Distannoxane speciation during esterification catalysis: revealing insights provided by electrospray ionization mass spectrometry†

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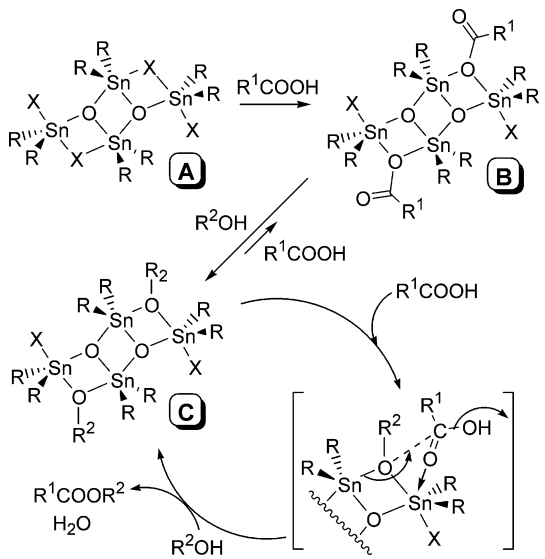
Dimeric tetraalkyldistannoxanes are have been reported to catalyze esterification reactions, but are difficult to investigate in detail due to the lack of suitable spectroscopic handles. Electrospray ionization mass spectrometry (ESI-MS), in conjunction with a tethered charge on a tin atom, reveals that immediate decomposition to mono-tin carboxylate compounds occurs in the presence of carboxylic acid.

Tetraalkyldistannoxanes have an unusual, ladder-like dimeric structure[1] and are effective catalysts for a variety of functional group transformations of carbonyl compounds.[2] Most interestingly, they have been reported to catalyze both *esterification* ($R^1COOH + R^2OH \rightarrow R^1COOR^2 + H_2O$)[3] and *transesterification* ($R^1COOR^2 + R^3OH \rightarrow R^1COOR^3 + R^2OH$) reactions,[4] making them potentially useful in the production of biodiesel from waste oil (which is often contaminated with free fatty acids). A major impediment to the further development of these catalysts is a lack of understanding of the mechanism by which they operate or what the active species is, partly due to a lack of informative structural probes. NMR has been frequently employed but provides limited information: ^{1}H and ^{13}C NMR probe only the uninformative alkyl groups, and while ^{119}Sn NMR can reveal the number of tin environments, mixtures lead to very complex spectra.[5] Product distributions are often the only mechanistic information gleaned.[6]

Distannoxane-catalyzed (trans)esterification has been studied in detail, including systems that include fluorous "ponytails" to enable catalysis in a biphasic context.[7] The only mechanism proposed to date for esterification involves first formation of a carboxydistannoxane, followed by ligand exchange to produce an alkoxydistannoxane that is thought to coordinate the carbonyl oxygen of the acid *via* a peripheral tin atom, thus promoting nucleophilic attack on the carbonyl carbon by the alkoxy group (Scheme 1).[8]

Electrospray ionization mass spectrometry (ESI-MS)[9] is capable of detecting organometallic catalysts at very low concentrations, in complicated mixtures, under anaerobic conditions and in a wide range of solvents.[10] These abilities make it well-placed to provide insight into distannoxane-catalyzed reactions. ESI-MS has been used to investigate a methanol/water solution of $(Cl^tBu_2SnOSnMe_2Cl)_2$,[11] but no distannoxane species were observed, certainly due to the fact that they are neutral and hence invisible in ESI-MS, which detects only charged species.



Scheme 1 Esterification mechanism (adapted from ref. 8).

An acetonitrile solution of $SnCl_2(CH_2SiMe_3)_2$ revealed a variety of di-, tri- and tetratin compounds detectable as $[M+X]^-$ (X = Cl or OH) anions in the negative ion mode.[12] Neither of these studies examined catalysis *in situ*.

Distannoxanes are conveniently prepared by combining R_2SnO and R_2SnX_2,[13] and we have designed a synthetic route to a mixture of $[SnBrX(C_4H_8Br)(C_4H_8NC_5H_5)]^+$ Br^- (**1a**, X = Cl; **1b** X = Br), thus solving the ESI-MS ionization problem by introducing an inherently charged pyridinium group (see supplementary information†). The mixture of bromo and chloro compounds results from a comproportionation of SnR_4 + $SnCl_4$ to make SnR_2Cl_2, followed by treatment with HBr that replaces most but not all of the Cl with Br. The comproportionation with $SnBr_4$, which would have alleviated the slight complication arising from the mixture of **1a** and **1b**, did not proceed in satisfactory yield. Reaction of **1a+b** with Bu_2SnO in acetonitrile provides a dimeric distannoxane with one tin atom having a charge appended, *mono*cationic $[Sn_4O_2Br_nCl_{(4-n)}Bu_6(C_4H_8Br)(C_4H_8NC_5H_5)]^+$ ($n = 0$, 1, 2), (Fig. 1).

The other species detected in solution were primarily starting materials, suggesting that the relatively coordinating solvent partially suppresses distannoxane formation. The X_4 distannoxane corresponds to compound **A** in Scheme 1.

The reaction of **1a+b** and Bu_2SnO in methanol proceeds slightly differently (Fig. 2), due to the involvement of the solvent. In addition to compounds where X = Cl and Br, X = OH and OMe are also observed, lending an extra level of complexity to the interpretation of the spectra.

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† Electronic supplementary information (ESI) available: Experimental preparations; ^{1}H and ^{13}C NMR data; additional ESI-MS(/MS); catalytic data. See DOI: 10.1039/b913492a

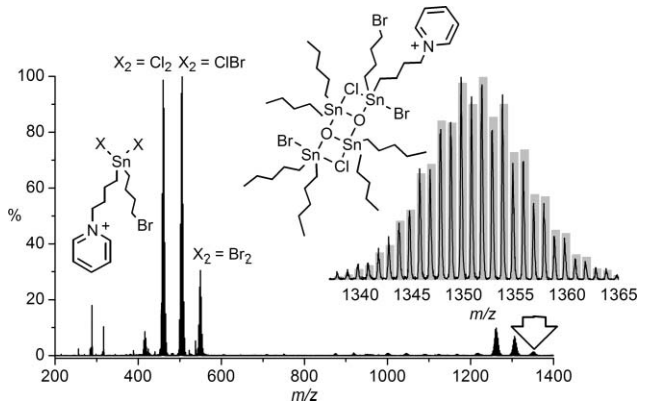

Fig. 1 Positive-ion ESI-MS of **1a+b** + Bu_2SnO in acetonitrile. Inset shows calculated and experimental (line) isotope patterns for the cationic distannoxane $[Sn_4O_2Cl_2Br_2Bu_6(C_4H_8Br)(C_4H_8NC_5H_5)]^+$.

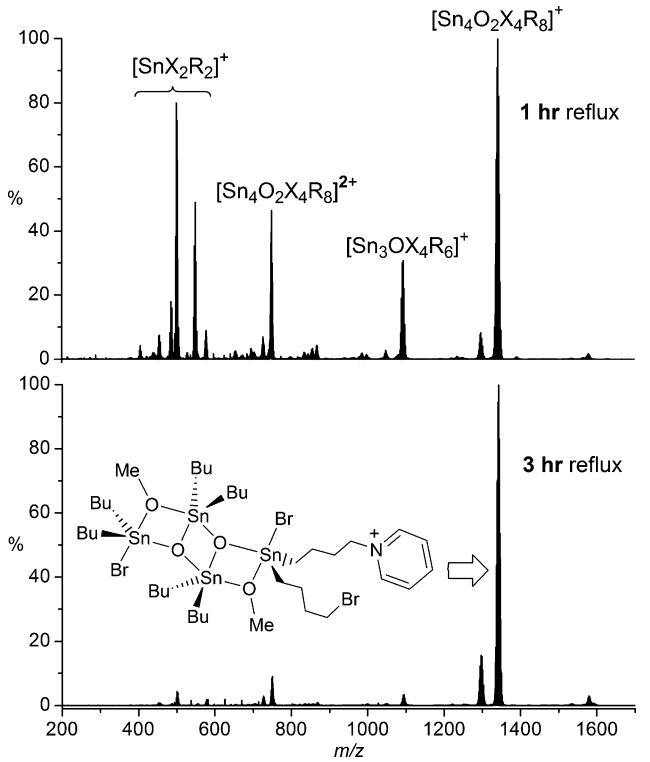

Fig. 2 Positive-ion ESI-MS of the product mixture from reaction of **1a+b** with Bu_2SnO in methanol, after reflux for 1 hour (top) and 3 hours (bottom). X = Cl, Br, OH or OMe; R = Bu, C_4H_8Br or $C_4H_8NC_5H_5^+$. One possible isomer only is shown.

Despite the combinatorial possibilities, remarkably few of these manifest themselves, and after three hours of reflux, the spectrum is dominated by just one species, the dimeric distannoxane $[Sn_4O_2(OMe)_2Br_2Bu_6(C_4H_8Br)(C_4H_8NC_5H_5)]^+$. This distannoxane species is precisely analogous to that implicated in Scheme 1 as the active catalyst, **C**. Initially, the reaction mixture contains only the monotin species $[SnX_2(C_4H_8Br)(C_4H_8NC_5H_5)]^+$ (X = Br, Cl, OMe), but higher nuclearity species rapidly appear including the dicationic distannoxane $[Sn_4O_2(OMe)_2Br_2Bu_4(C_4H_8Br)_2(C_4H_8NC_5H_5)_2]^{2+}$ and $[Sn_3O(OMe)_2Br_2Bu_4(C_4H_8Br)(C_4H_8NC_5H_5)]^+$, which probably has a $\frac{3}{4}$-ladder structure. These other species disappear almost completely after three hours, and the distannoxane was isolated as a white solid. Regardless of solvent, ligand redistribution clearly occurs between X and O, a process known to be facilitated by the presence of halide (present here as the counterion).[14] The reason why the monocationic distannoxane dominates over the dicationic distannoxane in the spectra is presumably due to the greater insolubility of $[SnO(C_4H_8Br)(C_4H_8NC_5H_5)]^+$ Br^- compared to $SnOBu_2$, and it is probable that some neutral distannoxane $Sn_4O_2X_4Bu_8$ is also forming in the reaction.

The stability of the distannoxane in methanol solution and its correspondence to the putative active species **C** was very encouraging, and we expected that addition of carboxylic acid would produce a charged distannoxane with a structure equivalent to **B**. Accordingly, addition of 0.05 mol% of the isolated distannoxane to CH_3OH and CH_3COOH resulted in esterification at reflux temperature, with formation of CH_3COOCH_3 (by ^1H NMR). The reaction proceeded at essentially the same rate as the neutral distannoxane $Sn_4O_2Cl_4Bu_8$, confirming that the remote charged group was not affecting the reactivity. Monitoring of the same solution by ESI-MS also revealed instant reactivity, but not to any species analogous to **B**; instead, all peaks at high *m/z* disappeared, including the distannoxane, and a range of low molecular weight species readily identifiable by *m/z* and isotope pattern as $[SnX(OAc)(C_4H_8Br)(C_4H_8NC_5H_5)]^+$ (X = Cl, OAc, Br) formed (Fig. 3).

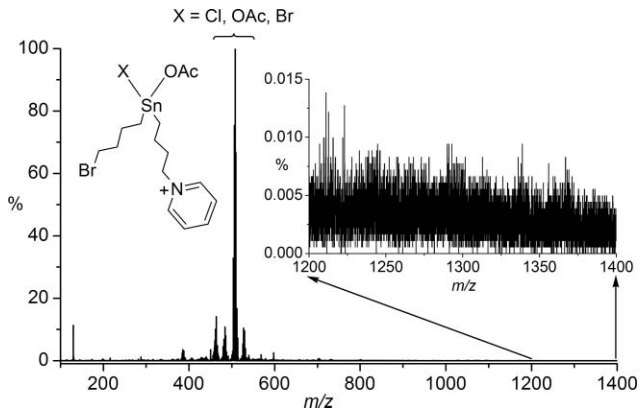

Fig. 3 Positive-ion ESI-MS of the reaction mixture of **1a+b** and Bu_2SnO (see Fig. 2), methanol and acetic acid. Inset shows the absence of higher mass species in the presence of carboxylic acid.

Regardless of temperature, time of reaction and ratio of methanol to acetic acid, the monotin species remained the only significant tin-containing ions present. This result suggested that if the distannoxane is unstable in the presence of an excess of carboxylic acid, perhaps a monotin precursor alone is capable of catalyzing the esterification. The reaction was repeated with 0.05 mol% **1a+b**, and found to proceed slightly faster than the "distannoxane-catalyzed" reaction (41% after 2 hours compared to 29%), and the ESI-MS spectrum was identical to that seen in Fig. 3. The reaction was repeated with HCOOH and CH_3CH_2COOH and analogous results were obtained, *i.e.* the three acids provided $[SnX(OOCR)(C_4H_8Br)(C_4H_8NC_5H_5)]^+$ (X = Cl, OOCR, Br; R = H, Me, Et) species only.

Examination of the high mass region of the spectrum reveals that no distannoxane species survive in the presence of the

Table 1 Completion of the $CH_3OH + CH_3COOH \rightarrow CH_3COOCH_3 + H_2O$ reaction after 2 hours at reflux

Catalyst	Conc. (mol%)	% ester after 2 hours	% ester after 4 hours
None	0	25%	35%
$Sn_4O_2Cl_4Bu_8$	0.05	29%	41%
1a+b + Bu_2SnO	0.05	26%	38%
1a+b	0.05	41%	63%
HBr	0.1	67%	69%

carboxylic acid. Above 1200 *m/z* there is only noise; if any high mass species are present their concentrations must be less than 0.01% of the abundance of the monotin compounds (Fig. 3, inset). This observation is in stark contrast to the same material in methanol alone (Fig. 2), in which distannoxane species compose the bulk of the ions present. Note that while ESI-MS is not a quantitative technique (in the absence of careful calibration to internal standards) and even permanently charged species can differ in their response by up to a factor of 10 (due to differences in "surface activity"),[15] it should be noted that the ratio of monotin compounds: distannoxane has changed from ~1:20 to at least 10^4:1, representing a change in concentration of more than five orders of magnitude.

Formation of the monotin species (Equation 1; anion is Br^-) necessarily results in the release of HBr, and Brønsted acids readily catalyze esterification.[16]

$$[Sn_4O_2(OMe)_2Br_2Bu_6(C_4H_8Br)(C_4H_8NC_5H_5)]^+ + 4RCOOH \rightarrow [Sn(OOCR)_2(C_4H_8Br)(C_4H_8NC_5H_5)]^+ + 2SnOBu_2 + Sn(OOCR)_2Bu_2 + 2ROH + 2HBr \quad (1)$$

Accordingly, the same esterification reaction was repeated in the presence of 0.1 mol% HBr, and proceeded to 67% completion (close to the equilibrium position) after 2 h, faster than either the distannoxane (26%) or **1a+b** (41%). To control for any possible effect of the tethered charge the catalytic activity of the neutral distannoxane $Sn_4O_2Cl_4Bu_8$ was examined, and the reaction went to 29% completion. To control for the rate of the uncatalyzed reaction, the catalyst was omitted and the reaction still went to 25% completion after 2 h at reflux (see Table 1 for summary).

It has been reported that fluorous distannoxanes are not isolated in pure form after esterification reactions, but rather "a portion of the catalyst was converted into unidentifiable species, which were presumably organotin carboxylate derivatives".[7d] The recovered material exhibited similar catalytic ability to the original distannoxane. These experimental observations are in keeping with our own: the "unidentifiable species" we have shown to consist of $R_2Sn(OAc)X$ (X = Br, Cl, OAc) compounds, and its activity is little different to the uncatalyzed reaction. However, the postulated mechanism for esterification in Scheme 1 is probably unnecessary, as the results we report suggest that if distannoxanes catalyze *esterification* at all, the observed activity could be explained by the release of HX upon reaction with RCOOH.

We are currently studying the catalysis of *transesterification* by distannoxanes, and plan to exploit the ability of tethered charges to confer both amenability to analysis by ESI-MS and potential for immobilization for the purposes of biphasic catalysis.[17] Our preliminary work confirms the activity of distannoxanes in this reaction, as the charged (and neutral) distannoxanes effect the transformation but **1a+b** and HBr do not.

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Notes and references

1 A. G. Davies, *J. Chem. Res.*, 2004, 309.
2 (*a*) J. Otera and H. Nozaki, *Tetrahedron Lett.*, 1986, **27**, 5743; (*b*) J. Otera, T. Yano, A. Kawabata and H. Nozaki, *Tetrahedron Lett.*, 1986, **27**, 2383; (*c*) J. Otera, T. Mizutani and H. Nozaki, *Organometallics*, 1989, **8**, 2063.
3 H. Takahashi, T. Hayakawa and M. Ueda, *Chem. Lett.*, 2000, 684.
4 J. Otera, *Chem. Rev.*, 1993, **93**, 1449.
5 D. L. Hasha, *J. Organomet. Chem.*, 2001, **620**, 296.
6 B. Jousseaume, C. Laporte, M. C. Rascle and T. Toupance, *Chem. Commun.*, 2003, 1428.
7 (*a*) J. Otera, *Acc. Chem. Res.*, 2004, **37**, 288; (*b*) Y. Imakura, S. Nishiguchi, A. Orita and J. Otera, *Appl. Organomet. Chem.*, 2003, **17**, 795; (*c*) J. N. Xiang, A. Orita and J. Otera, *J. Organomet. Chem.*, 2002, **648**, 246; (*d*) J. N. Xiang, A. Orita and J. Otera, *Angew. Chem., Int. Ed.*, 2002, **41**, 4117.
8 J. Otera, N. Danoh and H. Nozaki, *J. Org. Chem.*, 1991, **56**, 5307.
9 W. Henderson and J. S. McIndoe, *Mass Spectrometry of Inorganic and Organometallic Compounds: Tools, Techniques, Tips*, Wiley, Chichester, 2005.
10 (*a*) P. J. Dyson and J. S. McIndoe, *Inorg. Chim. Acta*, 2003, **354**, 68; (*b*) P. J. Dyson, J. S. McIndoe and D. Zhao, *Chem. Commun.*, 2003, 508; (*c*) A. T. Lubben, J. S. McIndoe and A. S. Weller, *Organometallics*, 2008, **27**, 3303; (*d*) M. A. Henderson and J. S. McIndoe, *Chem. Commun.*, 2006, 2872; (*e*) N. J. Farrer, R. McDonald and J. S. McIndoe, *Dalton Trans.*, 2006, 4570.
11 D. Dakternieks, K. Jurkschat, S. vanDreumel and E. R. T. Tiekink, *Inorg. Chem.*, 1997, **36**, 2023.
12 J. Beckmann, M. Henn, K. Jurkschat, M. Schurmann, D. Dakternieks and A. Duthie, *Organometallics*, 2002, **21**, 192.
13 R. Okawara and M. Wada, *J. Organomet. Chem.*, 1963, **1**, 81.
14 D. L. Tierney, P. J. Moehs and D. L. Hasha, *J. Organomet. Chem.*, 2001, **620**, 211.
15 N. B. Cech and C. G. Enke, *Mass Spectrom. Rev.*, 2001, **20**, 362.
16 J. Clayden, N. Greeves, S. Warren and P. Wothers, *Organic Chemistry*, OUP, Oxford, 2001, p. 288.
17 D. M. Chisholm and J. S. McIndoe, *Dalton Trans.*, 2008, 3933.

