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A General Method For The Coupling of Vinyl Stannanes

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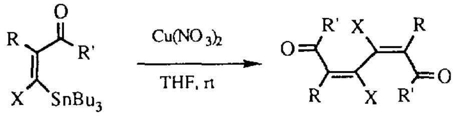
Abstract: *The inter- and intra- copper mediated coupling of functionalised vinyl stannanes is reported.*

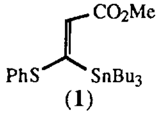
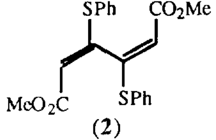
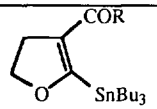
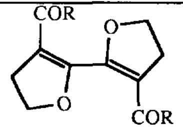
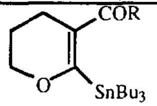
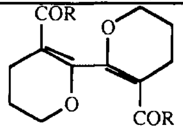
The synthesis of novel buta-1,3-dienes continues to be an area of much synthetic interest primarily for their use in Diels-Alder reactions[1], although recently other elegant uses of these compounds have been developed[2]. As a continuation of our interest in the chemistry of functionalised vinyl stannanes we wish to report a general method for the preparation of highly substituted, buta-1,3-dienes based upon a copper(II)-promoted coupling[3] reaction of vinyl stannanes. Execution of this reaction in an intramolecular sense provides a novel route to macrocyclic systems, **Scheme 1**.



Scheme 1

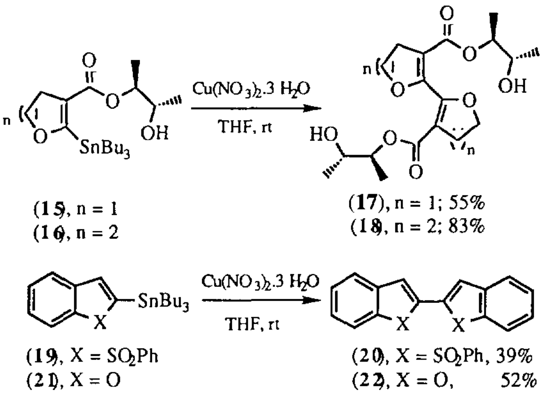
The coupling procedure adopted is operationally simple to carry out, and occurs at ambient temperatures over short reaction times (usually 10 minutes). The reaction conditions are tolerant to a range of functional groups (*e.g.* alkyl and benzyl esters, thioethers); in certain cases a small amount of protodestannylated starting material was also isolated as in the case of the stannane (**15**), where 7% of the corresponding enol ether was isolated. The yields are generally good, except in the case of substrates containing α,α,α-trichloromethylketone residues, substrates (**5**) and (**11**), where yields are moderate. In the case of the acyclic vinyl stannane (**1**), it was clear from an examination of the high field ^1H nmr spectrum that the homocoupled product was generated as a single diastereoisomer. Spectroscopic techniques were not able to provide an unambiguous stereochemical assignment, although a single crystal X-ray structure determination[4] conclusively demonstrated that the coupling reaction had proceeded with retention of configuration at both of the reacting sp^2- centres.

The coupling reaction also proceeded well in the presence of unprotected hydroxyl functionality as demonstrated in the case of the racemic stannanes (**15**) and (**17**). In addition, homocoupling of benzofused heterocyclic systems is also possible as exemplified by the preparation of the bis - indole and - benzofuran (**20**) and (**22**) respectively.

Stannane#	Diene¶	Yield
 (1)	 (2)	65%
 R = OMe, (3) R = CCl$_3$, (5) R = OBn, (7)	 R = OMe, (4) R = CCl$_3$, (6) R = OBn, (8)	84% 40% 65%
 R = OMe, (9) R = CCl$_3$, (11) R = OBn, (13)	 R = OMe, (10) R = CCl$_3$, (12) R = OBn, (14)	92% 46% 94%

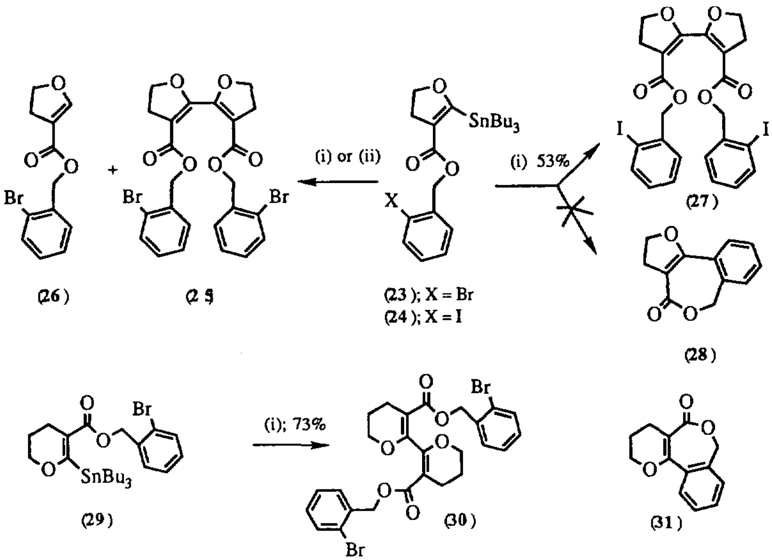
Preparation as in ref. 5. ¶ characterised by high field ^{1}H nmr, ir, and mass spectrometry.

Table



Scheme 2

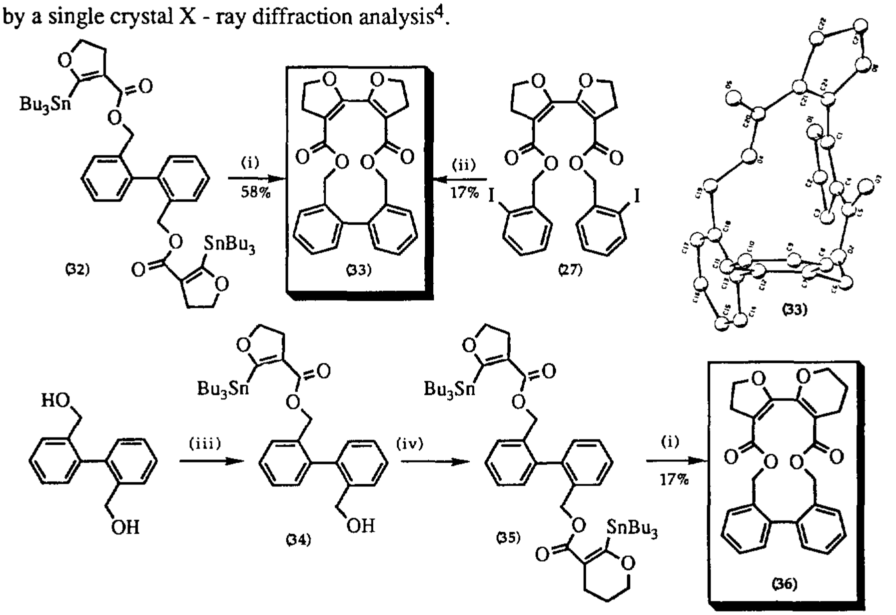
The recent report by Piers[6] concerning the *intramolecular* coupling of ω - halostannanes promoted by Cu(1) salts prompted us to prepare the halobenzyl esters (**23**) and (**24**). In our case, exposure of (**23**) to CuCl (3 eq.) in DMF at 70 °C afforded the diene (**25**) in 37% isolated yield together with a 17% yield of the protodestannylated compound (**26**). Upon changing to Cu(NO$_3$)$_2$.3H$_2$O in THF the diene (**25**) was isolated in 73% yield after 45 minutes reaction time; the corresponding iodobenzyl ester (**24**) underwent homocoupling to the diene (**27**) in 53% isolated yield after a reaction time of 90 minutes. None of the lactone[7] (**28**) (*i.e.* the poduct of a Piers - type coupling reaction) could be isolated from any of these reactions. Similarly, reaction of the ester (**29**) with CuCl in hot DMF afforded the diene (**30**) in 73% yield, again without isolation of the corresponding lactone[7] (**31**). Presumably stereoelectronic factors play a decisive role in diverting these coupling reactions from the intramolecular (Piers) to an intermolecular mode of coupling, **Scheme 3**.



Reagents: (i) CuCl (3 eq.); DMF; 70 °C; (ii) $Cu(NO_3)_2 . 2 H_2O$ (1 eq.); THF; 25 °C.

Scheme 3

At this juncture we decided to investigate the possibility of utilising the homocoupling reaction in an intramolecular sense. Brief exposure (25 minutes) of the readily available bis - stannane (**32**) with $Cu(NO_3)_2 . 3H_2O$ (2 eq.) in THF at ambient temperature afforded the macrocycle (**33**) in 58% yield after chromatography and recrystallisation (m.p. 229 - 230.5 °C), **Scheme 4**. The structural identity of (**33**) was confirmed by a single crystal X - ray diffraction analysis[4].

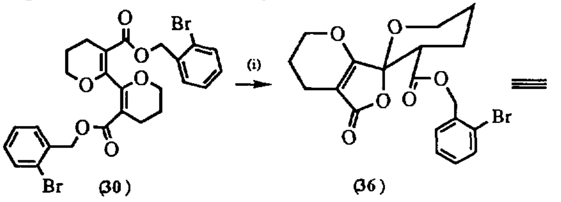


Reagents: (i) $Cu(NO_3)_2 . 2 H_2O$ (1 eq.); THF; 25 °C; (ii) $(Me_3Sn)_2$; Pd(0); toluene; 120 °C (iii) (**5**); DBU (2 eq.); 2 - pyridone (0. 2 eq.); (iv) (**11**); DBU (2 eq.); 2 - pyridone (0.2 eq.).

Scheme 4

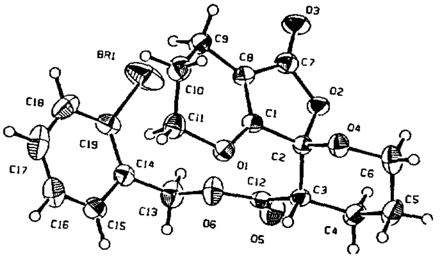
By way of comparison, the macrocycle (33) was also prepared in lower yield (17%) from the bis - iodide (27) using the elegant coupling procedure recently developed by Grigg[8] ($(Me_3Sn)_2$ (1.2 eq.); tri-o-tolylphosphine (20 mol%); $Pd(OAc)_2$; toluene; 120 °C; 20 hrs.). The structure of the macrocycle (33) was unambiguously assigned upon the basis of a single crystal X - ray diffraction analysis. Although we have yet to define the scope of this cyclisation reaction, we have shown that the analogous unsymmetrical bis - stannane (34) also undergoes cyclisation to afford the macrocycle (35), albeit in the somewhat lower yield of 17%, which is still comparable to many existing modes of macrocyclisation which proceed *via* C - C bond formation[9].

Having developed a general method for the synthesis of highly functionalised dienes such as (30), we have begun to study their chemistry. Whilst these dienes appear to be unreactive in Diels - Alder reactions, we have shown that dissolution of the bromobenzyl ester (30) in TFA (25 °C; 1 hr.) containing triethyl silane (10 eq.) led to the isolation of the the functionalised spiroketal[10] (36) in 72% isolated yield as a single diastereoisomer, **Scheme 5**. Again the structural identity of (36) was established primarily upon the basis of high field nmr spectroscopy and confirmed by single crystal X - ray diffraction analysis. Synthetic applications of this sequence are now underway.



(30) (36)

Reagents: CF_3CO_2H; Et_3SiH (10 eq.); 25 °C; 72%.



Scheme 5

General experimental procedure

To the vinyl stannane (1 mmol) in THF (20 ml) was added copper(II) nitrate (1 eq.) in a single portion. The mixture was stirred at ambient temperature for 10-40 minutes. The reaction mixture was diluted with ethyl acetate (60 ml) and washed with aqueous ammonia (45 ml; 5% soln.), water and then brine. The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. "Flash" chromatography of the residue afforded the homocoupled dienes[11] in 40-94% yield (**Table**).

Acknowledgements

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References and notes

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3. e.g. G-J. Boons, D. A. Entwistle, S. V. Ley, and M. Woods, *Tetrahedron Letters*, 1993, **34**, 5649.
4. Details of this structure determination will appear elsewhere
5. Booth, C.; Imanieh, H.; Quayle, P.; Lu, S. Y. *Tetrahedron Letters*, 1992, **33**, 413.
6. Piers, E.; Wong, T. *J. Org. Chem.*, 1993, **58**, 3609.
7. Lactones (**28**) and (**31**) were prepared indepedently; Zhao, Y. K.; Quayle, P. Unpublished.
8. Grigg, R.; Teasdale, A.; Sridharan, V. *Tetrahedron Letters*, 1991, 32, 3859.
9. *e.g.* Marsella, M. J.; Carroll, P. J.; Swager, T. M. *J. Am. Chem. Soc.*, 1994, **116**, 9347; Barrett, A. G. M.; Boys, M. L.; Boehm, T. L. *J. Chem. Soc., Chem. Commun.*, 1994, 1881. For recent improvements to bi - aryl coupling procedures see Lipshutz, B. H.; Kayser, F.; Liu, Z-P. *Angew. Chem., Intl. Edn. Engl.*, 1994, **33**, 1842 and refs. therein..
10. For a related reaction see Bateson, J. H.; Elsmere, S. A.; Elliot, R. L. *Synlett.*, 1994, 152.
11. All new compounds were fully characterised by high field ^1H and ^{13}C nmr, ir, mass spectrometry and or combustion microanalysis.

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