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# MÖSSBAUER SPECTRA OF ORGANOTIN AMINO-ACID AND GLUTATHIONE DERIVATIVES

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## SUMMARY

Mössbauer parameters are reported for compounds in which organotin entities are bonded to thiolate, carboxylate and sulfonate groups of simple ligands (L-cysteine and derivatives, DL-penicillamine, cysteic acid and Glutathione reduced) which have biological relevance. The relationship between the stereochemistry about the tin atom and the corresponding quadrupole splitting value is examined and the extension to the use of Mössbauer spectroscopy to determine the binding of organotins in more complex biochemical systems is discussed.

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The biochemistry of organotin compounds has been the subject of many investigations (1,2,3). Mössbauer spectroscopy is potentially a valuable technique for such studies since it makes possible the identification of the types of group that bind the organotin. In view of the complexity of biological systems, it would be useful to have data for simpler "model" compounds, such that sites binding organotins may, under favorable conditions, be identified by comparison with the

respective Mossbauer spectra. Study of simpler systems also enables the elucidation of factors that may be of major significance in the biochemistry of organctins: e.g. the role of hydrogen bonding, chelating or bridging ligands and the coordination states of tin when bound to different sites (4).

Compounds were prepared which contained organotins bound to thiolate, carboxylate and sulfonate groups. The data reported here extend those already published for trialkyltin derivatives of amino-acids (5) and for diorganotin derivatives (6,7). Structural investigations on L-cysteine and Glutathione derivatives have been reported (4,8,9).

## Experimental

(i) Synthesis

The preparations of some compounds containing the ligands L-cysteine, DL-penicillamine, N-acetyl L-cysteine, 2-thiolaminoethane and Glutathione (reduced) have been described previously (4,8).

1. Bis(tri-*n*-butyltin)cysteicate dihydrate.

   L-cysteic acid (5 mmol) was suspended in 50 $cm^3$ ethanol and bis(tri-*n*-butyltin)oxide (5 mmol) slowly added. The L-cysteic acid slowly dissolved and the solution was heated for *ca.* 1 hour to evaporate off half the solvent. The remaining solvent was removed with a rotary evaporator to yield a pale blue "plastic" product. M.Pt. 118-120°C. Yield 66%. Analysis. Calculated for $[(n\text{-}C_4H_9)_3Sn]_2[O_3SCH_2CH(NH_2)CO_2].2H_2O$ : C, 41.41; H, 8.10; N, 1.79; O, 14.30; S, 4.09%. Found: C, 41.46; H, 7.71; N, 1.79; O, 14.1; S, 4.2%.

2. Bis(triphenyltin)cysteicate.

   Prepared in a similar manner from equimolar quantities of bis(triphenyltin)oxide and L-cysteic acid in $CHCl_3$. The solvent was removed with a rotary evaporator and the "plastic" product kept in a vacuum desiccator for 2 weeks.

On standing, the product slowly converts into a white powder. Yield 73%. Analysis. Calculated for $[(C_6H_5)_3Sn]_2[O_3SCH_2CH(NH_2)CO_2]$ : C, 54.02; H, 4.07; O, 9.20; S, 3.69; Sn, 27.31%. Found : C, 54.69; H, 4.50; O, 9.8; S, 4.7; Sn, 29.7%.

3. α-Glutamyl cysteinato-glycinato (S-, O-)bis(triphenylstannane) IV, $[(Ø_3Sn)_2SG]$*

Equimolar quantities (10 mmol) of Glutathione (reduced) and bis(triphenyltin)oxide were mixed in 1:1 ethanol/water (1 ℓ) under an atmosphere of dinitrogen. This mixture was stirred for 3 days and then the solvent was allowed to air evaporate to about half the original volume. Another 500 $cm^3$ ethanol was added and the stirring continued for 2 more days, after which the solvent was allowed to air evaporate to half its volume then a further 300 $cm^3$ ethanol added. This mixture was allowed to stand for 2 more days during which time the solvent was reduced to 100 $cm^3$. Now 200 $cm^3$ $CHCl_3$ was added and the mixture was stirred and air evaporated to *ca.* 150 $cm^3$. Water was added and the chloroform layer separated. This was filtered and allowed to evaporate to 50 $cm^3$. Addition of *n*-pentane precipitated the product, which was filtered off and dried in a vacuum desiccator for 2 days. Yield 40%. Analysis. Calculated for $[(C_6H_5)_3Sn]_2[SG.H_2O]$: C, 53.99; H, 4.63; O, 10.94; S, 3.13; Sn, 23.20%. Found: C, 52.43; H, 4.37; O, 9.9; S, 4.1; Sn, 22.7%.

(ii) Recording the Mössbauer spectra.

The spectra were obtained using a conventional constant

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*Abbreviations employed hereafter are: Me, methyl; Et, ethyl; Bu, butyl; Ø, phenyl; L-cyst, L-cysteine; L-cyst eth, L-cysteine ethyl ester; DL-pen, DL-penicillamine; N-acet L-cyst, N-acetyl L-cysteine; SG, Glutathione.

TABLE: Mössbauer parameters of compounds analyzed (mm $sec^{-1}$). (The errors are ±0.01 mm $sec^{-1}$ in I.S. and $\Gamma$ and 0.02 mm $sec^{-1}$ in Q.S. for liquid nitrogen spectra).

| | Compound | I.S. | Q.S. | $\Gamma$ | $I_1/I_2$** | Calculated Q.S† | Structure |
|---|---|---|---|---|---|---|---|
| 1. | $Me_2Sn(Cl)$L-cyst.$H_2O$ | 1.33 | 3.26 | 1.16 | 1.03 | 3.0-3.3 | I |
| 2. | $Me_2Sn(Cl)$ DL.pen | 1.28 | 3.16 | 1.12 | 1.03 | 3.0-3.3 | I |
| | ditto (Room Temp.) | 1.23 | 3.05 | 0.96 | 1.14 | | I |
| 3. | $n$-$Bu_2Sn(Cl)$ L-cyst* | 1.44 | 3.15 | 1.38 | 1.00 | 3.0-3.3 | I |
| 4. | $Me_2Sn(Cl)$ L-cyst eth. | 1.27 | 2.84 | 1.08 | 1.05 | 3.0 | I |
| 5. | $Me_2Sn(Cl)SCH_2CH_2NH_2$ | 1.27 | 2.83 | 1.08 | 1.13 | 3.0 | I |
| | ditto (Room Temp.) | 1.21 | 2.77 | 0.74 | 0.86 | | I |
| 6. | $(n\text{-}Bu_3Sn)_2$N-acet.L-cyst* | 1.41 | 3.59 | 1.06 | 1.04 | 3.8 | II |
| | | 1.37 | 1.62 | 1.04 | 0.94 | - | Tetrahedral |
| 7. | $(n\text{-}Bu_3Sn)_2$L-cysteicate.$2H_2O$ | 1.37 | 3.54 | 0.98 | 1 | 3.8 | II |
| | | 1.28 | 2.31 | 0.94 | 1 | 2.3 | III |
| 8. | $(\phi_3Sn)_2$ L-cysteicate@ | 1.38 | 3.21 | 1.08 | 1 | 3.5 | IV |
| | | 1.02 | 3.06 | 1.04 | 1 | | |
| 9. | $(\phi_3Sn)_2$ SG. | 1.61 | 2.20 | 0.92 | 1.05 | 2.0 | III |
| | | 0.78 | 2.29 | 0.94 | 0.99 | | |
| 10. | $(n\text{-}Bu_3Sn)_2$ SG* | 1.40 | 3.43 | 1.00 | 1 | 3.5 | IV |
| | | 1.39 | 1.76 | 0.90 | | - | Tetrahedral |

* Spectra were not observed at room temperature.

@ The alternative assignment is I.S. = 1.24, Q.S. = 3.49 with $\Gamma$ = 0.98; I.S. = 1.16, Q.S. = 2.77 with $\Gamma$ = 1.10. The calculated Q.S. value is 3.3 if coordination by O is assumed.

† Calculated according to the procedure given in ref. 10.

** The ratio of the left to right hand peaks of the quadrupole doublet in a free fit.

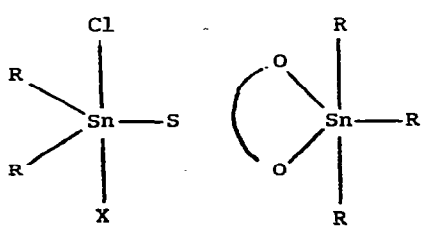
The value 1 indicates that the intensities were constrained to be the same.

acceleration drive connected to an electromechanical transducer. The absorber was mounted in the tail of a variable temperature cryostat, with the source maintained either at ambient or liquid nitrogen temperature and the spectrum accumulated into 1024 channels of a multi-channel analyzer.

Curve fitting was performed using a least squares program and a two-peak spectrum was fitted to single Lorentzians with no constraints. Four-peak spectra were fitted first by the single line procedure in order to obtain likely pairs, then with a doublet fitting procedure in which two lines corresponding to a quadrupole doublet were constrained to have the same height and $\Gamma$ value. This enabled different pairings to be tried in order to obtain the most probable assignment. In all cases except one (compound 8) this procedure permitted unambiguous assignments of the isomer shift (I.S.) and quadrupole splitting (Q.S) values to be made. The data are given in the Table.

## Discussion

The five-coordinate structural types for which Q.S. values were calculated are as follows:

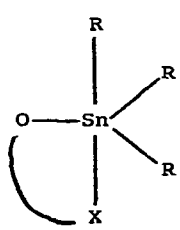



(X = N or O)

I

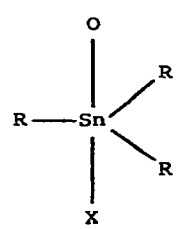



II




(X = S, N or O)

III




(X = N or O)

IV

Compounds 1-3 can be assigned structure I, but the question of intra- or intermolecular association is difficult to answer. The five-coordinate structures have been proposed from NMR and IR spectral

data (8) but whether coordination is *via* carboxylate or amino groups is unclear. The IR spectra suggest possible carboxylate coordination and the amino group involved in strong hydrogen bonding. Thus, an associated structure containing carboxylate groups coordinating to tin may be postulated - analogous to that of $Me_3SnSCH_2COOH$. That a room temperature spectrum of compound 2 is observable suggests an associated lattice, but this may be due either to intermolecular coordination or to hydrogen bonding. A detailed investigation of compounds 1 and 2 is in progress.

The structure of compound 4 has been determined by X-ray methods, and is of type I with a chelating ligand (11). Compound 5, however, appears to be associated *via* intermolecular N→Sn coordination, as suggested by the room-temperature spectrum.

The spectra of compounds 6-10 illustrate the potential of the Mössbauer technique for differentiating between two organotin moieties in the same complex which are in different chemical environments. The groups binding the organotin moiety in compounds 6,9 and 10 are thiol and carboxylate groups while those in compounds 7 and 8 are carboxylate and sulfonate. The $R_3Sn\text{-}S^{\nu}$ groups in compounds 6 and 10 give Q.S. values typical of triorganotin thiolate derivatives (12). Compound 9, however, shows an intriguing spectrum, with a very low I.S. value for one moiety, while the other compares favorably with the values reported (I.S. = 1.34 mm $sec^{-1}$, Q.S. = 2.35 mm $sec^{-1}$) for triphenyltin thioacetate in pyridine (12). The structure of this compound was proposed to be of type IV. On the other hand, the calculated Q.S. value for compound 9 suggests structure III. It is quite possible, however, that the triphenyltin moiety is considerably distorted. Other spectral data for this compound is difficult to obtain, but compound 10 has been investigated thoroughly and is associated *via* intermolecular coordination by nitrogen, so that its higher Q.S. value corresponds to structure IV, while the lower value is due to a tetrahedral *n*-$Bu_3Sn\text{-}S^{\nu}$ moiety (4). The analytical data for compound 9 and the infrared spectrum indicate the presence of water. The higher Q.S. value for the $Ø_3Sn\text{-}S^{\nu}$ moiety may then be due to water coordinating to that tin atom.

The other moiety, $\phi_3Sn\text{-}O^{\nu}$ may be type III (X=N) *via* inter- or intramolecular association. The infrared spectrum does not indicate carboxylate bridging, nor are the ν(C=O) and ν(N-H) bands typical of chelating groups. The difficulties in recording solution spectra for this compound preclude detailed studies which would determine if it is strongly associated like the butyltin derivative.

The Mössbauer spectra of the cysteicate compounds **7** and **8** provide interesting results. The values for compounds of the type $R_3SnO_3SR'$ have been reported to fall in the ranges I.S. = 1.4 - 1.6 mm $sec^{-1}$, Q.S. = 3.9 - 4.3 mm $sec^{-1}$ (13) while those for compounds $R_3SnO_2CR'$ lie in the area I.S. = 1.2 - 1.5 mm $sec^{-1}$, Q.S. *ca.* 3.5 mm $sec^{-1}$ for associated structures - with lower Q.S. values for those which are unassociated (14,15). The values for compounds **7** and **8** do not fall in the ranges expected, although the alternative assignment given for compound **8** would do so. The $^{13}C$ NMR spectrum of the tributyltin derivative shows equivalent chemical shifts for the butyl groups, indicating that at the temperature of the probe, both sulfonate and carboxylate groups were interchanging chelate/non-chelate ligands. Thus, the two organotin moieties may in fact be five coordinate in the solid, as suggested by the calculated Q.S. values, but additional information is required before a structure can be deduced for each tin moiety. Hydrogen bonding may modify the ability of amino, carboxylate and sulfonate groups to coordinate to a tin atom. Also, the possibility of mixed ligand chelation has to be considered. Thus it is difficult to make structural deductions simply from the Mössbauer spectra of these compounds.

Mössbauer spectroscopy in fact has been applied to studies related to the interaction of triethyltin chloride with rat liver mitochondria (16). A low affinity site was assigned (I.S. = 1.49 mm $sec^{-1}$, Q.S. = 2.78 mm $sec^{-1}$) together with a partitioned fraction (I.S. = 1.56 mm $sec^{-1}$, Q.S. = 3.44 mm $sec^{-1}$) and a high affinity site (I.S. = 1.59 mm $sec^{-1}$, Q.S. = 2.22 mm $sec^{-1}$). If a direct comparison between these values and those in the Table is assumed to be possible, it becomes apparent that the assignment

of the low affinity site to a $Et_3Sn-S^{\nu}$ entity is questionable. The Q.S. values for such a moiety in compounds 6 and 10 (1.62 and 1.76 mm $sec^{-1}$ respectively) are well below that reported. In fact, these compounds exhibit Q.S. values comparable to those of simpler $R_3Sn-SR'$ compounds. The low affinity site appears to compare favorably with $R_3Sn-$ carboxylate moieties which are unassociated, or perhaps in an environment more comparable to that in compound 7. The high affinity site may also be compared with the Q.S. value expected for structure III.

Our intention is not, however, to reassign the binding sites reported in reference 16, but rather to discuss the information that may be derived from the judicious use of Mössbauer spectroscopy. We feel that the difficulties that may be encountered in studying compounds of the type shown in the Table have been clearly demonstrated. The value of the Mössbauer spectrum is enhanced when it can be combined with information obtained from other techniques (e.g. reference 4). Thus a comparison between well-characterized compounds such as those already reported and other model compounds may provide valuable information on complicated biological systems.

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References

1. W.N. Aldridge and J.E. Cremer, Biochem. J., 61, 406, (1955).
2. W.N. Aldridge in "Organotin Compounds: New Chemistry and Applications" (J.J. Zuckerman, Ed.). Advances in Chemistry Series, Vol. 151, pp.186-195, American Chemical Society, Washington, D.C. (1976).
3. K. Cain, M.D. Partis and D.E. Griffiths, Biochem. J., 166, 593, (1977).

4. G. Domazetis, R.J. Magee and B.D. James, J. Organometal. Chem., in press.

5. B.Y.K. Ho and J.J. Zuckerman, Inorg. Chem., 12, 1552, (1973).

6. L. Pellerito, M.T. LoGuidice, G. Ruisi, N. Bertazzi and R. Barbieri, Inorg. Chim. Acta, 17, L21 (1976).

7. W.T. Hall and J.J. Zuckerman, Inorg. Chem., 16, 1239, (1977).

8. G. Domazetis, R.J. Magee and B.D. James, J. Organometal. Chem., 162, 239, (1978).

9. P.J. Smith, R.L. Hyams, J.S. Brooks and R.W. Clarkson, J. Organometal. Chem., 171, C29, (1979).

10. G.M. Bancroft, V.G. Kumar Das, T.K. Sham and M.G. Clark, J. Chem. Soc. (Dalton), 643, (1976).

11. G. Domazetis, M.F. Mackay, R.J. Magee and B.D. James, Inorg. Chim. Acta, 34, L247, (1979).

12. R.C. Poller and J.N. Ruddick, J. Chem. Soc. (Dalton), 555, (1972).

13. P.G. Harrison, R.C. Phillips and J.A. Richards, J. Organometal. Chem., 114, 47, (1976).

14. B.F.E. Ford and J.R. Sams, J. Organometal. Chem., 21, 345, (1970).

15. J.J. Zuckerman, Adv. Organometal. Chem., 9, 22, (1970).

16. G. Farrow and A.P. Dawson, Eur. J. Biochem., 86, 85, (1978).