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Palladium-catalysed cyclotrimerisation reactions of polycyclic alkenes under the Stille and Grigg coupling conditions

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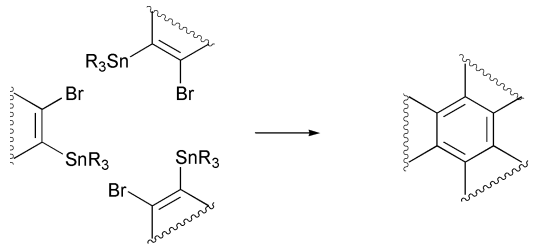
Preformed or *in situ* generated polycyclic bromostannylalkenes react under palladium catalysis under Stille or Grigg reaction conditions to afford cyclotrimerised adducts *via* a three-fold carbon–carbon coupling reaction.

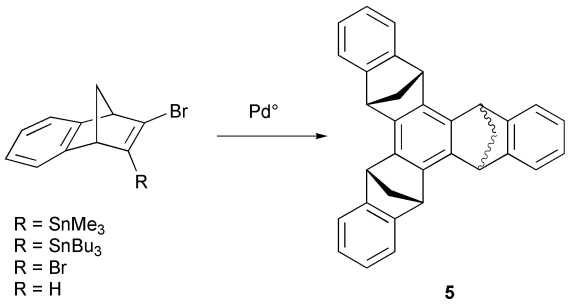
Due to their unusual electronic features, the class of molecules composed by trisannelated benzenes of polycyclic structures has attracted considerable interest in the past few years.[1] These molecules also have a peculiar cup-shaped structure that makes them suitable for use in molecular recognition as the component host.[2] Here we present a new and effective method of preparation of benzoannellated cyclotrimers which is based on the Stille coupling reaction.†[3] The cyclotrimerisation is accomplished by placing the metal center (the stannyl residue) and the leaving group (the bromine atom) (Scheme 1) at the two ends of the olefinic substrate.



Scheme 1

Bromostannylbenzonorborna-2,5-dienes‡ **1,2** were prepared by bromine–tin exchange from the dibromo derivative **3** or by LDA treatment of the bromobenzonorborna-2,5-diene **4** followed by quenching with trimethyltin chloride.[4] When **1** was heated at 70 °C for 24 h in DMF in the presence of palladium(II) acetate (10% mol eq.), triphenylphosphine (20% mol eq.) and LiCl a 4:1 mixture of *anti* and *syn* trimers **5** was obtained in 38% yield (Scheme 2). No detectable formation of dimers, as previously noticed in the reaction with copper nitrate, was observed.[4] Yields and *anti* to *syn* ratio are affected by temperature, solvent or by the changes to the other reaction conditions.

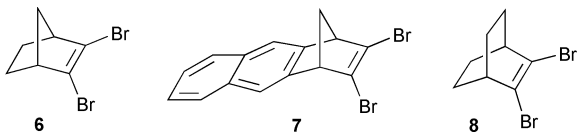
For example, the same reaction carried out in toluene at 120 °C affords, after 24 h, a 3:1 mixture of *anti* and *syn* isomers **5** in 30% yield. By comparison, in refluxing THF, the system is unreactive even after 94 h. The effect of co-catalysts has been considered. LiCl,[5] a well known Stille coupling activator, does not significally improve the yields of the reaction.



Scheme 2

Relevantly, the bromotributyltin derivative **2** treated with palladium(II) acetate (7% mol eq.) and triphenylphosphine (14% mol eq.) at 110 °C for 24 h in toluene leads to trimer **5** as only the *anti* isomer in 58% yield.

The toxic nature of tin compounds, which is especially crucial for the trimethyl derivative as well as the handling and storage of quantities of bromostannylalkenes, prompted us to test the feasability of the *in situ* reaction under the methodology developed by Grigg.[6] Accordingly, by heating a mixture of dibromobenzonorborna-2,5-diene **3**, palladium(II) acetate (10% mol eq.), triphenylphosphine (20% mol eq.) and hexamethylditin in refluxing toluene, cyclotrimer **5** is obtained in comparable yields with the Stille method (50%). In this case, however, only the *anti* isomer is formed. Remarkably the reaction can be achieved in much higher yields by using hexabutylditin, which besides being less toxic,[7] is less expensive than the methyl derivative. The latter reaction conditions, using hexabutylditin in place of hexamethylditin, gave **5** quantitatively, and were considered as the most convenient conditions for the desired transformation and were applied to other substrates for the determination of the scope of the method.§ All of the dibromoderivatives **6**–**8** afforded the respective trimer *anti*-**9**, *anti*-**10** and **11** in almost quantitative yields.¶[8]



The mechanism by which trimers are formed could be attractively envisaged as a 'head to tail' coupling amongst the tin and bromine termini of the double bonds. If this in indeed the case the cyclotrimerisation reaction of racemic **1** either preformed under the Stille reaction conditions or generated *in situ* with the Grigg method, should always afford a statistical 3:1 ratio of the *anti* and *syn* product.[1b] The formation of the *anti* product only suggests that the reaction occurs with the coupling of both antipods, while that derived from the coupling of the homochiral enantiomers does not form because of steric hindrance.[1b] Alternatively, the reaction may occur *via* an acetylene intermediate stabilised by complexation with palladium. However, no further data regarding the mechanism are available so far.

In conclusion we have reported the Stille reaction applied to an unusual bifunctional substrate that leads to a useful application and developed a method that, especially in the optimised Grigg variant, competes with the best method so far available for the cyclotrimerisation of polyclic alkenes both in terms of yields and safety.

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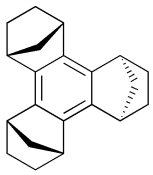
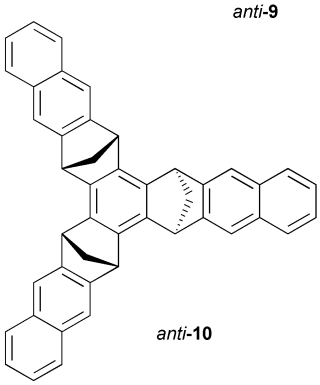
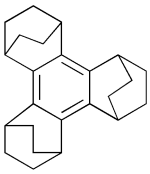


anti-**9**



anti-**10**



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Notes and references

† As reported in ref. 1*a*, 2-bromo-3-trimethyltinnorborna-2,5-diene does not undergo cyclotrimerisation under Stille-coupling conditions. The reason for this failure is assumed to be Pd complexation to the double bond between carbons 5 and 6 in this substrate.

‡ The IUPAC name for benzonorborna-2,5-diene is tricyclo[6.2.1.$0^{2,7}$]undeca-2,4,6,9-tetraene.

§ A mixture of 2,3-dibromobenzonorborna-2,5-diene (0.34 mmol), $Pd(OAc)_2$ (0.04 mmol), PPh_3 (0.08 mmol) and hexabutylditin (0.51 mmol) in dry toluene (3 mL) in a screw capped pyrex test tube was purged with argon, sealed and heated at reflux for 24 h. After cooling to rt, water (20 mL) was added and extracted with diethyl ether (3 × 30 mL), washed with brine, dried ($MgSO_4$) and concentrated at reduced pressure. The residue was purified by flash chromatography through a short silica gel column eluting with a hexane–dichloromethane gradient.

¶ It should be pointed out that the cyclotrimerisation reaction carried out on the boron derivative under Suzuki type reaction conditions afforded only a very moderate yield of cyclotrimer.

1 (*a*) C. Zonta, S. Cossu and O. De Lucchi, *Eur. J. Org. Chem.*, 2000, 1965; (*b*) C. Zonta, S. Cossu, P. Peluso and O. De Lucchi, *Tetrahedron Lett.*, 1999, **40**, 8185; (*c*) R. Rathore, S. V. Lindeman, A. S. Kumar and J. K. Kochi, *J. Am. Chem. Soc.*, 1998, **120**, 6012; (*d*) R. Durr, O. De Lucchi, S. Cossu and V. Lucchini, *J. Chem. Soc., Chem. Commun.*, 1996, 2447; (*e*) F. Cardullo, D. Giuffrida, F. H. Kohnke, F. M. Raymo, J. F. Stoddart and D. J. Williams, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 339; (*f*) N. L. Franck, K. K. Baldridge and J. S. Siegel, *J. Am. Chem. Soc.*, 1995, **117**, 2102; (*g*) K. Komatsu, S. Aonuma, Y. Jinbu, R. Tsuji, C. Hirosawa and K. Takeuchi, *J. Org. Chem.*, 1991, **56**, 195; (*h*) S. B. Singh and H. Hart, *J. Org. Chem.*, 1990, **55**, 3412; (*i*) P. G. Gassman and I. Gennick, *J. Am. Chem. Soc.*, 1980, **102**, 6863.

2 J. C. Ma and D. A. Dougherty, *Chem. Rev.*, 1997, **97**, 1303; R. Rathore, S. V. Lindeman and J. K. Kochi, *J. Am. Chem. Soc.*, 1997, **119**, 9393. General Reviews on supramolecular chemistry: C. A. Hunter, *Chem. Soc. Rev.*, 1994, 101; J.-M. Lehn, *Supramolecular Chemistry*, VCH, Weinheim, 1995; F. Diederich, *Cyclophanes*, The Royal Society of Chemistry, Cambridge, 1994; F. Vogtle, *Supramolekulare Chemie*, Teubner, Stuttgart, 1989.

3 S. P. Stanforth, *Tetrahedron*, 1998, **54**, 263; V. Farina, V. Krishnamurthy and W. J. Scott, *Org. React.*, 1997, **50**, 1; J. K. Stille, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 508.

4 R. Durr, S. Cossu, V. Lucchini and O. De Lucchi, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2805; S. Cossu, O. De Lucchi, V. Lucchini, G. Valle, M. Balci, A. Dastan and B. Demirci, *Tetrahedron Lett.*, 1997, **38**, 5319.

5 M. Fujita, H. Oka and K. Ogura, *Tetrahedron Lett.*, 1995, **36**, 5247; W. J. Scott and J. E. McMurry, *Acc. Chem. Res.*, 1988, **21**, 47.

6 R. Grigg, A. Teasdale and V. Sridharan, *Tetrahedron Lett.*, 1991, **32**, 3859.

7 M. Bragadin and D. Marton, *J. Inorg. Biochem.*, 1997, 76.

8 For **9**: see ref. 1*i*. For **10**: see ref. 1*a*. For **11**: see ref. 1*g*.