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Correlation of Coordination Geometries and Stability Factors in Organotin(IV) Derivatives of 4-Acylpyrazol-5-onates with their Fungicidal (Mycelial Control) and Insecticidal (Topical Toxicity, Larvicidal and Ovicidal) Activities

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The fungicidal and insecticidal activities of the 4-acetyl (HPMAP) and 4-benzoyl (HPMBP) derivatives of 3-methyl-l-phenylpyrazol-5-one and their complexes with diorganotins [$Bu_2Sn(PMAP)_2$, $Bu_2Sn(PMBP)_2$, $Ph_2Sn(PMAP)_2$ and $Ph_2Sn(PMBP)_2$] and triorganotins [$Bu_3SnPMAP$, $Ph_3SnPMAP$, $Bu_3Sn(PMBP)(H_2O)$ and $Ph_3SnPMBP$] have been determined and their ED_{50} (fungicidal activity) and LC_{50} (insecticidal activity) values are reported. An attempt has been made to correlate the type of coordination geometry around the tin atom [based on published ^{119}Sn NMR and ^{119}Sn Mössbauer data as well as on the crystal structures of $Bu_2Sn(PMBP)_2$ and $Bu_3Sn(PMBP)(H_2O)$] and the relative stabilities with the observed bioactivities in these compounds. The diorganotin complexes are more effective than the triorganotins as insecticides. The effect of disproportionation of R_3SnL to give R_4Sn and R_2SnL_2 is discussed with respect to insecticidal activity. The stability constants of the diorganotin compounds are reported, and they suggest that these compounds are sufficiently stable to prevent appreciable ligand exchange before their assimilation into the living tissues of the insects. © 1997 by John Wiley & Sons, Ltd.

Keywords: geometry; relative stability; organotin(IV) derivatives; 4-acylpyrazol-5-onates; fungicidal; insecticidal

INTRODUCTION

A possible dependence of bioactivity of triorganotin(IV) compounds on the geometry around tin has continued to attract the attention of many researchers.[1,2] For example, Blunden an Hill have shown that intramolecularly chelated five-coordinate R_3SnL (L = X—X′) compounds (Fig. 1) were less bioactive than the intermolecularly associated polymer (Fig. 2).[1] Also, biological activity in triorganotin(IV) compounds is reportedly higher in tetrahedral monomers of the type R_3SnX than in five-coordinate trigonal-bipyramidal *cis*-R_3SnX_2 compounds.[2]

The nature of the ligand in triorganotin(IV) derivatives of the type R_3SnX or R_3SnX_2 have, so far, been reported to have relatively very little influence on the observed bioactivity.[3,4] However, some recent studies have considered a possible contribution of the ligands (especially those that are bioactive) in the observed bio-

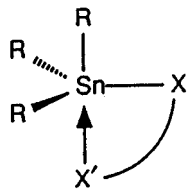

Figure 1 Five-coordinate R_3SnL compounds.

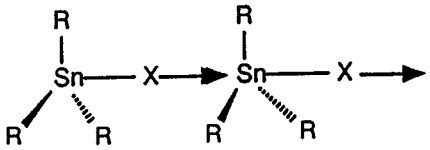

Figure 2 Intermolecularly associated and polymeric five-coordinate R_3SnX compounds.

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activity of the triorganotin(IV) derivatives.[3–5] In this regard, there is as yet limited interest in the bioactivity of organotin(IV) derivatives of β-diketonates.[5]

The 4-acylpyrazol-5-onates have been described as sophisticated examples of β-diketonates, and their potential bioactivities have been reported in many publications in the last decade.[5–9] Dibutylbis(4-benzoylpyrazol-5-onato) tin(IV) has also been reported to show some insecticidal activity against *Tribolium castaneum* (Herbst) and *Trogoderma granarium* (Everts) (both grain pests).[5] The molecular structures of many more diorganotin(IV) derivatives of the same ligand have been published recently.[10–12] We have also described the molecular structure of the first triorganotin(IV) derivative elsewhere.[13]

Hence, this study was commenced to investigate the possible fungicidal and insecticidal activities of 4-acetyl- (HPMAP) and 4-benzoyl-3-methyl-1-phenylpyrazol-5-ones (HPMBP) and their di- and tri-organotin(IV) derivatives, and to correlate any possible role of the coordination environment around tin, as well as stability factors, with the observed bioactivities.

RESULTS AND DISCUSSION

The syntheses and structural characterizations of the 4-acylpyrazol-5-ones [HPMAP and HPMBP (see Fig. 3)] and their organotin(IV) derivatives have been reported elsewhere.[10–12] The fungicidal and insecticidal activities of these compounds have been determined according to standard procedures in the literature, as described in the Experimental section.[4, 14]

Fungicidal activities

The fungicidal tests were designed to determine the concentrations (ppm) causing 50% inhibition (ED_{50}) of the lateral mycelial growth of the six fungi chosen: *Trichoderma viridae* (soil fungus), *Colletotrichum gloeospoioides* (banana fungus), *Verticillium fungicola* (dry bubble disease in mushrooms), *Pyricularia oryzae* rice blast disease), *Sclerotinia fruticola* (apricots) and *Fusarium culmorum* (cereal crops pathogen). The processed data for the relationship between the percentage inhibition of the fungi and concentration (ppm) of the test compounds are summarized in Table 1.

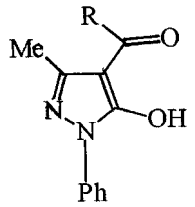

Figure 3 The 4-acyl-3-methyl-1-phenylpyrazol-5-ones [R = Me (HPMAP) or R = Ph (HPMBP)].

The 4-acylpyrazol-5-ones (HPMAP and HPMBP) in Fig. 3 show fungitoxicity against these species between 17.5 and 42.5 ppm. The organotin precursors for the new compounds were fungicidal at concentrations between 8 and 20 ppm (Bu_3SnOMe and Ph_3SnOEt) and 15 and 28 ppm (Bu_2SnCl_2 and Ph_2SnCl_2). They are generally less effective than the new organotin derivatives. The results show that *V.* fungicola and *C. gloeospoioides* show greater sensitivity to the *cis*-R_3SnL compounds (ED_{50} values in the ranges 0.5–1.0 and 2–5 ppm, respectively, compared with 10 ppm in *trans*-Bu_3SnLL' and 20–45 ppm in six-coordinated R_2SnL_2 compounds) (see Table 1). The level of control in the *cis*-R_3SnL compounds is comparable with those of Ph_3SnCl and Ph_3SnOAc (currently in some formulations of fungicides in the mushroom and banana industry).[15, 16] The *cis*-R_3SnL compounds also show strong fungicidal activity against *F. culmorum* and *P. oryzae*.

The triorganotin(IV) derivatives were more fungicidal than the diorganotin(IV) analogues under the same conditions. The general trend of observed fungitoxicity in the test compounds is summarized as

$$L < R_2SnL_2 < \textit{trans}\text{-}R_3SnLL' < \textit{cis}\text{-}R_3SnL$$

There have been only very few reports on the possible dependence of fungicidal activity on the geometry around tin.[1, 2] According to previous comparisons, compounds of the type Ph_3SnL, e.g. Ph_3SnSAL (SAL = salicylaldehyde) (*cis* five-coordinate chelate in the solid state), Ph_3SnPTA and Ph_3SnIMI (PTA = phthalic acid, IMI = imidazole derivative) (both *trans* trigonal-bipyramidal five-coordinate and polymeric in the solid state but break down to give four-coordinate species in solution) have been reported to demonstrate similarly high activities displayed by some four-coordinate monomers {$Ph_3SnMTC(pip)$ and $Ph_3SnDTC(pip)$[MTC(pip) = piperidyl monodithiocarbamate and DTC(pip) = piperidyl-

Table 1 Comparison of ED_{50} values for six fungal species of two 4-acylpyrazol-5-ones, their di- and tri-organotin(IV) derivatives[a]

	ED_{50} (ppm)							
Fungus	HPMBP	$Ph_3SnPMBP$	$Bu_3Sn(PMBP)(H_2O)$	$Ph_2Sn(PMBP)_2$	$Bu_2Sn(PMBP)_2$	Ph_3SnOAc	Ph_3SnOMe	Bu_3SnOEt
V. fungicola	42.5	0.5	10.0	25.0	20.0	0.5	13.0	9.0
P. oryzae	30.0	3.0	15.0	25.0	37.5	0.1	18.0	10.0
C. gloeospoioides	25.0	2.0	12.0	25.0	25.5	1.5	10.0	8.0
F. culmorum	25.0	0.5	20.0	35.0	38.5	1.0	20.0	16.0
T. viridae	35.0	1.0	25.0	37.5	38.5	5.0	8.0	10.0
S. fruticola	17.5	5.0	18.0	45.0	45.0	0.1	11.0	9.0
	HPMAP	$Ph_3SnPMAP$	$Bu_3Sn(PMAP)$	$Ph_2Sn(PMAP)_2$	$Bu_2Sn(PMAP)_2$	Ph_3SnCl	Ph_2SnCl_2[b]	Bu_2SnCl_2[b]
V. fungicola	38.0	0.5	0.1	30.0	45.0	0.1	25.0	15.0
P. oryzae	35.0	1.0	3.0	25.0	30.0	0.5	28.5	20.0
C. gloeospoioides	30.0	3.5	5.0	40.0	25.0	0.5	15.0	16.0
F. culmorum	42.0	2.0	2.0	20.0	30.0	0.5	24.0	18.0
T. viridae	24.5	20.0	15.0	20.0	45.0	10.0	20.5	20.0
S. fruticola	26.5	2.0	6.0	40.0	25.0	2.0	18.0	16.5

[a] See Experimental section for details of definition of ED_{50} (ppm) and the test methods involved.
[b] Compounds R_2SnCl_2 were used because they were starting materials for making the new diorganotin derivatives of 4-acylpyrazol-5-ones (see Ref. 10).

dithiocarbamate]}.[2] Crystal structure and ^{119}Sn Mössbauer spectral results have confirmed *trans* ligand coordination in hte trigonal-bipyramidal structure of $Bu_3Sn(PMBP)(H_20)$[13] and a distorted octahedral structure of $Me_2Sn(PMBP)_2$ and $Bu_2Sn(PMBP)_2$ in the solid state, and are retained in solution as confirmed by their ^{119}Sn NMR spectral data (see Table 2).[10–12] Five-coordinate *cis* chelate geometry has been proposed for R_3SnL (R = Bu or Ph, L = PMAP and R = Ph, L = PMBP) on the basis of their ^{119}Sn NMR and Mössbauer spectral data (Figs 4 and 5).

It has been suggested that the strength of inhibition of fungal growth reflects the extent of inhibition of oxidative phosphorylation.[17] Differences in fungicidal activity are thus considered to be due to differences in (i) permeability of the cell (which is in turn dependent on the effective partition coefficient of the compound between water and the cell membrane phospholipid bilayer) and also in (ii) intrinsic activity of the enzyme system.

Insecticidal activity

Results of topical, larvicidal and ovicidal bioassays of 4-acetyl- and 4-benzoyl-3-methyl-1-phenylpyrazol-5-ones (HPMAP and HPMBP, respectively) and their di- and tri-organotin(IV) derivatives against *T. castaneum* (Everts) and *T. granarium* (Herbst) are reported in Table 3.

Topical bioassay

The trimmed Spearman–Karber analysis[18] showed that the diorganotin compounds (particularly the dibutyltin derivatives) were more toxic (LC_{50} = *ca* 30 μg/insect) to adults of both *T. castaneum* and *T. granarium* than analogous triorganotins [LC_{50} = *ca* 115 μg/insect (*T. castaneum*) and *ca* 130 μg/insect (*T. granarium*)] (see Table 3). The results of tests on the organotin precursors (Bu_3SnOMe, Ph_3SnOEt, Bu_2SnCl_2 and Ph_2SnCl_2) were not unexpected. Insecticidal activity of the triorganotin alkoxides [LC_{50} = *ca* 22 μg/insect (*T. castaneum*) and *ca* 17 μg/insect (*T. granarium*)] are higher than is observed for the four new diorganotin derivatives of 4-acylpyrazol-5-ones. The new diorganotins are better topical insecticides than the diorganotin dichlorides [cf. LC_{50} = 42 μg/insect (*T. castaneum*) and *ca* 51 μg/insect (*T. granarium*)]. The 4-acylpyrazol-5-ones were found to be ineffective as topically applied insecticides against the insects. The 4-benzoylpyrazol-5-one was reported earlier to show very poor insecticidal activity (topical) against both insects in the present study.[5] However, coordination of these organic moieties to the tin centre appears to be responsible for the increased potency observed in the new diorganotin compounds (cf. activity of either of the precursors). The toxicity of commercially available pyrethrins (LC_{50} = 0.94 μg/insect) and chlorpyrifos (LC_{50} = 0.08 μg/insect) were about

Table 2 ^{119}Sn NMR and Mössbauer data of organotin(IV) derivatives of 4-acylpyrazol-5-onates

	^{119}Sn NMR			^{119}Sn Mössbauer	
Compound	δ (ppm)	$^2J(^1H–^{119}Sn)$ (Hz)	$^1J(^{13}C–^{119}Sn)$ (Hz)	i.s. (mm s^{-1})	q.s. (mm s^{-1})
$Ph_3SnPMAP$	237.7	—	—	1.14	2.53
$Bu_3SnPMAP$	102.0	—	470.0	1.18	2.49
$Ph_3SnPMBP$	207.8	—	—	1.26	2.64
$Bu_3Sn(PMBP)(H_2O)$	126.0	—	362.6	1.45	3.80
$Ph_2Sn(PMAP)_2$	483.1[b] 487.1[b]	—	—	—	—
$Bu_2Sn(PMAP)_2$	355.6[b]	125.4	844.6 892.0	—	—
$Ph_2Sn(PMBP)_2$	480.9[b] 486.0[b] 486.0[b] 500–503[b]	—	—	—	—
$Bu_2Sn(PMBP)_2$	355.0[b]	124.9	831.4	—	—

[a] Intermolecularly associated in the crystal structure (see Ref. 13).
[b] References 10–12.

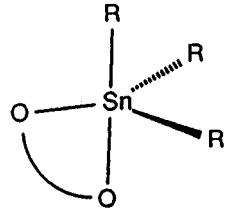

Figure 4 *cis*-R_3SnL coordination in the triorganotin(IV) pyrazol-5-onates ($Ph_3SnPMAP$, $Bu_3SnPMAP$ and $Ph_3SnPMBP$).

6 and 60 times, respectively, greater than the average of *ca* 30 μg/insect observed in the new diorganotin derivatives (see Table 3).

Larvicidal bioassay

The diorganotin derivatives were more toxic (LC_{50} = 12–38 μg g^{-1} in soil) to the larvae of both *T. castaneum* and *T. granarium* than the triorganotin analogues [LC_{50} = 59–69 μg g^{-1} in soil (*T. castaneum*) and 47–102 μg g^{-1} in soil (*T. granarium*)] (see Table 3). The 4-acylpyrazol-5-ones were inactive against the two insect species. The triorganotin alkoxide precursors again showed higher larvicidal activity [LC_{50} = *ca* 14 μg g^{-1} in soil (*T. castaneum*) and *ca* 11 μg g^{-1} in soil (*T. granarium*)] than the new diorganotin compounds. The trend that coordination of the 4-acylpyrazol-5-ones enhances insecticidal activity is also established in the results of larvicidal tests. The diorganotin dichloride precursors (for synthesis of the new diorganotin compounds) showed larvicidal activity at *ca* 32 μg g^{-1} in soil (*T. castaneum*) and *ca* 44 μg g^{-1} in soil (*T. granarium*) (see Table 3). The standard, chlorpyrifos, was about 10 times more toxic (LC_{50} = 1.4 μg g^{-1} in soil) than $Bu_2Sn(PMAP)_2$, which is the most effective organotin larvicide [LC_{50} = 14 μg g^{-1} in soil (*T. castaneum*)] and 12 times more than $Bu_2Sn(PMBP)_2$, which is most toxic against larvae of *T. granarium*.

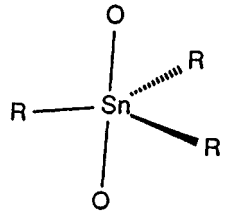

Figure 5 *trans*-R_3SnLL' coordinaton in $Bu_3Sn(PMBP)(H_2O)$.

Ovicidal bioassay

The triorganotin derivatives demonstrate ovicidal activity [percentage inhibition of egg hatch = *ca* 64–78 (*T. castaneum*) and 48–88 (*T. granarium*)], and also those of the diorganotin analogues [percentage inhibition = 77–79 (*T. castaneum*) and 92–100 (*T. granarium*)] (see Table 3). The trends in relative topical toxicity levels and larvicidal activity among the organotin compounds are also observed here. The diorganotin dichloride precursors demonstrate weaker ovicidal activity [percentage inhibition = *ca* 93 (*T. castaneum*) and 97 (*T. granarium*)] among the organotins tested. The free 4-acylpyrazol-5-ones deomonstrated limited ovicidal activity [percentage inhibition = *ca* 15 (*T. castaneum*) and 25 (*T. granarium*) against eggs of the two species at the test medium concentration of 833 μg g^{-1}.

Evaluation of the toxicity data reveals that the new diorganotin derivatives were generally better insecticides than their triorganotin analogues, as either topical biocides, larvicides or as ovicides. The 4-acylpyrazol-5-ones (HPMAP and HPMBP) are poor insecticides in the concentration ranges tested (0–50 ppm), showing slight activity against the eggs and none against the larvae and the adults. This appears to suggest possible correlation between the dosage and size (of insect) in the observed bioactivity. There is only a small difference in the level of susceptibility of the two insect species to the test compound, indicating that the mode of action is probably similar in the two insects. The present results do not show significant differences in the insecticidal activities of *cis*-R_3SnL chelates and *trans*-$Bu_3Sn(PMBP)(H_2O)$. Bioactivity in organotin compounds is reported to increase with the number of organic substituents (peaking at the triorganotins).[19] Earlier literature reports show that attempts to prepare simple triorganotin derivatives of the 4-acylpyrazol-5-ones from R_3SnCl (R = Ph, Bu or Me) yielded only the diorganotin products.[10, 11] We also reported our attempt to crystallize triphenyl(4-acetylpyrazol-5-onato)tin(IV) ($Ph_3SnPMAP$) from dilute toluene solution, which led to production of crystals of Ph_4Sn [and residues of $Ph_2Sn(PMAP)_2$] after a few days in solution.[13] This fact has been attributed to the result of the disproportionation of Eq. [1], which probably proceeds slowly in some solvents,[10, 13]

$$R_3SnL \xrightarrow[(L = HPMAP \text{ or } HPMBP)]{} R_4Sn + R_2SnL_2 \qquad [1]$$

Table 3 Insecticidal (topical, larvicidal and ovicidal) activity of 4-acylpyrazol-5-ones and their di- and tri-organotin(IV) derivatives

	Insecticidal activity													
	Topical						Larvicidal						Ovicidal[c]	
	T. castaneum			*T. granarium*			*T. castaneum*			*T. granarium*			*T. castaneum*	
Compound	LC_{50} (μg/fly)	Cl[a]	N[b]	LC_{50} (μg/fly)	Cl[a]	N[b]	LC_{50} (μg g^{-1} in soil)	Cl[a]	N[b]	LC_{50} (μg g^{-1} in soil)	Cl[a]	N[b]	Inhibition (% of egg hatch)	N[b]
HPMAP	—	—	120	—	—	120	—	—	120	—	—	120	5	200
HPMBP	—	—	120	—	—	120	—	—	120	—	—	120	25	200
$Ph_3SnPMAP$	120	115–125	120	156	150–159	120	71.5	65–75	120	60	55–65	120	78	200
$Bu_3SnPMAP$	115	111–119	120	130	125–135	120	81.4	75–84	120	97	93–105	120	64	200
$Ph_3SnPMBP$	135	130–142	120	108	103–112	120	59	64–74	120	102	97–106	120	68	200
$Bu_3Sn(PMBP)(H_2O)$	110	106–114	120	162	156–166	120	89.8	85–94	120	46.5	41–50	120	70	200
$Ph_2Sn(PMAP)_2$	35	30–39	120	35	30–38	120	24	20–30	120	36	31–40	120	87	200
$Bu_2Sn(PMAP)_2$	28	24–34	120	20	15–26	120	14	10–20	120	22	18–28	120	97	200
$Ph_2Sn(PMBP)_2$	32	26–38	120	45	40–50	120	28.6	22–34	120	18	14–22	120	77	200
$Bu_2Sn(PMBP)_2$	25	22–30	120	38	35–45	120	16.5	11–19	120	12	8–18	120	92	200
Bu_2SnCl_2[d]	40	36–45	120	48.5	43–52	120	28	24–36	120	39.5	35–45	120	92	200
Ph_2SnCl_2[d]	45.5	41–49	120	56	50–59	120	34	28–38	120	48	44–54	120	88	200
Bu_3SnOMe[d]	21	16–25	120	15.5	11–19	120	10	6–14	120	8.5	3–14	120	96	200
Ph_3SnOEt[d]	23.5	18–30	120	21.5	16–26	120	16	11–19	120	13	7–17	120	90	200
Chlorpyrifos(Std)	0.08	0.02–0.2	120	0.08	0.06–0.4	120	1.2	0.5–1.5	120	1.2	0.8–1.8	120	—	—
20% Pyrethrins(Std)[e]	0.94	0.6–1.5	120	0.94	0.6–1.9	120	—	—	—	—	—	—	100	200

[a] 95% confidence interval (Cl), not adjusted for multiple interferences. Activity is considered significantly different when the 95% Cls fail to ove
[b] Number of insects tested.
[c] 833 μg g^{-1} of test compound in solution was used for all ovicidal tests.
[d] These R_2SnCl_2 and R_3SnOR compounds are used because they were the precursors for making the new organotin derivatives of 4-acylpyrazol-5
and 11).
[e] Adjusted for 20% (AI).

Thus, it would appear that the new triorganotin complexes are not very stable in solution on long standing. The preference for coordination of a molecule of water in $Bu_3Sn(PMBP)(H_2O)$ (instead of coordination of the second oxygen atom of the 4-acylpyrazol-5-onate) could suggest that the triorganotin ions form stronger bonds with water, and thus are very susceptible to hydrolysis.[13] We propose that substantially similar disproportionation of the triorganotin derivatives takes place, and so it is essentially the residual diorganotin analogues that are actually responsible for the observed bioactivity. The diorganotins have previously been reported to be very stable.[10, 11] The higher insecticidal activity of the R_2SnL_2 complexes (cf. R_3SnL complexes) is probably a result of the difference in the amount of the diorganotin product retained in solution, at the point of assimilation into the insects. This is also supported by the relatively higher activity of the triorganotin alkoxides (cf. the insecticidal action of the R_2SnL_2 compounds) (see Table 3).

We have also determined the stability constants and the rates of dissociation of the R_2Sn^{2+} derivatives of 4-acylpyrazol-5-onates. Although the stability constant for $Me_2Sn(acac)$ (acac = acetylacetonate ion) was reported earlier in the literature, we are not aware of any previous kinetic studies of the organotin derivatives of 4-acylpyrazol-5-onates (which have been described elsewhere as sophisticated analogues of acetylacetonate).[6, 20] When a dioxane solution of the diorganotin ion, R_2Sn^{2+} (R = Me, Bu, Ph), is added to $PMAP^-$ or $PMBP^-$, the reaction product is yellow or brown, and the colour is retained for at least 24 h.[10–12] From the spectra of solutions containing a large excess of the organometallic ion, the maximum wavelengths and the corresponding molar extinction coefficients were obtained (see Table 4). The values were useful in the spectrophotometric determination of the stability constants. The complex formation reaction was considered to be as represented in Eqn [2].

$$R_2Sn^{2+} + 2HL \rightarrow R_2SnL_2 + 2H^+ \qquad [2]$$

Unlike acetylacetone, which is a weak acid and so is unable to prevent appreciable hydroxo complex formation, the 4-acylpyrazol-5-ones were found to form very strong chelate bonds with R_2Sn^{2+}, in agreement with earlier reports.[10–12] They displaced water in some of their complexes with transition metals.[20–22] The acid dissociation constants of HPMAP and HPMBP were determined for the 0.1 M ClO_4^- medium by amperometric measurements following the procedure of Yasuda and Tobias.[23] The values were $K_{HPMAP} = -4.3$ and $K_{HPMBP} = -5.1$. The value for K_{Hacac} was given earlier as -8.65.[23] A summary of the chelate formation constants of HPMAP and HPMBP determined spectrophotometrically at 25 °C in aqueous 20% (v/v) dioxane is reported in Table 5. The stability constants are much higher than was observed for $Me_2Sn(acac)$. The strength of the bonds formed, as supported by their formation constants (see Table 5), leads us to suggest that the diorganotin(IV) derivatives are sufficiently stable to prevent appreciable ligand exchange (especially hydrolysis) before assimilation of the molecules of these compounds into the living tissues, in the presence of functional groups on the enzymes in the biochemical system. The data in Table 5 suggest that stability of the R_2Sn^{2+} compounds decreases in the order Ph > Bu > Me. A similar trend has been observed elsewhere, and is justified on the basis of an increase in the length of the R-groups attached to tin.[23]

Table 4 Absorption data of 4-acyl-3-methyl-1-phenyl-pyrazol-5-onate (HPMAP and HPMBP) chelates in aquoeus 20% dioxane

Compound	λ_{max} (nm)	ε ($\times 10^3$)
HPMAP		
Me_2Sn^{2+}	553.0	29.3
Bu_2Sn^{2+}	558.0	31.2
Ph_2Sn^{2+}	566.0	30.8
HPMBP		
Me_2Sn^{2+}	566.0	30.6
Bu_2Sn^{2+}	560.0	32.2
Ph_2Sn^{2+}	569.0	31.4

EXPERIMENTAL

Chemicals

Triphenyltin(IV) chloride, triphenyltin(IV) acetate, triphenyltin(IV) ethoxide, tributyltin(IV) methoxide, diphenyltin(IV) dichloride, dibutyltin(IV) dichloride, chlorpyrifos, certified acetone, 20% pyrethrins and potato dextrose agar (PDA) were obtained commercially and used without further purification. The 4-acetyl- and

Table 5 Chelate formation constants of HPMAP and HPMBP determined spectrophotometrically at 25 °C in aqueous 20% dioxane

Compound	No. of protons released on complex formation	R_2Sn^{2+}: ligand ratio in the complex	K	log K_f
HPMAP				
Me_2Sn^{2+}	2.0	1:2	8.2	12.75
Bu_2Sn^{2+}	2.0	1:2	187.0	13.33
Ph_2Sn^{2+}	2.0	1:2	375.0	14.35
HPMBP				
Me_2Sn^{2+}	2.0	1:2	11.0	12.54
Bu_2Sn^{2+}	2.0	1:2	155.0	13.98
Ph_2Sn^{2+}	2.0	1:2	352.0	14.67
acac				
Me_2Sn^{2+} [a]	2.0	1:1	6.6	—

[a] See Ref. 23.

4-benzoyl-3-methyl-1-phenylpyrazol-5-ones (HPMAP and HPMBP, respectively) were isolated according to the procedure of Okafor.[21, 22] The diorganotin(IV) derivatives were synthesized according to published procedures,[10–12] and characterized by their analytical data and their melting points. The syntheses and structural characterization of the triorganotin(IV) derivatives is described elsewhere.[13]

Physical measurements

A Pye–Unicam spectrophotometer (Model SP8-150), a Cary spectrophotometer (Model 11) and a Radiometer pHM84 research pH-meter equipped with a combined electrode (Model GKC 2401) were used in the spectrophotometric determinations. Amperometric titrations were performed using a dropping electrode as the cathode and a saturated calomel electrode as anode.

In the experiments for measurement of the kinetic parameters, commercial-grade dioxane was dried using benzophenone and distilled under a nitrogen atmosphere. Dioxane perchlorate solutions were prepared by dissolving weighed amounts of R_2SnO in excess of standard perchloric acid. The dialkyltin content of the solutions was determined by amperometric titration with 8-hydroxyquinoline (R = Me, Bu, Ph).[23, 24] In order to calculate the constants K for reaction [2], known amounts of R_2Sn^{2+}, of HPMAP (or HPMBP) solution in dioxane and of standard perchloric acid were introduced into 25-ml volumetric flasks, and the solutions were diluted with sodium perchlorate solution and dioxane so that 20% (v/v) dioxane would be present and the ionic strength would be equal to 0.1 M ClO_4^-. The R_2Sn^{2+} ions yield precipitates with potassium ferrocyanide in the amperometric titrations. The general calculations have employed the methods described by earlier workers.[23, 24]

Fungicidal activity assay

The fungitoxicity of the test compoinds were determined according to previously published procedures.[4]

The test compounds were made into appropriate solutions in acetone for all the fungicide tests, since most of the organotin derivatives are insoluble in water: 15 mg of each test compound was added to 10 ml of certified acetone to make a stock solution. Appropriate dilutions were then made to give final concentrations of 0, 0.1, 0.5, 1.0, 1.5, 2.0, 5.0, 10.0, 30.0, and 50.0 ppm in PDA contained in Petri dishes. Five concentrations in the ppm range (based on results of range-finding experiments) were replicated three times for the final testings.

A 5 mm diameter inoculum disc from an eight-day culture of each fungal isolate was placed in the centre of each of the three replicates, for each fungicide concentration. Colony size across two diameters was measured for each plate after two days (for fast-growing fungi) or eight days of incubation at 24 °C.

ED_{50} values (concentration of the fungicide required to reduce radial growth of mycelium to 50% of the control) were calculated, in order to assess the toxicity of the various compounds

compared with two commercial fungicides (Ph_3SnOAc and Ph_3SnCl) and with an acetone control.

Insecticidal bioassay

Topical activity assay
Acure toxicity was examined with *T. granarium* (Everts) and *T. castaneum* (Herbst) (10 days after eclosion, susceptible strain).

A micropipette was used to deliver 1 μl of acetone solution of the test compound to the *pronata* of the insects. Initial studies were conducted (between 0 and 50 ppm) to determine appropriate ranges of testing concentrations. Technical-grade chlorpyrifos and 20% pyrethrins served as the standards for comparison, as they are well-known spotting insecticides. Certified acetone was used as the control treatment.

A minimum of four concentrations (μg/insect; based on results of range-finding experiments) were replicated three times (10 insects per replication) for the final testings. Mortality was assessed 24 h after treatment. The trimmed Spearman–Karber method[18] was used to estimate LC_{50} values.

Larvicidal activity assay
A concentrated stock solution was made for the test compound in acetone. Appropriate amounts of the stock solution were added to 1 ml of acetone and 12 ml of distilled water. Preliminary studies were conducted (200–1000 mg g^{-1} of soil) to determine the appropriate concentration range to select for the tests.

The mixture [test compound, acetone, distilled water (treatment); chlorpyrifos, acetone, distilled water (standard); aor acetone and distilled water only (control)] was added to a 100 mm × 15 mm glass Petri dish containing 50 g of autoclaved, untreated, sand–clay–loam soil (*ca* 50% sand, 24% silt, 22% clay; 4% organic matter, pH = 5.7). The treated soil was mixed thoroughly, and the Petri dishes remained uncovered for 10 min to allow evaporation of acetone. The concentrations were calculated in terms of μg of the test compound per gram of soil. Ten third-instar test insects of the same species were then placed in each dish. The petri dishes were covered and put in an incubator set at 25 ± 2 °C with a photoperiod of 12:12 (light/dark, h:h). Mortality was assessed at 48 h. LC_{50} values were estimated by the trimmed Spearman–Karber method.[18]

Ovicidal activity assay
Eggs of *T. granarium* (or *T. castaneum*) were bathed in treatment medum (833 μg g^{-1} of the test compound in solvent) to determine the ovicidal properties of each compound.

A 15 mg portion of each test compound was added to 2 ml of certified acetone to make a concentrated stock solution, of which 600 μl was then added to 5.4 ml of distilled water to obtain 833 μg g^{-1} treatment solution. 1500 μl of each treatment was dispensed into a treatment jar (1.5 cm diameter, 2 cm height) containing 50 eggs (< 12 h old). The jars were agitated gently to disperse eggs throughout the treatment medium, sealed with paraffin film, and placed in an incubator (25 ± 2°C) with a photoperiod of 12:12 (light/dark, h:h) for the duration of the test. A mixture of acetone and distilled water (prepared as described earlier) was used as control, and pyrethrins; [20% (AI)] was the standard for comparison. Each test was replicated at least four times and terminated when the control eggs had hatched. The numbr of hatched larvae and the total number of eggs were counted. Percentage inhibition of hatch was determined using the formula given by Sharma and Saxena,[25]

$$\text{Percentage inhibition of egg hatching} = \frac{100(X - Y)}{X}$$

where X = control percentage hatch, and Y = treated percentage hatch.

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