the literature procedure from 2-hydroxyaniline (10).

2-Chloro-1,3,2-benzoxathiastibole (IIa).

Method A.

To a stirred solution of Ia (50 mmoles) in benzene (50 ml.) a solution of antimony trichloride (50 mmoles) in benzene (50 ml.) was added dropwise and the mixture was refluxed until the hydrogen chloride vapours completely disappeared. The yellow precipitate was filtered off and recrystallized from benzene, yield 80%.

The reaction of equimolar amounts of 2-hydroxythiophenol (Ia) or 1,2-benzodiol (Ib) with antimony trichloride gave good yields of IIa and IIb. The structure of IIa was determined from spectroscopic data, while the structure of IIb was already known (1c). In fact the mass spectrum of IIa shows the molecular ion at m/e 280 and the ir spectrum shows bands characteristic of the Sb-Cl bond at 260 cm^{-1} (3), of a 1,2-disubstituted benzene at 755 cm^{-1} and of $=\text{C}-\text{O}$ group at 1080 and 1220 cm^{-1} (4), while the OH and SH stretching are absent from the spectrum.



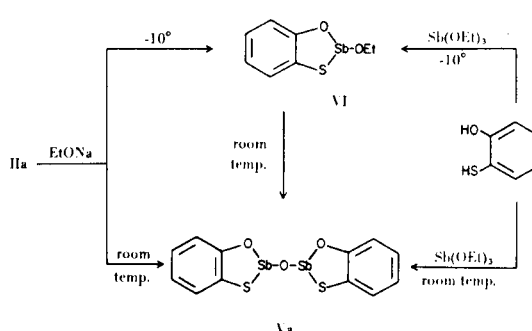
The reaction of 2-hydroxythiophenol with antimony trichloride also gave the compound III.

We determined the structure of the compound III, obtained in a different way from other authors (1a), from elemental analytical data and by nmr, ir and mass spectra. A tricoordinate structure was assigned to this compound on the basis of its ir and nmr spectra; we were not able to observe an equilibrium between tricoordinate and pentacoordinate forms like that observed for similar phosphorus compounds (5). The ir spectra gave no evidence of the Sb-H stretching bands between 1850 and 1880 cm^{-1} (6). The nmr spectra did not show any Sb-H signal, as would be expected for a possible pentacoordinate form, at high and low fields, with polar and non-polar solvents; on the

contrary the OH phenolic signal at δ 7.10 ppm is always present.

The compounds IVa-b were also obtained by reaction of compounds IIa-b with sodium or pyridine. Attempted substitution of the halogen with butyl or phenyl radicals, using butyllithium or phenyllithium, gave compounds IVa-b. The structures of the compounds IVa-b were determined by spectroscopic data.

Analogous treatment of IIa-b with sodium hydroxide, or sodium ethoxide, or phenoxide, in order to substitute the halogen, led to compounds Va-b. These results were obtained when the reactions were performed at room temperature as well as at higher temperature. In addition to Va-b, we always noted ethereal compounds arising from the organic radical of the organometallic reagent in an equimolar amount with respect to Va-b. Perhaps the reaction proceeds *via* the formation of 2-OR substituted stiboles, 2 molecules of which then react to give the compounds Va-b. Some support for this is given by the fact if the reaction of IIa with sodium ethoxide was carried out at -10° , the compound VI was isolated, which at room temperature gave Va. Attempts to obtain VI by treating 2-hydroxythiophenol with triethoxystibine gave the same results.



If the reaction was carried out with triphenoxystibine, at -10° and at room temperature, the starting material was obtained, but at a $80-100^\circ$, compound Va and diphenyl ether were obtained.

Reaction of 2-hydroxythiophenol or 1,2-benzodiol with ethoxy- or phenoxydichlorostibine did not give the expected results (VI or Va-b): only the compounds IIa-b were obtained at low and higher temperatures.

m.p. $189-191^\circ$; ir: $1450, 1430, 1280, 1225, 1215, 1120, 1030, 835, 760, 750, 680, 635, 560, 440, 390, 305, 260\text{ cm}^{-1}$; the nmr spectrum contained only aromatic signals at δ 7.10 ppm; molecular ion: m/e 280 (Calcd. 280).

Anal. Calcd. for $\text{C}_6\text{H}_4\text{ClOSSb}$: C, 25.61; H, 1.43; Cl, 12.60; S, 11.39; Sb, 43.27. Found: C, 25.64; H, 1.35; Cl, 12.45; S, 11.15; Sb, 43.10.

Method B.

To a stirred solution of Ia (30 mmoles) in dry hexane (20 ml.), kept at room temperature, the dichloroethoxystibine (11) (30 mmoles) was added dropwise under nitrogen. When the addition

was completed, the mixture was stirred for almost four hours. The yellow precipitate, filtered off and crystallized from benzene, was identified as IIa by mixed melting point with an authentic sample and comparison of ir and mass spectral data, yield 76%.

The same result was obtained performing the reaction at -20° or treating Ia with dichlorophenoxystibine (Ic).

2-(2'-Hydroxyphenyl)thio-1,3,2-benzoxathiastibole (III).

Reaction of IIa (Method A), by evaporating the benzene solution, gave a residue of crude III. Purification of III was effected by stirring with 10 ml. of 10% aqueous sodium hydroxide, filtering to remove undissolved solid and then acidifying with concentrated hydrochloric acid to precipitate III, which crystallized as orange crystals, yield 15%, m.p. $>300^{\circ}$; ir: 3400, 1610, 1480, 1435, 1300, 1080, 1020, 1000, 740, 685, 600, 460, 260 cm^{-1} ; nmr: δ 7.00 (m, 8 H arom) and 7.10 ppm (1 H, OH, deuterium oxide exchanged); molecular ion: m/e 371 (Calcd. 371).

Anal. Calcd. for $\text{C}_{12}\text{H}_9\text{O}_2\text{S}_2\text{Sb}$: C, 38.84; H, 2.44; S, 17.28; Sb, 32.81. Found: C, 38.64; H, 2.35; S, 17.09; Sb, 32.68.

2-Chloro-1,3,2-benzodioxastibole (IIb).

Method A.

A mixture of Ib (50 mmoles), benzene (100 ml.) and antimony trichloride (50 mmoles) was worked up in the same manner described for the synthesis of IIa giving white crystals, yield 94%, m.p. $>300^{\circ}$ [lit. (Ic) m.p. $>300^{\circ}$].

Method B.

The same procedure as for IIa under B was employed, starting from Ib (30 mmoles), hexane (20 ml.) and dichloroethoxystibine (30 mmoles); yield 81%, m.p. $>300^{\circ}$.

Reactions of 2-chlorostiboles (IIa-b).

(a) With Sodium.

A mixture of IIa (20 mmoles), sodium (20 mmoles) and dry xylene (100 ml.) was refluxed with stirring until the sodium completely disappeared. After cooling, the yellow precipitate formed was collected and washed thoroughly with water. After drying the compound had m.p. $274\text{--}275^{\circ}$ and was identified as 2,2'-bi-(1,3,2-benzoxathiastibole) (IVa), yield 74%; ir: 1550, 1440, 1430, 1275, 1250, 1220, 1110, 1020, 840, 745, 680, 630, 605, 560, 480, 420, 380, 260, 230 cm^{-1} ; the nmr spectrum consisted of aromatic signals at δ 6.85 ppm; molecular ion: m/e 490 (Calcd. 490).

Anal. Calcd. for $\text{C}_{12}\text{H}_8\text{O}_2\text{S}_2\text{Sb}_2$: C, 29.30; H, 1.64; S, 13.04; Sb, 49.51. Found: C, 29.10; H, 1.59; S, 13.11; Sb, 49.30.

(b) With *n*-Butyllithium.

To a stirred solution of *n*-butyllithium in hexane (34 ml., 10 mmoles) a solution of IIa (10 mmoles) in dry tetrahydrofuran (100 ml.) was added dropwise under an atmosphere of nitrogen at room temperature. When the addition was completed the mixture was stirred under reflux for two hours. After cooling, the mixture was poured into water and the yellow crystalline product separated by filtration. Upon drying the compound was identified as IVa and was identical in all respects to the product obtained by method (a) above, yield 80%.

The same product IVa was obtained performing the reaction at -50° or when the compound IIa was treated with phenyllithium.

Similar treatment of IIb with sodium or *n*-butyllithium gave a white solid, 2,2'-bi-(1,3,2-benzodioxastibole) (IVb), yield 69% and 75%, respectively, m.p. $>300^{\circ}$; ir: 1580, 1475, 1315, 1245, 1190, 1100, 1020, 900, 855, 810, 790, 740, 730, 620, 610, 540,

340 cm^{-1} ; the nmr spectrum consisted of aromatic signals at δ 6.80 ppm; molecular ion: m/e 458 (Calcd. 458).

Anal. Calcd. for $\text{C}_{12}\text{H}_8\text{O}_4\text{Sb}_2$: C, 31.35; H, 1.75; Sb, 52.97. Found: C, 31.19; H, 1.68; Sb, 52.81.

(c) With Sodium Ethoxide at 100° and at Room Temperature.

A solution of IIa (3.5 mmoles), sodium ethoxide (3.5 mmoles) and dimethylformamide (or dimethylsulfoxide) (10 ml.) was kept at 100° for six hours. The reaction mixture was then cooled and poured into water. The resulting yellow crystalline precipitate was filtered and washed with water. After drying the compound had m.p. 280° and was identified as 2,2'-bi-(1,3,2-benzoxathiastibole) oxide (Va), yield 56%; ir: 1620, 1570, 1475, 1450, 1430, 1280, 1260, 1240, 1145, 1115, 1055, 1025, 835, 790, 745, 710, 680, 635, 605, 565, 480, 435, 380, 290 cm^{-1} ; the nmr spectrum consisted of aromatic signals at δ 6.85 ppm; molecular ion: m/e 506 (Calcd. 506).

Anal. Calcd. for $\text{C}_{12}\text{H}_8\text{O}_3\text{S}_2\text{Sb}_2$: C, 28.38; H, 1.59; S, 12.65; Sb, 47.95. Found: C, 28.24; H, 1.50; S, 12.51; Sb, 47.84.

The same product Va was obtained performing the reaction at room temperature or when the compound IIa was treated with sodium hydroxide or sodium phenoxide. In the latter case the presence of diphenyl ether was found in an equimolar amount with respect to the product Va.

Similar treatment of IIb gave a white product, 2,2'-bi-(1,3,2-benzodioxastibole) oxide (Vb), m.p. $>300^{\circ}$, yield 61%; ir: 1630, 1580, 1470, 1380, 1310, 1245, 1185, 1100, 1020, 900, 855, 810, 795, 730, 620, 540, 440, 335, 290 cm^{-1} ; the nmr spectrum contained only aromatic signals at δ 7.00 ppm; molecular ion: m/e 474 (Calcd. 474).

Anal. Calcd. for $\text{C}_{12}\text{H}_8\text{O}_5\text{Sb}_2$: C, 30.30; H, 1.69; Sb, 51.19. Found: C, 30.19; H, 1.54; Sb, 51.05.

(d) With Sodium Ethoxide at -10° .

If the reaction of IIa with sodium ethoxide was carried out at -10° , the 2-ethoxy-1,3,2-benzoxathiastibole (VI) was isolated in 65% yield, m.p. $63\text{--}65^{\circ}$; ir: 2980, 2820, 1550, 1445, 1425, 1375, 1275, 1255, 1215, 1145, 1110, 1040, 1020, 925, 880, 835, 745, 680, 620, 600, 560, 485, 435, 425, 385, 330, 295, 255, 230 cm^{-1} ; nmr: δ 1.35 (t, 3 H, $\text{CH}_3\text{-CH}_2\text{-}$), 3.50 (q, 2 H, $\text{CH}_3\text{-CH}_2\text{-}$) and 6.90 ppm (m, 4 H arom); molecular ion: m/e 290 (Calcd. 290).

Anal. Calcd. for $\text{C}_8\text{H}_9\text{O}_2\text{SSb}$: C, 32.02; H, 3.12; S, 11.02; Sb, 41.84. Found: C, 31.90; H, 3.03; S, 10.89; Sb, 41.68.

(e) With Ia and Triethylamine.

To a stirred solution of IIa (5 mmoles) in anhydrous tetrahydrofuran (10 ml.) at room temperature a solution of Ia (5 mmoles), dry triethylamine (10 mmoles) and anhydrous tetrahydrofuran (5 ml.) was added dropwise under an atmosphere of nitrogen. The resulting mixture was stirred under reflux for six hours. The crude yellow mixture of amine salt and product was chilled to 20° and poured into water; the insoluble fraction was collected, washed with hot tetrahydrofuran, air dried and recrystallized from benzene-tetrahydrofuran (1:1); the compound had m.p. $145\text{--}147^{\circ}$ and was identified as 2,2'-spirobi[1,3,2-benzoxathiastibole]-2-triethylamine (VIIa), yield 76%; ir: 3010, 2990, 2970, 2700, 2600, 2560, 1445, 1435, 1385, 1260, 1230, 1115, 1055, 1025, 930, 840, 750, 720, 680, 595, 575, 560, 445, 415, 370, 240 cm^{-1} ; nmr: δ 1.20 (t, 9 H, $\text{CH}_3\text{-CH}_2\text{-}$), 3.10 (q, 6 H, $\text{CH}_3\text{-CH}_2\text{-}$) and 6.80 ppm (m, 8 H arom); mass spectrum: 370 ($\text{M}^+ \text{-Et}_3\text{N}$), 101 (Et_3N).

Anal. Calcd. for $\text{C}_{18}\text{H}_{23}\text{NO}_2\text{S}_2\text{Sb}$: C, 45.87; H, 4.92; N, 2.97; S, 13.61; Sb, 25.84. Found: C, 45.80; H, 4.83; N, 2.89; S, 13.50; Sb, 25.73.

Similar treatment of IIb with Ia and triethylamine gave a yellow solid, spiro[1,3,2-benzodioxastibole-2,2'-[1,3,2]benzoxathia-stibole]-2-triethylamine (VIIc), which was crystallized from water, yield 66%, m.p. 90-91°; ir: 3040, 3000, 2780, 2195, 1570, 1550, 1470, 1450, 1430, 1390, 1260, 1240, 1115, 1055, 1025, 925, 840, 785, 750, 715, 675, 590, 560, 510, 460, 420, 370, 335, 235 cm⁻¹; nmr: δ 1.20 (t, 9 H, CH₃-CH₂-), 3.05 (q, 6 H, CH₃-CH₂-) and 6.80 ppm (m, 8 H arom); mass spectrum: 354 (M⁺ - Et₃N), 101 (Et₃N).

Anal. Calcd. for C₁₈H₂₃NO₃SSb: C, 47.49; H, 5.09; N, 3.08; S, 7.04; Sb, 26.75. Found: C, 47.32; H, 5.00; N, 3.03; S, 6.93; Sb, 26.67.

(f) With Ib and Triethylamine.

The same product VIIc was obtained performing the reaction of IIa with Ib and triethylamine, yield 50%.

In the same manner the 2,2'-spirobi[1,3,2-benzodioxastibole]-2-triethylamine (VIIb) was obtained from IIb, Ib and triethylamine, as white crystals, which were crystallized from water; yield 78%, m.p. > 300°; ir: 3040, 3000, 2680, 2500, 1575, 1480, 1445, 1395, 1330, 1260, 1240, 1210, 1090, 1020, 905, 860, 790, 740, 630, 595, 505, 450, 335, 235 cm⁻¹; nmr: δ 1.20 (t, 9 H, CH₃-CH₂-), 3.10 (q, 6 H, CH₃-CH₂-) and 6.40 ppm (m, 8 H arom); mass spectrum: 337 (M⁺ - Et₃N), 101 (Et₃N).

Anal. Calcd. for C₁₈H₂₃NO₄Sb: C, 49.23; H, 5.28; N, 3.19; Sb, 27.73. Found: C, 49.09; H, 5.16; N, 3.14; Sb, 27.58.

(g) With Pyridine.

A mixture of IIa (2 mmoles) and dry pyridine (8 ml.) was refluxed with stirring for six hours. After cooling, the crude product was poured into water; the insoluble fraction was collected and washed with hot tetrahydrofuran. Upon drying the compound was identified as IVa; yield 62%.

Similar treatment of IIb with pyridine gave the compound IVb; yield 68%.

(h) With Triethylamine.

A mixture of IIa (2 mmoles) and dry triethylamine (10 ml.) was refluxed with stirring for eight hours. After cooling, the reaction mixture was poured into water and filtered; the precipitate was refluxed for one hour with tetrahydrofuran and filtered. The tetrahydrofuran layer, which contained the starting material, was discarded and the residue was added to 20 ml. of water and heated. After refluxing for about thirty minutes, the hot mixture was filtered and the residue, after drying, was identified as IVa, yield 35%. The aqueous solution, after cooling, deposited a yellow solid, which was identified as VIIa, yield 23%.

The first aqueous solution was extracted repeatedly with diethyl ether; the ethereal extracts, dried on magnesium sulphate and analyzed by glc, showed a peak with the same retention time as 2-hydroxythiophenol.

Similar treatment of IIb gave the compounds IVb and VIIb.

(i) With Phenol and Triethylamine.

A mixture of IIa (3.5 mmoles), phenol (3 mmoles), dry triethylamine (4 ml.) and dry tetrahydrofuran (10 ml.) was refluxed and stirred under an atmosphere of nitrogen for five hours. After cooling, the reaction mixture was poured into water. The residue was refluxed with tetrahydrofuran and filtered. The precipitate was added to 30 ml. of water and this mixture was warmed for

thirty minutes and filtered while hot. The mass spectrum of the residue showed two peaks at m/e 490 and 506, attributable to the molecular ions of IVa and Va.

The aqueous solution after cooling deposited a solid which was identified as VIa. The ratio of VIIa, IVa and Va was 7:1.5:1.5.

Similar treatment of IIb gave the compounds VIIb, IVb and Vb.

Action of Triethoxystibine on Ia.

A mixture of Ia (70 mmoles) and triethoxystibine (11) (70 mmoles) was heated at 50° under a nitrogen atmosphere for five minutes. Then a distillation device with a Vigreux column was attached. The mixture was heated initially at 60° and the temperature then raised to 110°. Ethanol and diethyl ether were distilled over. After cooling the yellow crystals obtained were identified as Va, yield 85%.

When the reaction was carried out at -10° the 2-ethoxy-1,3,2-benzoxathia-stibole (VI) was isolated in 89% yield.

Action of Triphenoxystibine on Ia.

With the same procedure, described above, with Ia and triphenoxystibine (Ic) at -10° and at room temperature the starting material was obtained. If the reaction was carried out at 80-100° compound Va (yield 76%), phenol and diphenyl ether were obtained.

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