SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL STUDIES OF NOVEL ORGANOBISMUTH(III) COMPLEXES

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Abstract: The Present Manuscript deals the synthesis of some novel organobismuth(III)aryloxyacetates followed by their characterization by melting points, elemental analysis, U.V., I.R and NMR spectral analysis to confirm their structures and geometry. The compounds were also screened for their antibacterial and antifungal efficacy against pathogenic bacterial and fungal strains. It was found that these compounds exhibit higher activity than the standard drug for bactericidal and fungicidal activity.

Keywords: Organobismuth, aryloxyacetates, antibacterial, antifungal.

Introduction

The acetates in organic derivatives of group 15 elements could behave as monodentate, bidentate or as bridging ligands depending on the oxidation state (+3 or +5); physical state of the compound (solid or solution) and the various substituents present on the acetate group itself [1-10]. It has been found that major influences in determining mode of bonding, geometry and stability of the acetate system in general are the absence of ligand atom trans to an organic substituent present on t

Experimental

The diorganobismuth (III) chloride, R₂BiCl₃ and organobismuth (III) dichloride, R₂BiCl₂ was prepared by the redistribution reaction [20]. The syntheses of some representative compounds are as follows.

Reaction of (C₆H₅)₂Bi(III)Cl with (C₆H₅OCH₂COOH) (1)

In the stirring solution of diphenylbismuth(III)chloride (0.398gm;1mmol), phenoxycetic acid (0.152gm;1mmol) was added in presence of triethylamine (1 ml) in benzene and was stirred in anhydrous oxygen free, nitrogen conditions for 6h, followed by refluxing for 2h to ensure completion of the reaction. A flocculent white precipitate of Et₃N·HCl (M.P.240°C) was formed which was filtered off. The filtrate on concentration gave a light brown solid which was recrystallised by petroleum ether (40°-60°C).

Reaction of (C₆H₅)₂Bi(III)Cl with (p-CH₃C₆H₄OCH₂COOH) (2)

In the stirring solution of diphenylbismuth(III)chloride (0.398gm;1mmol), p-methyl phenoxycetic acid (0.166gm;1mmol) was added in presence of triethylamine (1ml) in benzene and was stirred in anhydrous oxygen free, nitrogen atmosphere for 6h, followed by refluxing for 2h to ensure completion of the reaction. A flocculent white precipitate of Et₃N·HCl (M.P.240°C) was formed which was filtered off. The filtrate on concentration afforded a light brown solid which was recrystallised by petroleum ether (40°-60°C).

Reaction of (C₆H₅)₂Bi(III)Cl with (p-C₆H₅OCH₂COOH) (3)

In the stirring solution of diphenylbismuth(III)chloride (0.398gm;1mmol), p-chloro phenoxycetic acid (0.186gm;1mmol) was added in presence of triethylamine (1ml) in benzene and was stirred in anhydrous oxygen free, nitrogen atmosphere for 6h, followed by refluxing for 2h to ensure completion of the reaction. A white
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colour precipitate of Et₂N.HCl (M.P.240°C) was formed which was filtered off and the filtrate on concentration in vacuum afforded a light brown solid which was recrystallised by petroleum ether (40°-60°C).

Reaction of \((\text{C}_6\text{H}_5\text{CH}_2\text{O})\) with \((\text{Bi})(\text{III})\) chloride (\(0.578\, \text{g}; 1\, \text{mmol}\)) in benzene and was stirred in anhydrous oxygen free, nitrogen conditions for 6h, followed by refluxing for 2h to ensure completion of the reaction. A flocculent white precipitate of \(\text{Et}_2\text{N.HCl}\) (M.P.240°C) was formed which was filtered off. The filtrate on concentration gave a light brown solid which was recrystallised by petroleum ether (40°-60°C).

Antibacterial activity

The antibacterial activity of these organobismuth(III) compounds was determined by disc diffusion method [21]. In this technique, the filter paper (Whatman No. 1) sterile discs of 5 mm diameter, impregnated with the test compounds (10 µg/ml of ethanol) were placed on the nutrient agar plate at 37°C for 24 hrs. The inhibition zones around the dried impregnated discs were measured after 24 hrs. The activity was classified as 'highly active' (diameter > 14 mm); "moderately active" (diameter = 10-14 mm) and 'slightly active' (diameter = 6-10). The diameter less than 6 mm was regarded as inactive.

**Results and Discussion**

All the reactions were conducted at room temperature and the products were recrystallised from petroleum ether (40°-60°C) or in benzene. The complexes are off-white to light brown solids and obtained as a sticky mass which on treatment with sodium in dry benzene gets solidified and subsequently crystallized with benzene/pet-ether. The complexes are fairly stable on air and moisture and have sharp melting point. There is no regular trend of the melting point of the complexes and they melt without decomposition. Complexes are also soluble in chloroform and acetonitrile. They can be stored at room temperature without decomposition for several weeks. The consistency in melting points after repeated recrystallization as well as TLC run in chloroform hexane mixture (1:1) with the observation of a single spot excluded the presence of mixture of reactants. The molar conductance value of 10-3 S.m².mol⁻¹ solution of these compounds were recorded in methanol and found in the range of 15-25 Ω⁻¹. m².mol⁻¹ indicating the absence of ionic species in solution. The complexes were found to be monomeric in nitrobenzene.

IR Spectra

As expected infrared absorptions inherent to phenyl and fluoroaryl groups bound to bismuth have no difference appreciably and hence not discussed. The infrared absorptions having diagnostic value for organobismuth aryloxyacetates, related to the ligand, have been identified which on preliminary stage indicates the mode of bonding with arylxy ligand. The characteristic ν(OH) absorption band of ligands which appeared around 3400 cm⁻¹ in the free ligand, was found missing in the newly synthesized complexes. A medium strong intensity band appearing at 1690-1700 cm⁻¹ can confidently be assigned to ν(C=O) of the aryloxyacetate moiety. The deformation mode as a medium intensity band at around 1370 cm⁻¹ which can be attributed to ν(C–O) of the aryloxyacetate moiety in the complexes. This may be due to the presence of aryloxyacetate moiety and different amplitudes (2300 cm⁻¹) which are in solvents (2900 cm⁻¹). The vibrational bands of the aryloxyacetate moiety (2300 cm⁻¹) in solvents (2900 cm⁻¹) are very weak.

**HNM R Spectra**

The IR spectra of the compounds with those of respective ligands in solution states did not show any significant shift in ν(C=O), ν(OH) and ν(C–O) deformation bands in which showed the lack of coordination with bismuth through C–O=O or C–O–Ar center of the ligand. Since the separation observed in the present compounds is fairly large (2300 cm⁻¹), monomolecular conformation seems to be most plausible where bismuth would be a coordination number three. This observation is clearly sharp contrast to organol complexes of aryloxyacetates which have been found to be polymeric involving carboxylic bridges. In addition to this intermolecular interaction involving the ethereal oxygen has also been demonstrated in some cases particularly.
internal reference at 25°C. The disappearance of OH proton signals (89.1 ppm) present in the ligand clearly indicates the formation of arylxyocetate derivatives. The appearance of singlet for -CH₃ protons at 8.85 ppm showed the ligand is in one plane. The phenyl protons for both the derivatives appear as multiplets in the range 7.80-7.20 ppm. 

UV Spectra

| S.N. | Compounds | Formula | M.P. (°C) | Color | Yield (%) | Solvent |
|------|-----------|---------|-----------|-------|-----------|---------|
| 1    | (C₆H₅)Bi(OOC.CH(OCH₃))₂ | C₂H₆Bi₂O₂ | 190       | Light Brown | 60       | Pet-ether |
| 2    | (C₆H₅)Bi(OOC.CH(OCH₃)CH₃)₂ | C₂H₆Bi₂O₄ | 156       | Light Brown | 75       | Pet-ether |
| 3    | (C₆H₅)Bi(OOC.CH(OCH₃)Cl)₂ | C₂H₆Bi₂O₂Cl₂ | 214    | Light Brown | 70       | Pet-ether |
| 4    | (p-F₃C₆H₄)Bi(OOC.CH(OCH₃))₂ | C₂F₆H₄Bi₂O₂ | 184    | Light Brown | 65       | Pet-ether |
| 5    | (C₆F₃Bi(OOC.CH(OCH₃)CH₃)₂ | C₂F₆Bi₂O₄ | 176       | Light Brown | 60       | Pet-ether |
| 6    | (C₆F₃Bi(OOC.CH(OCH₃)Cl)₂ | C₂F₆Bi₂O₂Cl₂ | 204    | Light Brown | 60       | Pet-ether |
| 7    | (p-F₃C₆H₄)Bi(OOC.CH(OCH₃)CH₃)₂ | C₂F₆H₄Bi₂O₄ | 192    | Light Brown | 60       | Pet-ether |
| 8    | (p-F₃C₆H₄)Bi(OOC.CH(OCH₃)Cl)₂ | C₂F₆H₄Bi₂O₂Cl₂ | 182    | Light Brown | 75       | Pet-ether |
| 9    | (p-F₃C₆H₄)Bi(OOC.CH(OCH₃)Cl)₂ | C₂F₆H₄Bi₂O₂Cl₂ | 198    | Light Brown | 70       | Pet-ether |

IR Absorption frequencies in mm⁻¹ (OCO) 
- C₁H₁Bi: 1385, 1694, 1397
- C₂F₆Bi: 1385, 1397, 1394
- C₂H₂Bi: 1385, 1397, 1394

Aspergillus flavus: 76.6
- Control: 80.2
- p-F₃C₆H₄Bi: 76.6
- p-F₃C₆H₄Bi: 76.6

Staphylococcus aureus: 80.2
- Control: 80.2
- p-F₃C₆H₄Bi: 80.2
- p-F₃C₆H₄Bi: 80.2

Klebsiella pneumoniae: 80.2
- Control: 80.2
- p-F₃C₆H₄Bi: 80.2
- p-F₃C₆H₄Bi: 80.2

Antibacterial activity

The organobismuth (III) arylxyocetates were tested for antibacterial activity against three bacterial strains Pseudomonas aeruginosa, Staphylococcus aureus and Klebsiella pneumoniae using 10 µg/ml concentration of test compound. All the compounds show higher to moderate activity against the bacterial strains. It was found that compounds having fluoro and pentafluorophenyl ring are more effective because of their water and lipid solubility. The fluorine containing compounds may generally form complexes with metalloenzymes, particularly those which responsible in basic physiology such as cytochrome oxidase. These compounds may react with peptidoglycan layer of bacterial cell wall and damage it by penetrating in such a manner that the phenyl ring gets inside the cell by puncturing it followed by death of bacterial cell. Sometimes these compounds in low concentration may cause bacteriostatic condition by slow down the growth of bacteria.

On the basis of IR, NMR and UV spectral analysis data, it may tentatively concluded that arylxyocetate under the present study behaves as a monodentate ligand. Conduction measurement and molecular Wight data showed that these arylxyocetates have monomorphic nature and are non conducting in nature. The experimental data are thus consistent with three coordinate pyramidal structures.
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**Antifungal Activity**
The antifungal activity of organobismuth (III) compounds was tested against *Aspergillus flavus* and *Aspergillus niger* using 50 μg/ml concentration. The activity of these compounds was found variable at 50μg/ml concentration against fungal strains. Presence of nitrogen, phenyl and pentafluorophenyl ring along with bismuth in +3 oxidation state are considered for fungal activity. The role of different arylxoyacetates as ligands was also commendable. These compounds generally damage the fungal strains by puncturing the cell wall similarly as in the case of bacteria. Water and lipid solubility of these compounds, due to presence of fluorine, also increases the activity due to presence of fluorine.

**Application of research:** Applicable for study of antimicrobial activity of Organobismuth compounds

**Research Category:** Antibacterial activity

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