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The development of a 'safety-catch' arylgermane for biaryl synthesis by palladium-catalysed germyl-Stille cross-coupling

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The Pd(0) catalysed cross-coupling of arylgermanes with aryl bromides is shown to require at least two labile heteroatom ligands on the Ge centre to allow efficient nucleophilic activation by fluoride. Dichloroarylgermanes 7a and 7b are shown to cross-couple to a series of aryl bromides with moderate efficiency using activation by KF in DMF. Bis(2-naphthylmethyl)arylgermane 18b is identified as a 'safety-catch' precursor to this type of cross-coupling substrate. The 2-naphthylmethyl substituents can be removed via photolytic oxidation in the presence of $Cu(BF_4)_2$ and the resulting species, although not characterized, participates in cross-coupling using activation by TBAF in DMF. Copyright © 2007 John Wiley & Sons, Ltd.

KEYWORDS: germanium; cross-coupling; palladium; photooxidation; solid-phase; fluorous-phase

INTRODUCTION

Biaryls are found widely in bioactive natural products, pharmaceuticals, agrochemicals, dyes, organic semiconductors and ligands/auxiliaries for asymmetric synthesis.[1] Additionally, the biaryl motif has been identified as a privileged motif for disrupting protein–protein interfaces (PPIs)[2] and so is of increasing importance in contemporary genome-driven pharmaceutical discovery.[3,4] Biaryls are generally prepared by cross-coupling between aryl metals such as boronic acids/trifluoroboronates (Suzuki coupling),[5–7] zinc halides (Negishi coupling)[8] or trialkylstannanes (Stille coupling)[9] and aryl halides or pseudohalides (e.g. triflates and nonoflates).[1] The most robust of these aryl metal species are the aryl trifluoroboronates and trialkylstannanes; however, neither can be carried through complex synthetic sequences due to their reactivity towards electrophiles and nucleophiles.[10] The arylsilicon derivatives used for Hiyama–Denmark cross-coupling reactions are also sensitive to electrophiles and nucleophiles because activated derivatives such as aryldialkylsilanols/silylchlorides are required for coupling to occur (i.e. containing at least one heteroatom on Si).[11–16] A number of 'safety-catch'[17] all-carbon-substituted silane precursors to these species have been developed for alkenyl coupling, including alkenylmethylcyclobutylsilanes,[18] dimethylsilyl hydrides,[19] dimethyldimethyl(2-pyridyl)silanes,[20–27] dimethyl(2-thienyl)silanes,[28,29] [3,5-bis(trifluoromethyl)phenyl]silanes,[30] (4-trifluoromethylphenyl)silanes,[30] dimethylbenzylsilanes,[31–33] dimethylphenylsilanes[34] and allyldiphenylalkynylsilanes,[35] but the only safety-catch silanes for aryls are the triallylsilanes developed by Hiyama[36–38] and these are not robust towards multistep synthesis.

We were interested in developing an aryl metal cross-coupling precursor that would address this deficiency. Specifically, we wanted to develop a precursor that could be readily introduced early in a synthetic sequence, that would be non-toxic, that would be robust to a wide range of subsequent elaboration steps and that would be amenable to

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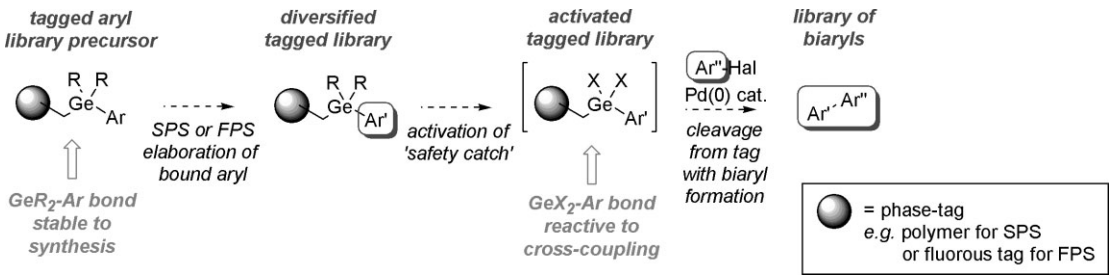
chemoselective activation to allow cross-coupling later in the synthesis. Herein, we describe the development of a type of aryl trialkylgermane that promises to fulfill these criteria in that it should display high levels of stability towards bases and nucleophilies (but only limited stability towards acids and electrophiles) and can be activated by photooxidation to enable cross-coupling with aryl bromides to give biaryls. Moreover, it offers the opportunity for attachment of a phase-tag[39] to facilitate synthesis in a parallel fashion with rapid purification prior to cleavage from the phase-tag [e.g. for solid phase synthesis (SPS)[40] or fluorous phase synthesis (FPS)[41,42]].

Arylgermanes are distinguished on the one hand from aryl stannanes by their lack of toxicity and relative stability towards electrophiles and nucleophiles and on the other hand from arylsilanes/silanols by their stability towards nucleophiles. This endows arylgermanes with arguably an optimal stability profile for multistep synthesis among group 14 aryl metals. The reason for the relative inertness of arylgermanes relative to their silane and stannane congeners is that, although Ge is located between Si and Sn in the periodic table, the electronegativity of Ge is the closest to that of C among group 14 metals (C, 2.50; Si, 1.74; Ge, 2.02; Sn, 1.72).[43] This has been suggested to be the result of 'scandide contraction'; i.e. the shielding of the Ge nuclear charge by its 3d electrons is relatively inefficient and renders the Ge atom anomalously electronegative.[44] This ensures that C–Ge bonds are less polarized than C–Si and C–Sn bonds.[45] It also means that activation of the C–Ge bond is required for cross-coupling.

The first reported organogermane cross-coupling reactions were those of α-styryltrimethylgermane with a series of aryl diazonium salts by Ikenaga in 1990.[46] Kosugi then reported the first arylgermane cross-coupling reaction using phenyl-carbagermatrane and 4-tolylbromide in 1996.[47] Subsequently, the groups of Oshima, Faller and Wnuck have developed protocols for cross-coupling aryl/alkenyl trifurylgermanes[48,49] with aryl iodides/bromides, aryl/alkenyl/alkynyl germatranes/triethoxygermanes[50–53] with aryl iodides/chlorides/triflates, and alkenyl tris(trimethylsilyl)germanes[54–56] with aryl iodides/bromides/chlorides, respectively. Additionally, Kosugi has reported the cross-coupling of aryltrichlorogermanes with aryl bromides.[57] Kosugi's carbagermatrane derivatives, which contain a nitrogen substituent constrained so as to render the Ge centre permenantly pentavalent,[58,59] can be coupled in the absence of nucleophilic activators, but all the other derivatives have substituents on Ge that are displaced by fluoride or hydroxide ions under the coupling conditions to facilitate formation of hypervalent species that are prone to transmetallation to Pd and thus allow cross-coupling.[60]

In the context of a program to develop arylgermane-based linkers for phase-tagged synthesis of heterocyclic libraries[61,62] and of high purity oligothiophenes[63,64] for 'plastic electronic' applications, we required a 'safety-catch' linker that would allow cleavage from the phase-tag with concomitant C–C bond formation.[65] It was envisaged that such a method of cleavage in which the arylgermane, following 'activation' of the safety-catch, could be enticed to participate in Pd(0)-catalysed cross-coupling with aryl halides would constitute a powerful method of diversification via biaryl formation in these and other applications (Scheme 1).

A number of linkers for phase-tagged synthesis have been developed that allow for cleavage from a phase-tag concomitant with introduction of diversity via transition metal catalysed cross-coupling processes.[66] They can be divided into two types: those constituting phase-tagged electrophiles and those constituting phase-tagged nucleophiles (cf. our envisaged linker). The first such electrophilic linker for SPS was a benzylthioether linker introduced by Mioskowski in 2000.[67] Subsequently, Holmes,[68,69] Cammidge,[70] Ganesan,[71] Park[72] and Tsukamoto[73] have reported aryl sulfonate linkers and Steel has reported a vinyl phosphonate linker for SPS all of which can be cleaved by Pd(0)/Ni(0)-catalysed cross-coupling with either aryl boronates or Grignard reagents.[74] Related linkers for FPS have also been described.[75] The only phase-tagged nucleophilic linkers reported are resin and fluorous-tagged stannanes such as the vinyl stannane linker used by Nicolaou for the SPS of (*S*)-zearalenone in 1998,[76] and resin or fluorous-tagged arylboronic esters such as described by Burgess[77] and Qing,[78] respectively. These nucleophilic linkers suffer from the limitations discussed above for Suzuki and Stille reactions respectively: they are not robust enough to survive much synthesis prior to cleavage. The envisaged



Scheme 1. Envisaged arylgermane-based 'safety-catch' linker for phase-tagged synthesis enabling Pd(0)-mediated cleavage from the phase-tag with concomitant C–C bond formation.

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safety-catch arylgermanes would therefore constitute a valuable addition to the repertoire of diversity/multifunctional linkers for phase-tagged parallel synthesis.[66]

RESULTS AND DISCUSSION

It was unclear when we embarked on this project exactly what was required to activate an arylgermane towards cross-coupling.[17] From the literature precedent summarized above, it was clear that the Ge centre needs to be rendered hypervalent in order to activate the aryl–Ge bond towards transmetallation with Pd. This has been achieved either via *intra*molecular coordination of a suitably tethered tertiary amine (as in Kosugi's carbagermatranes), or via *inter*molecular coordination of a halide/hydroxide nucleophile to a susceptible *tri*-halo-, hydroxyl- or alkoxy arylgermane precursor (as in the methods of Oshima, Faller and Wnuck, and for Kosugi's trichlorogermanes). We were particularly attracted to this latter approach as it offered the prospect of the development of an architecturally relatively simple linker. However, in all the aforementioned cases *three*, labile, heteroatom ligands are present on the Ge centre to allow coordination of a fourth to give the presumed pentavalent activated arylgermane coupling partner. Since we required one, stable, alkyl ligand for attachment to the phase-tag our first objective was to establish the optimal number of heteroatom ligands on Ge for cross-coupling. Analogous studies on variously fluorinated arylsilanes by Hiyama demonstrated that just one such ligand on Si was sufficient to allow efficient coupling;[79,80] hence the prevalence of mono-silanols in recent procedures. It was expected *a priori*, that Ge would require additional such ligands to offset its greater electronegativity relative to Si (see above). To evaluate this, we prepared 4-tolyl and 4-anisyl, mono- and dichlorogermane substrates **3, 10, 6b** and **7b** from trichlorogermane **1** (Scheme 2)

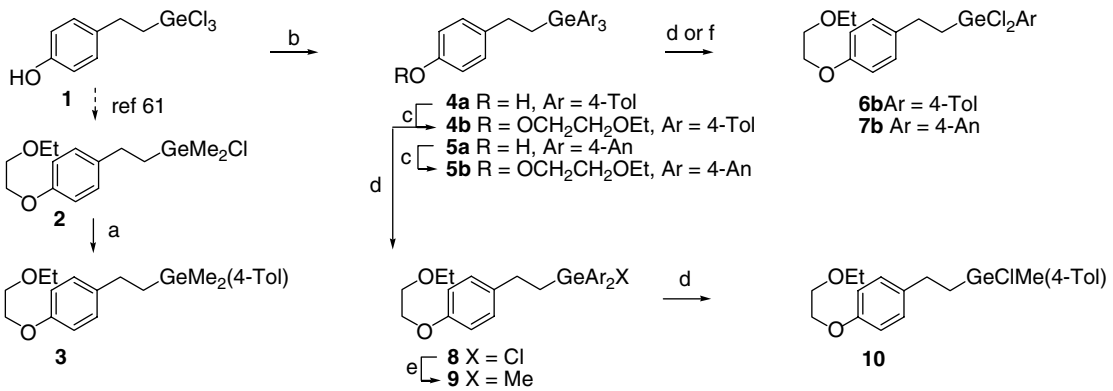
As in our previous studies,[61] the ethoxyethyl ether in these derivatives was envisioned to act as a surrogate for the polyethyleneglycol (PEG) chain of a PEG-grafted polystyrene resin for SPS such as Tentagel®.

Using conditions described by Hiyama for the coupling of ethyl(4-tolyl)dichlorosilane with aryl bromides [NaOH as nucleophilic activator in THF with $Pd(OAc)_2/PPh_3$ at 66 °C for 24 h][81] as a starting point for our investigation, we found that trialkyl(4-tolyl)germane **3** and dialkyl(4-tolyl)chlorogermane **10** were unreactive but that alkyl(4-tolyl)dichlorogermane **6b** was competent for cross-coupling (Table 1, entries 1–4).

Systematic optimization of the solvent (→ DMF), nucleophilic activator (→ KF), Pd(0) source [→ $PdCl_2(MeCN)_2$] and ligand (→ dppp) enabled synthetically useful yields of biaryls **11a–i** to be obtained using dichlorogermane **6b** (entries 5–7). Dichloro 4-anisyl congener **7b** was also competent for cross-coupling under these optimized conditions (entries 8–13). However, no conditions could be found that would allow cross-coupling products be obtained from the trialkyl or mono-chloro analogues **3** or **10**.

Having established that aryldichlorogermanes **6b** and **7b** were suitable precursors for Pd(0) catalysed cross-coupling we next prepared a series of potential safety-catch precursors to these compounds (and related di-heteroligated congeners), namely dihydridogermanes **12** and **13**, di(2-furyl)germane **14b**, diallylgermane **15b**, di(2-pyridyl)germane **16b**, dibenzylgermane **17b** and bis(2-naphthylmethyl)germane **18b** (Scheme 3).

Denmark has shown that alkenylsilylhydrides can act as safety-catch alkenylsilanes for cross-coupling. Thus, alkenyl di(isopropyl)silyl hydrides can be cross-coupled with aryl iodides using either TBAF or TBAOH as the nucleophilic promoter with $[allylPdCl]_2$ as the catalyst in THF.[19] Although the mechanistic details have not been unequivocally established, it seems that rather than occurring via Pd insertion into the Si–H bond, these derivatives act as precursors to silanols via *in situ* base-promoted hydrolysis



Scheme 2. Synthesis of trialkyl-, dialkylchloro- and alkyldichloro arylgermanes **3, 10, 6b** and **7b**. Reagents and conditions: (a) 4-TolMgBr, toluene (76%); (b) 4-TolMgBr, THF (**4a** 79%; **5a** 74%); (c) $ClCH_2CH_2OEt$, Cs_2CO_3, TBAI, MeCN (**4b** 90%; **5b** 78%); (d) MSA, CH_2Cl_2 then HCl (**8** 96%, **10** 94%, **6b** 97%); (e) MeMgI, THF (93%); (f) HCl, CH_2Cl_2 (**7b** 82%).

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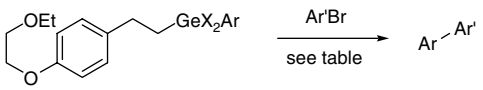
Table 1. Cross-coupling of variously chlorinated arylalkylgermanes



3 X_2 = Me_2, Ar = 4-Tol
10 X_2 = Me,Cl, Ar = 4-Tol
6b X_2 = Cl_2, Ar = 4-Tol
7b X_2 = Cl_2, Ar = 4-An

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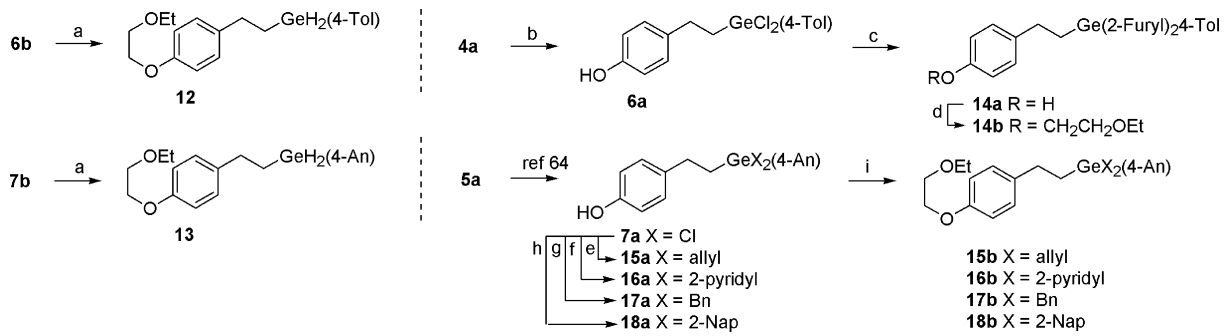
No.	Germane	Ar′	Method[a]	Yield (%)
1	**2**	3,5-$(CF_3)_2C_6H_3$	A	0
2	**10**	3,5-$(CF_3)_2C_6H_3$	A	0
3	**6b**	3,5-$(CF_3)_2C_6H_3$	A	32[b] (**11a**)
4	**6b**	4-AcC_6H_4	A	28 (**11b**)
5	**6b**	4-AcC_6H_4	B	60[c] (**11b**)
6	**6b**	3,5-$(CF_3)_2C_6H_3$	B	63 (**11a**)
7	**6b**	1-Nap	B	79 (**11c**)
8	**7b**	Ph	B	36 (**11d**)
9	**7b**	3-$CF_3C_6H_4$	B	51 (**11e**)
10	**7b**	3,5-$(CF_3)_2C_6H_3$	B	71 (**11f**)
11	**7b**	1-Nap	B	56 (**11g**)
12	**7b**	3-Py	B	44 (**11h**)
13	**7b**	4-$NO_2C_6H_4$	B	47 (**11i**)

[a] Method A: (i) NaOH (6 equiv.), THF, RT, 4 h; (ii) ArBr (1 equiv.), $Pd(OAc)_2$ (5 mol%), PPh_3 (10 mol%), 66 °C, 24 h. Method B: (i) KF (6 equiv.), DMF, RT, 3 h; (ii) ArBr (1 equiv.), $PdCl_2(MeCN)_2$ (5 mol%), dppp (5 mol%), 120 °C, 24 h.
[b] $PhGeCl_3$ coupled in 43% yield under these conditions.
[c] 4-AcC_6H_4I coupled in 25% yield under these conditions.

under the coupling conditions. Given that germyl hydrides are also susceptible to hydrolysis, we considered that dihydrogermanes **12** and **13** might represent interesting safety-catch germanes. However, under both Denmark's conditions and the optimized conditions for coupling dichlorogermanes **6b** and **7b** described above, we were unable to achieve any coupling using either compound.

Oshima has shown that alkenyl and aryltri(2-furyl)germanes can be cross-coupled with aryl iodides and bromides using TBAF as the nucleophilic promoter and $Pd_2(dba)_3 \cdot CHCl_3/P(2\text{-furyl})_3$ as the catalyst in NMP.[48,49] Oshima has suggested that the active intermediates are probably the corresponding trihydroxygermanes with the hydroxyl groups being supplied by the water (ca. 5%) present in commercially available solutions of TBAF. Although we were able to reproduce the results of Oshima by cross-coupling phenyltri(2-furyl)germane with 3-(trifluoromethyl)phenylbromide (albeit in 34% cf. 64% yield),[48] we were unable to entice di(2-furyl)germane **14b** to couple under either these or the optimized conditions for coupling dichlorogermanes **6b** and **7b** described above. Moreover, we found that, unlike phenyltri(2-furyl)germane, di(2-furyl)germane **14b** is stable to treatment with $TBAF \cdot 3H_2O$ (3 equiv.) in refluxing THF for 3 h (as determined by ^1H NMR). It seems that three 2-furyl groups are required for hydrolysis to occur readily.[82]

Hiyama has shown that aryltriallylsilanes (and diaryldiallylsilanes) can be cross-coupled with aryl iodides, bromides and chlorides using TBAF as the nucleophilic promoter and $PdCl_2/PCy_3$ or $PdCl_2$/Buchwald's ligand[83] as the catalyst in DMSO-H_2O.[36–38] The active intermediates are proposed to be the corresponding trifluorosilanes formed by fluorodeallylation under the reaction conditions. We were able to reproduce the results of Hiyama by cross-coupling phenyltriallylsilane with 4-bromoacetophenone (albeit in 70% cf. 81% yield),[36] but diallylgermane **15b** did not couple under either these or the optimized conditions for coupling dichlorogermanes **6b** and **7b** described above. Moreover, phenltriallylgermane gave 4,4′-diacetylbiphenyl (80%) and just traces of cross-coupled product under the Hiyama conditions. ^1H NMR experiments revealed that, unlike phenyltriallylsilane, phenyltriallylgermane is stable to treatment with $TBAF \cdot 3H_2O$ in d_6-DMSO-D_2O at 80 °C for 1 h. These results underscore the stability of arylgermanes cf. arylsilanes towards basic/nucleophilic conditions, and militate against the use of allylgermanes as safety-catch germanes with hydrolytic activation. It is possible that fluorodeallylation



Scheme 3. Synthesis of potential safety-catch precursors to dichlorogermanes **6b** and **7b**. Reagents and conditions: (a) $LiAlH_4$, THF (**12** 100%; **13** 91%); (b) MSA, CH_2Cl_2 (82%); (c) *n*-BuLi/furan, THF (39%); (d) $ClCH_2CH_2OEt$, Cs_2CO_3, TBAI, MeCN (88%); (e) allyl-MgCl, THF (73%); (f) Mg/2-Br-Py, THF (20%); (g) Mg/BnCl, THF (81%); (h) 2-naphthylmethyl-MgBr, Et_2O (74%); (i) $ClCH_2CH_2OEt$, K_2CO_3, TBAI, DMF (**15b** 70%; **16b** 25%; **17b** 68%, **18b** 80%).

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using KHF_2/TFA[84] could be used to activate allylgermanes but this was not explored as selectivity over dearylation was anticipated to be problematic (an Si-methallyl moiety can be converted into an Si-F moiety, even on an alkenylsilane, using fluorinative protodesilylation with KHF_2/TFA; see Hatanaka *et al.*[85]).

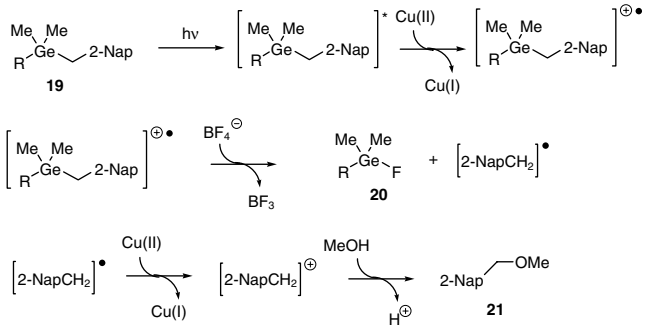
Yoshida has shown that 2-pyridyldimethylalkenyl- and benzylsilanes can be cross-coupled with aryl and heteroaryl iodides using TBAF as the nucleophilic promoter and $PdCl_2(PhCN)_2$ as the catalyst in THF.[21–26] The active intermediates are proposed to be the corresponding silanols with the hydroxyl group being supplied by the water in commercially available solutions of TBAF.[23] Although arylsilanes have not been coupled using this safety-catch we explored the use of this group in such a role on Ge. However, we found that di(2-pyridyl)germane **16b** was unstable even to chromatography on silica and could only be obtained in a pure state by rapid chromatography on alumina. We therefore did not examine its propensity to cross-couple.

Trost has shown that the benzyldimethylalkenylsilanes can be cross-coupled with aryl and alkenyl iodides and bromides using TBAF as the nucleophilic promoter and $Pd_2dba_3 \cdot CHCl_3$ as the catalyst in THF.[31,32,86,87] The benzyl group is reasonably stable to acidic and basic conditions, including some conditions used for deprotection of silyl ether protected alcohols, but is removed very rapidly on treatment with TBAF in THF. We found that aryldibenzylgermane **17b** was resistant towards cross-coupling under both Trost's conditions and the optimized conditions for coupling dichlorogermanes **6b** and **7b** described above. ^{1}H NMR studies showed that this compound was stable for >1 h towards TBAF in THF even at reflux. Undeterred, we considered that the inert nature of the benzylgermyl moiety would make it a very robust and therefore versatile safety-catch provided that conditions for selective debenzylative activation could be found.

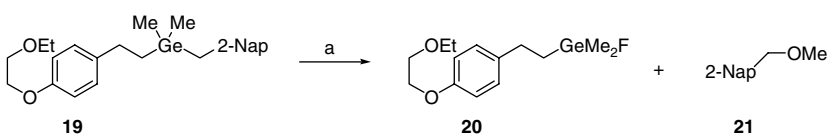
Benzylsilanes are known to be susceptible to nucleophile-assisted oxidative cleavage.[88,89] We therefore examined the stability of dibenzylgermane **17b** towards oxidation. Both CAN[90] and photooxidative[91] conditions gave a complex series of products, although it was apparent from the ^{1}H NMR spectra of both crude product mixtures that the signals for the benzylic methylene protons (δ 2.75 ppm) had disappeared. We considered that the photooxidative conditions offered the best prospect of being optimized as it seemed likely that the short wavelength output from our high pressure Hg lamp was probably responsible for the lack of selectivity for the desired photooxidation reaction. To test this idea, we decided to use a 2-naphthylmethyl group in place of the benzyl group.[91] The 2-naphthylmethyl group absorbs light at a longer wavelength than the benzyl group (ν_{max} 346 cf. 275 nm) and so allows the use of a Pyrex filter to substantially reduce the intensity of short wavelength radiation (<320 mn). Our first substrate was (2-naphthylmethyl)germane **19**, which we prepared by treating chlorogermane **2** with the Grignard reagent derived from 2-naphthylmethyl bromide. To our delight, photolysis of this compound using the same lamp, but through a Pyrex Schlenk tube, under the conditions developed by Otsuji[91] using $Cu(BF_4)_2$ (~2 equiv.) as the oxidant in a degassed MeCN/MeOH solvent system for ~30 min resulted in the clean formation of germyl fluoride **20** [^{19}F NMR δ − 196 ppm (app septet, $J^3_{H—F}$ 7 Hz)] along with 2-naphthylmethyl methyl ether **21** (Scheme 4).

The formation of a germyl fluoride was unexpected as Otsuji had proposed a mechanism in which methoxy germanes were formed in this type of process.[91] However, that fluoride from the copper tetrafluoroborate acts as a nucleophile to assist heterolysis of the benzylic Ge–C bond rather than MeOH as proposed by Otsuji is not surprising (Scheme 5).[92]

Encouraged by this photolysis result we subjected bis(2-naphthylmethyl)germane **18b** to photolytic oxidation, this time using ~4 equivalents of $Cu(BF_4)_2$. For this substrate, the ^{1}H NMR of the crude reaction product showed the presence of 2-naphthylmethyl methyl ether **21** as expected but the remainder of the material gave signals that were significantly more complex than we would have anticipated for the



Scheme 5. Possible mechanism of photooxidation of (2-naphthylmethyl)germane **19**.



Scheme 4. Photoactivation of (2-naphthylmethyl)germane **19** to give germyl fluoride **20**. Reagents and conditions: (a) hν (Hg-high pressure lamp, 125 W), Pyrex tube, $Cu(BF_4)_2$ (~2 equiv.), degassed MeOH/MeCN (3 : 1), 30 min (**20** ~87%).

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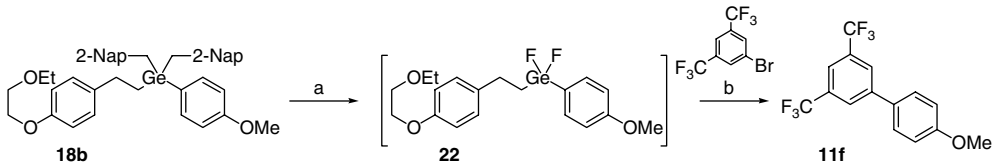

Scheme 6. Photooxidation/cross-coupling of bis(2-naphthylmethyl)germane **18b** with 3,5-bis(trifluoromethyl)bromobenzene. Reagents and conditions: (a) hν (Hg-high pressure lamp, 125 W), Pyrex tube, $Cu(BF_4)_2$ (~4 equiv.), degassed MeOH/MeCN (3 : 1); (b) $PdCl_2(MeCN)_2$ (10 mol%), $P(2\text{-Tol})_3$ (15 mol%), TBAF, CuI, DMF, 120 °C, 16 h (86%).

expected difluorogermane **22**. The ^{19}F NMR also showed three signals at ca. $\delta - 165$ ppm. Since this material could not be purified by chromatography, we subjected it directly to cross-coupling with 3,5-bis(trifluoromethyl)bromobenzene using the conditions optimized for dichlorogermane **7b**. This initial reaction afforded biaryl **11f** in 15% yield, but following re-optimization of the cross-coupling conditions based on the work of Li[93] [nucleophilic activator → TBAF and ligand → $P(2\text{-Tol})_3$] and the addition of CuI as a co-promotor[94,95] the yield for this two-step photoactivation/cross-coupling process was 86% (Scheme 6).

This exceeds the yield obtained directly from the isolated dichlorogermane **7b** (Table 1, entry 10, 71%). We are currently exploring the scope of this two-step photoactivation/cross-coupling process with respect to both the electronic and steric demand of the arylgermane and aryl bromide partners.

CONCLUSIONS

The Pd(0)-catalysed cross-coupling of arylgermanes with aryl bromides has been shown to require at least two labile heteroatom ligands present on the Ge centre to allow efficient nucleophilic activation by fluoride, presumably via a pentavalent intermediate. Dichloroarylgermanes **7a** and **7b** have been shown to cross-couple to a series of aryl bromides with moderate efficiency using KF in DMF. Subsequent efforts to identify a safety-catch precursor to this type of cross-coupling substrate, so as to allow for the use of the method in multi-step synthesis, identified bis(2-naphthylmethyl)arylgermane **18b** as being suitable. Both the 2-naphthylmethyl substituents could be removed via photolysis in the presence of $Cu(BF_4)_2$ as stoichiometric oxidant and the resulting species, although not characterized, participated in cross-coupling with 3,5-bis(trifluoromethyl)bromobenzene.

Once the scope of this new two-step photoactivation/cross-coupling process has been delineated, our efforts will focus on fully characterizing the photolysis-derived coupling precursor species, adapting the process to a phase-tagged protocol, evaluating the stability profile of the bis(2-naphthylmethyl)germane unit and applying the method in target-orientated synthesis.

EXPERIMENTAL

General

Solvents and reagents

Solvents were distilled as follows: THF and Et_2O over Na-benzophenone ketyl, toluene over Na, CH_2Cl_2 and DMF over CaH_2; HPLC-grade EtOAc and petrol were used as commercially supplied. Reagents were used as commercially supplied unless otherwise stated and handled in accordance with COSHH regulations.

Chromatography

Flash chromatography (FC) was carried out on Silica gel (BDH Silica gel for FC) according to the method described by Still,[96] or by using either Isolute Flash Silica (1, 5 or 50 g) or Varian Bond Elut Si (10 g) SPE cartridges in conjunction with a Varian Vac-Elut-20 vacuum manifold. Alumina was grade 1 basic supplied by BDH. TLC was performed on aluminium-backed silica gel plates (Merck Silica gel 60 F_{254}) which were developed with UV fluorescence (254 nm and 365 nm) and $KMnO_4(aq)/\tilde{\Delta}$.

^1H NMR spectra

These were recorded at 250 MHz on Bruker AC-250 instrument or at 400 MHz on a Bruker AM-400 instrument. Chemical shifts (δ_H) are given in parts per million (ppm) as referenced to the appropriate residual solvent peak. Broad signals are assigned as b.

^{13}C NMR spectra

These were recorded at 63 MHz on a Bruker AC-250 instrument or at 101 MHz on a Bruker AM-400 instrument. Chemical shifts (δ_C) are given in parts per million (ppm) as referenced to $CHCl_3$, and are assigned as s, d, t, and q, for C, CH, CH_2, and CH_3 respectively.

^{19}F NMR spectra

These were recorded at 367 MHz on a Bruker AM-400 instrument. Chemical shifts (δ_F) are given in parts per million (ppm) as referenced to $CFCl_3$.

Mass spectra

Low- and high-resolution spectra were recorded on a VG Prospec spectrometer, with molecular ions and major peaks being reported. Intensities are given as percentages of the

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base peak. Molecular weights were calculated using ^{74}Ge, ^{35}Cl and ^{79}Br isotopes. HRMS values are valid to ±5 ppm.

GC/MS

Analyses were carried out using a Perkin Elmer Turbomass mass spectrometer and Autosystem XL gas chromatograph. GC retention times are given in minutes. MS data is reported as above and all EI spectra were compared with the NIST database to confirm identity.

LC/MS

Analyses were carried out using a Micromass LCZ mass spectrometer and Hewlett Packard 1100 liquid chromatograph. LC methods are outlined where appropriate and retention times are given in minutes. MS data is reported as above.

Elemental analysis

Analyses were carried out by either by Mr Alan Jones of University of Sheffield using a Perkin Elmer 2400 CHN elemental analyser or by Mr Steven Boyer of London Metropolitan University Services Ltd.

Melting points

Analyses were carried out using a Khofler hot stage and are uncorrected.

Photochemistry

Photolytic oxidation was carried out using a 125 W Cathodeon high pressure Hg vapour lamp (type HPK 125) cooled by a rotary fan.

4-{[2-Dimethyl-(4-methylphenyl)germyl]ethyl} phenyl-(2-ethoxyethyl)ether 3

4-{[2-Chlorodimethylgermyl]ethyl}phenyl (2-ethoxyethyl) ether[61] (**2**, 0.553 g, 1.67 mmol) was placed in an N_2 atmosphere and dissolved in 10 ml toluene immediately after purification. A solution of 4-TolMgBr in Et_2O (6.30 ml, 6.30 mmol, 1.0 M) was added via a syringe with stirring. The solution was then heated at reflux for 14 h. Distilled H_2O (20 ml) was added dropwise to destroy remaining 4-TolMgBr, forming a white precipitate. 1M HCl (75 ml) was added to dissolve precipitates; Et_2O (100 ml) was added to dissolve organic components. The phases were separated, and the aqueous phase was extracted with Et_2O (3 × 75 ml). Organic washings were combined, dried with $MgSO_4$, and evaporated. The resulting mixture was purified by FC (7 × 18 cm Silica gel eluted with CH_2Cl_2/toluene, 8:2) to give 4-tolylgermane **3** as a dark brown oil (0.493 g, 76%). R_f 0.42 (CH_2Cl_2/toluene, 8:2); ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.48 (6H, s, Ge(CH_3)$_2$), 1.36 (3H, t, *J* 7.0, CH_3CH_2O), 1.38 (2H, m, $ArCH_2CH_2Ge$), 2.46 (3H, s, $ArCH_3$), 2.78 (2H, m, $ArCH_2CH_2Ge$), 3.70 (2H, q, *J* 7.0, CH_3CH_2O), 3.87 (2H, t, *J* 5.0, OCH_2CH_2OAr), 4.19 (2H, t, *J* 5.0, OCH_2CH_2OAr), 6.95 (2H, d, *J* 8.5, OCCHCHCCH$_2$), 7.20 (2H, d, *J* 8.5, OCCHCHCCH$_2$), 7.30 (2H, d, *J* 8.0, GeCCHCHCCH$_3$), 7.49 (2H, d, *J* 8.0, GeCCHCHCCH$_3$); ^{13}C NMR (63 MHz, $CDCl_3$) δ −3.5 (2q), 15.3 (q), 18.2 (t), 21.5 (q), 30.4 (t), 66.9 (t), 67.6 (t), 69.2 (t), 114.7 (2d), 128.8 (2d), 129.4 (2d), 133.4 (2d), 137.1 (s), 137.7 (s), 138.1 (s), 157.1 (s); IR (neat) ν_{max} 2927, 2869, 1611, 1510, 1246, 1125, 1089, 1067, 795, 593 cm^{-1}; MS (EI$^+$) *m/z* 388 (M$^+$, 7%), 195 (100%); HRMS calcd for $C_{21}H_{30}O_2{}^{74}Ge$ 388.1458, found 388.1457, Δ −0.16 ppm; analysis for $C_{21}H_{30}O_2Ge$, expected C 65.17%, H 7.81%, found C 65.14%, H 8.07%.

4-{2-[Tri-(4-methylphenyl)germyl]ethyl}phenol 4a

4-Bromotoluene (13.6 g, 79.6 mmol) dissolved in THF (10 ml) was added to a suspension of magnesium turnings (1.99 g, 82.0 mmol) in THF (60 ml). The solution was briefly warmed by hand to initiate the reaction and then allowed to stir for 1 h at RT. 4-(2-Trichlorogermylethyl)phenol[61] (**1**, 2.02 g, 6.7 mmol) was dissolved in THF (10 ml) and then added to the solution of Grignard reagent, the resulting mixture was refluxed for 22 h. Distilled water was carefully added dropwise to destroy excess Grignard and aqueous HCl (1.0 M, 75 ml) was added to dissolve inorganics. The solution was then extracted with Et_2O (3 × 70 ml) after which the organic washings were combined, dried with $MgSO_4$ and concentrated *in vacuo*. Purification by FC (8 × 10 cm silica gel, eluted with petrol/EtOAc, 19:1 → petrol/EtOAc, 9:1) to give tri-(4-tolyl)germylphenol **4a** as a clear colourless oil (2.48 g, 79%). R_f 0.42 (petrol/EtOAc, 9:1); **^{1}H NMR** (250 MHz, $CDCl_3$) δ 1.80 (2H, m, CH_2CH_2Ge), 2.39 (9H, s, $ArCH_3$), 2.77 (2H, m, CH_2CH_2Ge), 4.69 (1H, s, O*H*), 6.74 (2H, d, *J* 8.5, HOCCHCHC), 7.07 (2H, d, *J* 8.5, HOCCHCHC), 7.22 (6H, d, *J* 8.0, GeCCHCHCCH$_3$), 7.41 (6H, d, *J* 8.0, GeCCHCHCCH$_3$); ^{13}C NMR (63 MHz, $CDCl_3$) δ 16.4 (t), 21.5 (3q), 30.3 (t), 115.1 (2d), 128.9 (2d), 129.1 (6d), 133.5 (3s), 134.9 (6d), 137.2 (s), 138.7 (3s), 153.5 (s); IR (neat) ν_{max} 3402, 2920, 1512, 1228, 1087, 799 cm^{-1}; MS (EI$^+$) *m/z* 468 (M$^+$, 2%), 376 (19%), 347 (100%), 255 (10%), 181 (17%), 165 (21%), 91 (32%); HRMS calcd for $C_{29}H_{30}{}^{74}GeO$ 468.1509, found 468.1518, Δ −2.0 ppm; analysis for $C_{29}H_{30}GeO$ expected C 74.56%, H 6.47%, found C 74.20%, H 6.55%.

4-{2-[Tri-(4-methylphenyl)germyl]ethyl}phenyl-(2-ethoxyethyl)ether 4b

Caesium carbonate (1.50 g, 4.56 mmol), TBAI (0.128 g, 0.345 mmol) and 2-chloroethyl ethyl ether (1.8 ml, 1.78 g, 16.4 mmol) were added to a solution of tri-(4-tolyl)germylphenol **4a** (1.50 g, 3.21 mmol) in MeCN (50 ml), and the resulting mixture heated at 80 °C for 16 h. The crude reaction mixture was then partitioned between Et_2O (75 ml) and aqueous HCl (1 M, 75 ml), and the aqueous layer further extracted with Et_2O (2 × 25 ml). The organic washings were combined, dried with $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was then filtered through silica gel (3 × 6 cm, petrol/EtOAc, 85:15), before being concentrated to give tri-(4-tolyl)germane **4b** as a clear colourless oil (1.56 g, 90%). R_f 0.65 (petrol/EtOAc, 9:1); ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.28 (3H, t, *J* 7.0, CH_3CH_2O), 1.81 (2H, m, CH_2CH_2Ge), 2.39

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(9H, s, $ArCH_3$), 2.78 (2H, m, CH_2CH_2Ge), 3.63 (2H, q, *J* 7.0, CH_3CH_2O), 3.80 (2H, t, *J* 5.0, OCH_2CH_2OAr), 4.12 (2H, t, *J* 5.0, OCH_2CH_2OAr), 6.85 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 7.11 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 7.22 (6H, d, *J* 8.0, $GeCCHCHCCH_3$), 7.42 (6H, d, *J* 8.0, $GeCCHCHCCH_3$); ^{13}C NMR (63 MHz, $CDCl_3$) □ 15.3 (q), 16.4 (t), 21.5 (3q), 30.3 (t), 66.9 (t), 67.5 (t), 69.1 (t), 114.6 (2d), 128.7 (2d), 129.1 (6d), 133.6 (3s), 135.0 (6d), 137.2 (s), 138.7 (3s), 157.0 (s); IR (neat) ν_{max} 2921, 1509, 1245, 1124, 1086, 798 cm^{-1}; MS (EI^+) *m/z* 540 (M^+, 4%), 448 (10%), 347 (100%), 271 (15%), 255 (9%), 165 (16%), 91 (20%); HRMS calcd for $C_{33}H_{38}{}^{74}GeO_2$ 540.2084, found 540.2082, Δ 0.4 ppm; analysis for $C_{33}H_{38}{}^{74}GeO_2$ expected C 73.50%, H 7.10%, found C 73.43%, H 7.51%.

4-{2-[Chlorodi-(4-methylphenyl)germyl]ethyl} phenyl-(2-ethoxyethyl)ether 8

Tri-(4-tolyl)germane **4b** (0.275 g, 0.510 mmol) was dissolved in a solution of MSA in CH_2Cl_2 (0.25 M, 12.3 ml) and stirred at RT for 55 min. The reaction mixture was added dropwise to distilled water (10 ml) and shaken, the phases were separated and the aqueous layer extracted with CH_2Cl_2 (2 × 20 ml). The combined organic layers were shaken with conc. HCl (50 ml), phases separated and the acid layer extracted with CH_2Cl_2 (2 × 20 ml). The organic washings were combined, dried with $MgSO_4$, filtered and concentrated *in vacuo* to give chlorodi-(4-tolyl)germane **8** as a pale brown oil (0.237 g, 96%). ^1H NMR (250 MHz, $CDCl_3$) δ 1.25 (3H, t, *J* 7.0, CH_3CH_2O), 1.87–1.94 (2H, m, CH_2CH_2Ge), 2.39 (6H, s, $ArCH_3$), 2.81–2.88 (2H, m, CH_2CH_2Ge), 3.61 (2H, q, *J* 7.0, CH_3CH_2O), 3.79 (2H, t, *J* 5.0, OCH_2CH_2OAr), 4.09 (2H, t, *J* 5.0, OCH_2CH_2OAr), 6.82 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 7.09 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 7.24 (4H, d, *J* 8.0, $GeCCHCHCCH_3$), 7.47 (4H, d, *J* 8.0, $GeCCHCHCCH_3$); ^{13}C NMR (63 MHz, $CDCl_3$) δ 15.2 (q), 21.1 (t), 21.5 (2q), 29.1 (t), 66.8 (t), 67.5 (t), 69.0 (t), 114.7 (2d), 128.8 (2d), 129.4 (4d), 132.3 (2s), 133.4 (4d), 135.6 (s), 140.3 (2s), 157.2 (s); IR (neat) ν_{max} 2923, 1610, 1511, 1244, 1124, 910, 799, 733 cm^{-1}; MS (EI^+) *m/z* 484 (M^+, 6%), 291 (32%), 248 (35%), 192 (100%), 91 (22%), 45 (39%); HRMS calcd for $C_{26}H_{31}Cl^{74}GeO_2$ 484.1224, found 484.1229, δ − 0.9 ppm.

4-{2-[Methyldi-(4-methylphenyl)germyl]ethyl} phenyl-(2-ethoxyethyl)ether 9

A solution of methyl magnesium iodide in Et_2O (1 ml, 3 mmol, 3.0 M) was added to a solution of chlorodi-4-tolylgermane **8** (0.233 g, 0.481 mmol) dissolved in THF (9 ml), and the resulting mixture heated at reflux for 22 h. Distilled water was added dropwise to destroy excess Grignard reagent, and the mixture then partitioned between Et_2O (5 ml) and aqueous HCl (5 ml), the acid layer was further extracted with Et_2O (2 × 5 ml). The organic layers were combined and washed with saturated aqueous $Na_2S_2O_3$ solution (5 ml), before being dried with $MgSO_4$, filtered and concentrated *in vacuo* to give methyldi-(4-tolyl)germane **9** as a clear colourless oil (0.207 g, 93%). R_f 0.56 (petrol/EtOAc, 9:1); ^1H NMR (250 MHz, $CDCl_3$) δ 0.57 (3H, s, $GeCH_3$), 1.24 (3H, t, *J* 7.0, CH_3CH_2O), 1.52 (2H, m, CH_2CH_2Ge), 2.34 (6H, s, $ArCH_3$), 2.67 (2H, m, CH_2CH_2Ge), 3.59 (2H, q, *J* 7.0, CH_3CH_2O), 3.77 (2H, t, *J* 5.0, OCH_2CH_2OAr), 4.08 (2H, t, *J* 5.0, OCH_2CH_2OAr), 6.82 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 7.06 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 7.17 (4H, d, *J* 8.0, $GeCCHC_HCCH_3$), 7.37 (4H, d, *J* 8.0, $GeCCHCHCCH_3$); ^{13}C NMR (63 MHz, $CDCl_3$) δ − 5.0 (q), 15.2 (q), 16.9 (t), 21.5 (2q), 30.2 (t), 66.8 (t), 67.5 (t), 69.1 (t), 114.6 (2d), 128.7 (2d), 129.0 (4d), 134.0 (4d), 135.6 (2s), 137.0 (s), 138.4 (2s), 156.9 (s); IR (neat) ν_{max} 2922, 1510, 1245, 1125, 799 cm^{-1}; MS (EI^+) *m/z* 464 (M^+, 6%), 449 (6%), 347 (41%), 271 (100%), 195 (54%), 181 (49%), 165 (33%), 91 (44%); HRMS calcd for $C_{27}H_{34}{}^{74}GeO_2$ 464.1771, found 464.1785, Δ − 3.2 ppm; analysis for $C_{27}H_{34}GeO_2$ expected C 70.02%, H 7.40%, found C 70.31%, H 7.76%.

4-{2-[Chloromethyl-(4-methylphenyl)germyl] ethyl}phenyl-(2-ethoxyethyl)ether 10

A solution of MSA in CH_2Cl_2 (0.23 M, 6 ml) was added to methyldi-(4-tolyl)germane **9** (0.122 g, 0.262 mmol) and the mixture stirred for 30 min before being added dropwise to saturated aqueous $NaHCO_3$ (10 ml). The aqueous layer was then extracted with CH_2Cl_2 (2 × 10 ml), and the combined organic washings treated with conc. HCl (20 ml), the phases were separated again, and the acid layer was further extracted with CH_2Cl_2 (2 × 10 ml). The combined organic layers were then dried with $MgSO_4$, filtered and concentrated *in vacuo* to give chloromethyl-4-tolylgermane **10** as a pale brown oil (0.101 g, 94%). ^1H NMR (250 MHz, $CDCl_3$) δ 0.79 (3H, s, $GeCH_3$), 1.26 (3H, t, *J* 7.0, CH_3CH_2O), 1.71 (2H, m, CH_2CH_2Ge), 2.39 (3H, s, $ArCH_3$), 2.84 (2H, m, CH_2CH_2Ge), 3.61 (2H, q, *J* 7.0, CH_3CH_2O), 3.79 (2H, t, *J* 5.0, OCH_2CH_2OAr), 4.11 (2H, t, *J* 5.0, OCH_2CH_2OAr), 6.85 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 7.10 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 7.25 (2H, d, *J* 8.0, $GeCCHCHCCH_3$), 7.45 (2H, d, *J* 8.0, $GeCCHCHCCH_3$); ^{13}C NMR (63 MHz, $CDCl_3$) δ 1.7 (q), 15.2 (q), 21.5 (q), 22.4 (t), 29.1 (t), 66.9 (t), 67.5 (t), 69.0 (t), 114.7 (2d), 128.9 (2d), 129.4 (2d), 132.6 (2d), 134.2 (s), 135.2 (s), 140.2 (s), 157.2 (s); IR (neat) ν_{max} 2925, 2868, 1610, 1511, 1246, 1197, 1125, 797 cm^{-1}; MS (EI^+) *m/z* 408 (M^+, 10%), 357 (3%), 301 (3%), 215 (24%), 192 (100%), 120 (16%), 91 (17%), 73 (27%), 45 (69%); HRMS calcd for $C_{20}H_{27}Cl^{74}GeO_2$ 408.0911, found 408.0918, δ − 1.6 ppm.

4-{2-[Dichloro-(4-methylphenyl)germyl]ethyl} phenyl-(2-ethoxyethyl)ether 6b

A solution of MSA in CH_2Cl_2 (6.04M, 12 ml) was added to tri-(4-tolyl)germane **4b** (0.141 g, 0.261 mmol) and stirred at RT for 3 h, before being added to distilled water (20 ml). The phases were separated and the aqueous layer extracted with CH_2Cl_2 (2 × 20 ml). The combined organic washings were then shaken with conc. HCl (50 ml), before being separated and the acid layer further extracted with CH_2Cl_2 (2 × 10 ml). The organic washings were combined, dried with $MgSO_4$, filtered and concentrated *in vacuo* to give dichloro-4-tolylgermane **6b** as a pale brown oil (0.109mg, 97%). ^1H NMR (250 MHz, $CDCl_3$) δ 1.26 (3H, t, *J* 7.0, CH_3CH_2O), 2.09 (2H, m, CH_2CH_2Ge), 2.40 (3H, s, $ArCH_3$), 2.96 (2H, m,

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CH_2CH_2Ge), 3.62 (2H, q, *J* 7.0, CH_3CH_2O), 3.79 (2H, t, *J* 5.0, OCH_2CH_2OAr), 4.10 (2H, t, *J* 5.0, OCH_2CH_2OAr), 6.84 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 7.11 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 7.27 (2H, d, *J* 8.5, $GeCCHCHCCH_3$), 7.47 (2H, d, *J* 8.5, $GeCCHCHCCH_3$); ^{13}C NMR (63 MHz, $CDCl_3$) $\dot{\delta}$ 15.2 (q), 21.6 (q), 27.7 (t), 28.5 (t), 66.9 (t), 67.5 (t), 69.0 (t), 114.8 (2d), 129.0 (2d), 129.6 (2d), 132.0 (2d), 132.2 (s), 133.7 (s), 142.0 (s), 157.5 (s); IR (neat) ν_{max} 2975, 2926, 2870, 1512, 1248, 1125, 800 cm^{-1}; MS (EI^+) *m/z* 428 (M^+, 16%), 235 (10%), 192 (33%), 120 (39%), 91 (45%), 73 (49%), 45 (100%); HRMS calcd for $C_{19}H_{24}Cl_2{}^{74}GeO_2$ 428.0365, found 428.0352, δ 3.0 ppm.

4-{2-[Tri-(4-methoxyphenyl)germyl]ethyl} phenol 5a

4-Bromoanisole (11.2 g, 0.0599 mol) was added to a suspension of magnesium turnings (1.54 g, 0.0632 mol) in THF (130 ml), and the resulting solution stirred until it had cooled to RT. A solution of 4-(2-trichlorogermylethyl)phenol[61] (**1**, 3.00 g, 10.0 mmol) dissolved in THF (20 ml) was then added to the Grignard reagent and heated at reflux for 17 h. The reaction mixture was quenched with methanol (20 ml) and then partitioned between distilled water (100 ml) and EtOAc (3 × 100 ml). Acid was not used in the work-up to avoid cleavage of the germanium-aryl bonds. The organic washings were dried with $MgSO_4$, filtered and concentrated *in vacuo*. Purification with a SPE cartridge (50 g, petrol → petrol/EtOAc, 19:1 → petrol/EtOAc, 9:1 → petrol/EtOAc, 8:2 → petrol/EtOAc, 7:3) gave tri-(4-anisyl)phenol **5a** as a clear colourless oil (3.82 g, 7.42 mmol, 74%). R_f 0.21 (petrol/EtOAc, 8:2); ^1H NMR (250 MHz, $CDCl_3$) δ 1.77 (2H, m, CH_2CH_2Ge), 2.76 (2H, m, CH_2CH_2Ge), 3.84 (9H, s, $ArOCH_3$), 6.74 (2H, d, *J* 8.0, $HOCCHCHCCH_2$), 6.95 (6H, d, *J* 8.5, $GeCCHCHCOCH_3$), 7.05 (2H, d, *J* 8.0, $HOCCHCHCCH_2$), 7.41 (6H, d, *J* 8.5, $GeCCHCHCOCH_3$); ^{13}C NMR (63 MHz, $CDCl_3$) □̇ 16.7 (t), 30.3 (t), 55.1 (3q), 114.0 (6d), 115.2 (2d), 128.2 (3s), 128.9 (2d), 136.2 (6d), 137.0 (s), 153.6 (s), 160.3 (3s); IR (neat) ν_{max} 3417, 2931, 1592, 1498, 1279, 1246, 1179, 1091, 1029, 816, 793 cm^{-1}; MS (EI^+) *m/z* 516 (M^+, 1%), 395 (100%), 347 (13%), 271 (18%), 181 (17%), 120 (17%), 107 (16%), 91 (31%); HRMS calcd for $C_{29}H_{30}{}^{74}GeO_4$ 516.1356, found 516.1358, Δ − 0.3 ppm; analysis for $C_{21}H_{30}GeO_2$ expected C 67.72%, H 5.87%, found C 67.41%, H 5.78%.

4-{2-[Tri-(4-methoxyphenyl)germyl]ethyl} phenyl-2-ethoxyethylether 5b

Caesium carbonate (2.17 g, 6.65 mmol), TBAI (0.157 g, 0.42 mmol) and 2-chloroethyl ethyl ether (2.5 ml, 2.47 g, 22.8 mmol) were added to a solution of tri-(4-anisyl)phenol **5a** (2.33 g, 4.52 mmol) dissolved in MeCN (75 ml), and the resulting solution heated at 80 °C for 15 h. The crude reaction mixture was then partitioned between distilled water (100 ml) and EtOAc (2 × 100 ml, 50 ml). The organic washings were combined, dried with $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was then filtered through silica (5 g SPE cartridge, petrol/EtOAc, 9:1), before being concentrated to give tri-(4-anisyl)germane **5b** as a pale yellow oil (2.06 g, 3.51 mmol, 78%). R_f 0.44 (petrol/EtOAc, 8:2); ^1H NMR (250 MHz, $CDCl_3$) δ 1.25 (3H, t, *J* 7.0, CH_3CH_2O), 1.76 (2H, m, CH_2CH_2Ge), 2.75 (2H, m, CH_2CH_2Ge), 3.61 (2H, q, *J* 7.0, CH_3CH_2O), 3.79 (2H, t, *J* 5.0, OCH_2CH_2OAr), 3.83 (9H, s, $ArOCH_3$), 4.10 (2H, t, *J* 5.0, OCH_2CH_2OAr), 6.83 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 6.93 (6H, d, *J* 8.5, $GeCCHCHCOCH_3$), 7.08 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 7.40 (6H, d, *J* 8.5, $GeCCHCHCOCH_3$); ^{13}C NMR (63 MHz, $CDCl_3$) $\dot{\delta}$ 15.2 (q), 16.7 (t), 30.3 (t), 55.1 (3q), 66.8 (t), 67.5 (t), 69.0 (t), 114.0 (6d), 114.6 (2d), 128.2 (3s), 128.7 (2d), 136.1 (6d), 137.1 (s), 153.6 (s), 160.3 (3s); IR (neat) ν_{max} 2929, 1592, 1511, 1290, 1253, 1181, 1094, 1027, 823 cm^{-1}; MS (EI^+) *m/z* 588 (M^+, 2%), 480 (8%), 395 (100%), 347 (16%), 271 (66%), 181 (31%), 91 (46%); HRMS calcd for $C_{33}H_{38}{}^{74}GeO_5$ 588.1931, found 588.1939, Δ − 1.4 ppm; analysis for $C_{33}H_{38}GeO_5$ expected C 67.5%, H 6.5%, found C 67.1%, H 6.6%.

4-{2-[Dichloro-(4-methoxyphenyl)germyl]ethyl} phenyl-2-ethoxyethylether 7b

Tri-(4-anisyl)germane **5b** (2.04 g, 3.47 mmol) was dissolved in CH_2Cl_2 (27 ml). To the resulting solution aqueous HCl (1 M, 4.5 ml, 4.5 mmol) was added dropwise over 2 min with vigorous stirring. After 5 min, conc. HCl (53 ml, 0.530mol) was added, dropwise to begin with, to give a vivid violet coloured organic layer. The resulting biphasic mixture was vigorously stirred at RT for 3 h, whereupon the organic layer was pipetted out and filtered through a hydrophobic frit. The acid layer was shaken with further CH_2Cl_2 (2 × 20 ml), which was also removed and filtered through a hydrophobic frit, and the combined organic washings concentrated *in vacuo*, with further volatiles removed under a high vacuum to give dichloro-4-anisylgermane **7b** as a pale brown oil (1.27 g, 2.86 mmol, 82%). ^1H NMR (250 MHz, $CDCl_3$) $\dot{\delta}$ 1.26 (3H, t, *J* 7.0, CH_3CH_2O), 2.09 (2H, m, CH_2CH_2Ge), 2.96 (2H, m, CH_2CH_2Ge), 3.61 (2H, q, *J* 7.0, CH_3CH_2O), 3.79 (2H, t, *J* 5.0, OCH_2CH_2OAr), 3.85 (3H, s, $ArOCH_3$), 4.10 (2H, t, *J* 5.0, OCH_2CH_2OAr), 6.84 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 6.97 (2H, d, *J* 8.5, $GeCCHCHCOCH_3$), 7.11 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 7.49 (2H, d, *J* 8.5, $GeCCHCHCOCH_3$); ^{13}C NMR (63 MHz, $CDCl_3$) $\dot{\delta}$ 15.2 (q), 27.8 (t), 28.6 (t), 55.3 (q), 66.9 (t), 67.5 (t), 69.0 (t), 114.5 (2d), 114.8 (2d), 126.5 (s), 129.0 (2d), 133.7 (2d), 157.5 (s), 162.2 (s), one quaternary carbon not observed; IR (neat) ν_{max} 2930, 1592, 1512, 1290, 1253, 1181, 1094, 1027, 824, 795 cm^{-1}; MS (EI^+) *m/z* 444 (M^+, 18%), 251 (5%), 192 (68%), 120 (41%), 107 (100%), 92 (74%), 78 (46%), 45 (78%); HRMS calcd for $C_{19}H_{24}Cl_2{}^{74}GeO_3$ 444.0314, found 444.0302, δ 2.9ppm.

Cross-coupling reactions (Table 1, entries 3 and 4, method A)

Entry 3: 4-methyl-3′,5′-bis(trifluoromethyl)biphenyl ***11a***[97]

Method A: according to the method of Hiyama,[81] powdered sodium hydroxide (0.0464 g, 1.16 mmol) was added to dichlorotolylgermane **6b** (0.101 g, 0.235 mmol) dissolved in THF (1 ml), and then stirred at RT for 3 h. Palladium(II) acetate

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(0.0118 g, 0.0526 mmol) and triphenylphosphine (0.0256 g, 0.0976 mmol) were dissolved in THF (2 ml) and stirred at RT for 1 h. A 1 ml aliquot of the resulting catalyst solution was then added to the solution of hydrolysed chlorogermane, along with 3,5-bis(trifluoromethyl)bromobenzene (34 μl, 0.057 g, 0.195 mmol). The reaction mixture was then heated at reflux for 24 h, before being partitioned between Et_2O (3 × 10 ml) and distilled water (10 ml). Organic washings were combined, dried with $MgSO_4$, filtered and concentrated *in vacuo*, before being purified on a silica SPE cartridge (5 g, cyclohexane) to give 4-methyl-3′, 5′-bis(trifluoromethyl)biphenyl **11a**[97] as a clear liquid (0.0189 g, 32%). R_f 0.65 (cyclohexane); ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.44 (3H, s, ArC*H*$_3$), 7.33 (2H, d, *J* 8.0, CH_3CC*H*CHCAr), 7.52 (2H, d, *J* 8.0, CH_3CCHC*H*CAr), 7.84 (1H, s), CF_3CC*H*CCF_3, 8.01 (2H, s, ArCC*H*CCF_3); **MS** *m/z* (EI$^+$) 304 (M$^+$, 91%), 285 (19%), 235 (66%), 215 (39%), 165 (100%), 91 (66%), 69 (25%).

Entry 4: 4-Acetyl-4′-methylbiphenyl ***11b***[98]

Using *method A*, powdered sodium hydroxide (0.0556 g, 1.39 mmol), dichlorotolylgermane **6b** (0.100 g, 0.234 mmol), palladium(II) acetate (0.0104 g, 0.0463 mmol), triphenylphosphine (0.0230 g, 0.0876 mmol) and 4-bromoacetophenone (0.0421 g, 0.211 mmol) followed by mass-directed automated preparative LC/MS gave 4-acetyl-4′-methylbiphenyl **11b**[98] as a white powder (0.0124 g, 28%): R_f 0.41 (petrol/EtOAc, 9 : 1); ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.41 (3H, s, CH_3CAr), 2.64 (3H, sCH_3COAr), 7.28 (2H, d, *J* 8.0, CH_3CC*H*CHCAr), 7.54 (2H, d, *J* 8.0, CH_3CCHC*H*CAr), 7.67 (2H, d, *J* 8.0, ArCC*H*CHCCOCH_3), 8.02 (2H, d, *J* 8.0, ArCCHC*H*CCOCH_3); MS (ESI$^+$) *m/z* 211 [(M + H)$^+$, 100%]; (EI$^+$) *m/z* 210 (M$^+$, 42%), 195 (100%), 165 (25%), 152 (39%); LC R_t 3.49 min; m.p. 116.9–118.3 °C (cf. 114–115 °C[99], 121–122 °C[100]).

Optimization of cross-coupling conditions (method A → method B)

The cross-coupling reaction between dichlorogermane **6b** and 4-bromoacetophenone to give 4-acetyl-4′-methylbiphenyl **11b** was optimized by in an array format using a Radleys greenhouse with ESI LC/MS analysis of the crude product mixtures.

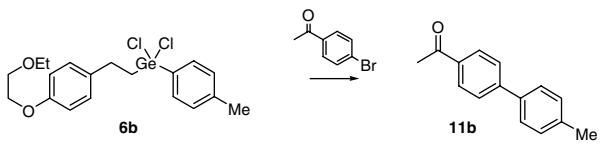
Agilent 1100 HPLC; Fisons VG Platform mass spectrometer. Ionization mode: ESI +ve and ESI −ve. Column: Supelcosil LC ABZ + PLUS (3.3 cm × 4.6 mm, 3 μm). Solvent A: 0.1% v/v HCO_2H and 0.01 M NH_4OAc in water. Solvent B: 0.05% v/v HCO_2H and 5% v/v water in MeCN. Temperature: room temperature. Gradient: 0 min 0%B, 0.7 min 0% B, 4.2 min 100% B, 5.3 min 100% B, 5.5 min 0% B. Flow rate: 3 ml/min. Run time: 5.5 min. Injection volume: 5 μl. Detection: UV between 215 and 330 nm.

Unsurprisingly dichlorogermane **6b** was not observed directly by LC/MS, but was ionized to give an ion corresponding to the protonated dihydroxygermane hydrolysis product. As both dichlorogermane **6b** and the 4-bromoacetophenone co-eluted under the LC conditions the UV peak area of the product **11b** {R_t 3.49 min, *m/z* 211 [M + H$^+$]} was compared with the combined UV peak area of **6b** (R_t 2.94 min, *m/z* 392 [hydrolysis product + H$^+$]) and 4-bromoacetophenone (R_t 2.89 min, not ionized). Using method A this reaction gave a yield of 28% (Table 1, entry 4).

Screen 1

Five sets of activator conditions and seven ligands were screened maintaining other conditions as for method A (Table 2). It was concluded that potassium fluoride at 120 °C was the most successful activator and that P(4-$C_6H_4F)_3$, dppp and IMes· HCl were superior ligands to PPh_3.

Table 2. Activator and ligand optimisation. Reagents and conditions: (i) activator (6 equiv.), THF or DMF, RT, 3 h; (ii) 4-bromoacetophenone, $Pd(OAc)_2$ (5 mol%), ligand (10 mol%), 60 or 120 °C, 24 h



	NaOH (s) THF 60 °C	NaOH (aq) THF 60 °C	NaOH (s) DMF 120 °C	NaOH (aq) DMF 120 °C	KF (s) DMF 120 °C[a]	δ
PPh_3	—	0.12	0	0	1.19 (11%)	1.32
P(2-Tol)$_3$	—	0.25	1.76	0	0.29	2.30
P(2-furyl)$_3$	—	0.12	1.20	0	0.98	2.29
P(4-$C_6H_4F)_3$	—	0	0.59	0	1.92 (34%)	2.50
Dppp[b]	—	0.15	0.95	0	2.21 (20%)	3.30
Dppf[b]	—	0.20	0	0	1.09	1.29
IMes·HCl[b]	—	0	0	0	2.11 (38%)	2.11
No ligand	—	0	0.40	0	1.65	2.05
δ		0.84	4.90	0.00	11.44	

[a] Isolated yields in brackets; [b] 5mol% of co-catalyst used.

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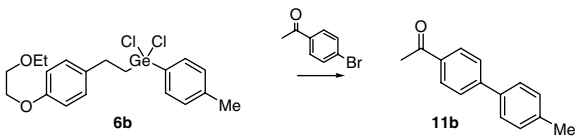
Table 3. Palladium source optimisation. Reagents and conditions: (i) KF (6 equiv.), DMF, RT, 3 h; (ii) 4-bromoacetophenone (**3b**), Pd source (5 mol%), ligand (10mol%), 120 °C, 24 h



	$Pd(OAc)_2$	$PdCl_2(MeCN)_2$[a]	APC dimer	$Pd_2(dba)_3$	$Pd(PPh_3)_4$	δ
PPh_3	1.26	2.48	0.71	1.26	1.35[b]	7.06
$P(4\text{-}C_6H_4F)_3$	1.53	0.48	0.82	1.52	1.65	6.00
Dppp[c]	2.52	2.73 (60)	0.89	1.34	1.81	9.30
IMes·HCl[c]	2.15	2.19	1.88	0.22	0.98	7.42
δ	7.47	7.87	4.30	4.35	5.79	

[a] Isolated yield in brackets; [b] excess PPh_3 was not added; [c] 5mol% of ligand used.

Screen 2

Five palladium sources were investigated next (Table 3). It was concluded that dppp and $PdCl_2(MeCN)_2$ was the best ligand/palladium source combination and so these conditions were adopted as method B (see below).

Cross-coupling reactions continued (Table 1, entries 5–13, method B)

*Entry 5: 4-acetyl-4′-methylbiphenyl **11b***[98]

Method B: dichloroarylgermane **6b** (0.112 g, 0.262 mmol) was dissolved in DMF (1 ml) and stirred with potassium fluoride (0.0926, 1.59 mmol) for 3 h at RT to furnish the activated arylgermane. During this time $PdCl_2(MeCN)_2$ (0.0097 g, 0.0374 mmol) and dppp (0.0129 g, 0.0313 mmol) were dissolved in DMF (1.5 ml) and stirred at RT for 1 h to give the active catalytic species. The 4-bromobenzophenone (0.0441 g, 0.222 mmol) and a 1 ml portion of the catalyst solution were then added to the arylgermane solution and the resulting mixture heated at 120 °C for 24 h. The crude reaction mixture was partitioned between distilled water (5 ml) and CH_2Cl_2 (5 ml) and filtered through a hydrophobic frit, which was rinsed with further CH_2Cl_2 (2 ml). The combined organics were washed with further water (5 ml) and filtered through a second frit, which was again rinsed with CH_2Cl_2 (2 ml). The organics were again combined and concentrated *in vacuo* to give the crude reaction mixture. Purification using Silica gel SPE cartridge (5 g, petrol → petrol/EtOAc, 97 : 3) gave 4-acetyl-4′-methylbiphenyl **11b** as a white powder (0.0276 g, 59%). Analytical data as above.

*Entry 6: 4-methyl-3′,5′-bis(trifluoromethyl)biphenyl **11a***[97]

Using method B, powdered potassium fluoride (0.0928, 1.60 mmol), dichlorotolylgermane **6b** (0.1012 g, 0.236 mmol), 3,5-bis(trifluoromethyl)bromobenzene (34.3 µl, 0.0583 g, 0.199 mmol), and 1 ml of a solution of $PdCl_2(MeCN)_2$ (0.0370 g, 0.143 mmol) and dppp (0.0574 g, 0.139 mmol) in DMF (1.5 ml) following purification on a silica SPE cartridge (5 g, cyclohexane) gave 4-methyl-3′, 5′-bis(trifluoromethyl)biphenyl **11a**[97] as a clear liquid (0.0378 g, 63%). Analytical data as above.

*Entry 7: 1-(4-methylphenyl)naphthalene **11c***[101]

Using method B, powdered potassium fluoride (0.0806 g, 1.39 mmol), dichlorotolylgermane **6b** (0.0953 g, 0.223 mmol), 1-bromonaphthalene (25 µl, 0.0372 g, 0.180 mmol), and 1 ml of a solution of $PdCl_2(MeCN)_2$ (0.0370 g, 0.143 mmol) and dppp (0.0574 g, 0.139 mmol) in DMF (1.5 ml) following purification using silica gel SPE cartridge (5 g, cyclohexane) gave 1-(4-methylphenyl)naphthalene **11c**[101] as a clear colourless film (0.0311 g, 79%). R_f 0.26 (cyclohexane); ^1H NMR (250 MHz, $CDCl_3$) δ 2.48 (3H, s, $ArCH_3$), 7.31–7.34 (2H, m, Ar CH′s), 7.40–7.57 (6H, m, Ar CH′s), 7.84–7.96 (3H, m, Ar CH′s); MS (EI^+) m/z 218 (M^+, 100%), 203 (73%), 189 (11%), 108 (27%), 95 (28%).

*Entry 8: 4-methoxybiphenyl **11d***[102]

Using method B, powdered potassium fluoride (0.0889 g, 1.53 mmol), dichloroanisylgermane **7b** (0.0997 g, 0.225 mmol), bromobenzene (20 µl, 0.0298 g, 0.190 mmol), and 1 ml of a solution of $PdCl_2(MeCN)_2$ (0.0277 g, 0.107 mmol) and dppp (0.0448 g, 0.109 mmol) in DMF (1.5 ml) followed by purification using silica gel SPE cartridge (5 g, cyclohexane) gave 4-methoxybiphenyl **11d**[102] as a white powder (0.0125 g, 36%). R_f 0.26 (cyclohexane); ^1H NMR (250 MHz, $CDCl_3$) δ 3.87 (3H, s, $ArOCH_3$), 6.98–7.01 (2H, m, $CH_3OCCHCHCAr$), 7.31–7.34 (1H, m, $ArCCHCHCH$), 7.40–7.46 (2H, m, Ar CH′s), 7.53–7.59 (4H, m, Ar CH′s); MS (EI^+) m/z 184 (M^+, 100%), 169 (57%), 141 (57%), 115 (46%), 76 (8%); m.p. 86.7–88.2 °C (cf. 87 °C[103]).

*Entry 9: 4-methoxy-3′-trifluoromethylbiphenyl **11e***[104]

Using method B, powdered potassium fluoride (0.0872 g, 1.50 mmol), dichloroanisylgermane **7b** (0.0971 g, 0.219 mmol), 3-bromobenzotrifluoride (26 µl, 0.0424 g, 0.188 mmol), and 1 ml of a solution of $PdCl_2(MeCN)_2$ (0.0277 g, 0.107 mmol) and dppp (0.0448 g, 0.109 mmol) in DMF (5 ml) following

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purification using silica gel SPE cartridge (5 g, cyclohexane) gave 4-methoxy-3′-trifluoromethylbiphenyl **11e**[104] as a clear colourless oil (0.0246 g, 52%): R_f 0.27 (cyclohexane); ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.87 (3H, s, ArOCH_3), 6.98–7.02 (2H, m, CH_3OCC*H*CHCAr), 7.52–7.56 (4H, m, Ar CH′s), 7.71–7.74 (1H, m, Ar CH), 7.79 (1H, s, ArCC*H*CCF$_3$); **MS** (EI$^+$) m/z 252 (M$^+$, 100%), 237 (41%), 209 (69%), 183 (17%), 139 (15%).

*Entry 10: 4-methoxy-3′,5′-bis(trifluoromethyl) biphenyl **11f***

Using method B, powdered potassium fluoride (0.0863 g, 1.49 mmol) dichloroanisylgermane **7b** (0.114 g, 0.257 mmol), 3,5-bis(trifluoromethyl)bromobenzene (34 µl, 0.0578 g, 0.197 mmol), and 1 ml of a solution of $PdCl_2(MeCN)_2$ (0.0160 g, 0.0617 mmol) and dppp (0.0245 g, 0.0594 mmol) in DMF (3 ml) following purification using silica gel SPE cartridge (5 g, cyclohexane) gave 4-methoxy-3′, 5′-bis(trifluoromethyl)biphenyl **11f** as a clear colourless oil (0.0451 g, 71%). R_f 0.22 (cyclohexane); ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.89 (3H, s, ArOCH_3), 7.04 (2H, d, *J* 9.0, CH_3OCC*H*CHCAr), 7.57 (2H, d, *J* 9.0, CH_3OCCHC*H*CAr), 7.81 (1H, s, CF_3CC*H*CCF$_3$), 7.98 (2H, s, ArCC*H*CCF$_3$); ^{13}C NMR ($CDCl_3$) δ 55.4 (q), 114.7 (2d), 120.2 (d), 126.6 (2d), 128.4 (2d), 7 quaternary carbons not seen; ^{19}F NMR (376 MHz, $CDCl_3$) δ − 62.8 (6F, s, 2 × CF_3); IR (neat) ν_{max} 2940, 2842, 1610, 1521, 1383, 1279, 1185, 1132, 1061, 830, 682 cm^{-1}; MS (EI$^+$) m/z 320 (M$^+$, 100%), 305 (16%), 301 (20%), 277 (60%), 251 (9%), 188 (13%); HRMS calcd for $C_{15}H_{10}F_6O$ 320.0636, found 320.0625, δ 3.4 ppm.

*Entry 11: 1-(4-methoxyphenyl)naphthalene **11g***[105]

Using method B, powdered potassium fluoride (0.0834 g, 1.44 mmol), dichloroanisylgermane **7b** (0.115 g, 0.259 mmol), 1-bromonaphthalene (28 µl, 0.0417 g, 0.201 mmol), and 1 ml of a solution of $PdCl_2(MeCN)_2$ (0.0160 g, 0.0617 mmol) and dppp (0.0245 g, 0.0594 mmol) in DMF (3 ml) following purification using silica gel SPE cartridge (5 g, petrol → petrol/EtOAc, 19 : 1) gave 1-(4-methoxyphenyl)naphthalene **11g**[105] as clear colourless prisms (0.0272 g, 58%). R_f 0.16 (cyclohexane); ^{1}H NMR (250 MHz, $CDCl_3$) $\dot{\delta}$ 3.91 (3H, s, ArOCH_3), 7.01–7.07 (2H, m, Ar CH′s), 7.40–7.56 (6H, m, Ar CH′s), 7.84–7.96 (3H, m, Ar CH′s); MS m/z (EI$^+$) 234 (M$^+$, 100%), 219 (38%), 203 (14%), 189 (55%), 163 (9%), 101 (23%), 95 (29%); m.p. 110.4–116.2 °C (cf. 114–115 °C[106]).

*Entry 12: 3-(4-methoxyphenyl)pyridine **4h***[107]

Using method B, powdered potassium fluoride (0.0887 g, 1.53 mmol), dichloroanisylgermane **7b** (0.0963 g, 0.217 mmol), 3-bromopyridine (18 µl, 0.0291 g, 0.184 mmol), and 1 ml of a solutuion of $PdCl_2(MeCN)_2$ (0.0277 g, 0.107 mmol) and dppp (0.0448 g, 0.109 mmol) in DMF (5 ml) following purification using silica gel SPE cartridge (5 g, cyclohexane → petrol/EtOAc, 9 : 1) gave 3-(4-methoxyphenyl)pyridine **11h**[107] as an off-white film (0.0150 g, 44%). R_f 0.13 (Petrol/EtOAc, 8 : 2); ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.87 (3H, s, ArOCH_3), 7.02 (2H, d, *J* 9.0, CH_3OCC*H*CHCAr), 7.35 (1H, dd, *J* 5.0, *J* 8.0, ArCCHC*H*CHN), 7.53 (2H, d, *J* 9.0, CH_3OCCHC*H*CAr), 7.85 (1H, d, *J* 8.0, ArCC*H*CHCHN), 8.55 (1H, d, *J* 5.0, ArCCHCHC*H*N), 8.83 (1H, s, ArCC*H*N); MS (EI$^+$) m/z 185 (M$^+$, 100%), 170 (55%), 142 (50%), 115 (27%), 89 (17%), 89 (17%).

*Entry 13: 4-methoxy-4′nitrobiphenyl **11i***[108]

Using method B, powdered potassium fluoride (0.0886 g, 1.52 mmol), dichloroanisylgermane **7b** (0.0970 g, 0.219 mmol), 4-nitrobromobenzene (0.0392 g, 0.194 mmol), and 1 ml of a solution of $PdCl_2(MeCN)_2$ (0.0277 g, 0.107 mmol) and dppp (0.0448 g, 0.109 mmol) in DMF (5 ml) followed by purification using silica gel SPE cartridge 95 g, cyclohexane → petrol/EtOAc, 97 : 3) gave 4-methoxy-4′-nitrobiphenyl **11i**[108] as a yellow amorphous powder (0.0217 g, 47%). R_f 0.35 (Petrol/EtOAc, 9 : 1); ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.89 (3H, s, ArOCH_3), 7.03 (2H, *J* 9.0, CH_3OCC*H*CHCAr), 7.59 (2H, *J* 9.0, CH_3OCCHC*H*CAr), 7.70 (2H, *J* 9.0, ArCC*H*CHCNO$_2$), 8.28 (2H, *J* 9.0, ArCCHC*H*CNO$_2$); MS (EI$^+$) m/z 229 (M$^+$, 100%), 199 (27%), 183 (18%), 168 (32%), 152 (22%), 139 (64%); m.p. 105.6–106.7 °C (cf. 107–108 °C[109]).

4-{2-[(4-Methylphenyl)germyl]ethyl}phenyl-(2-ethoxyethyl)ether 12

$LiAlH_4$ (0.0756 g, 1.98 mmol) was added to a solution of dichlorogermane **6b** (0.109 g, 0.254 mmol) in THF (10 ml) at 0 °C. the solution was then warmed to RT before being heated at reflux for 16 h. The crude reaction mixture was cooled to 0 °C before aqueous HCl (1 M, 1 ml) was added cautiously. Once effervescence had ceased, further aqueous HCl was added (1 M, 25 ml) and the acid layer extracted with CH_2Cl_2 (2 × 25 ml). The organics were combined and washed with HCl (1 M, 10 ml), before being dried with $MgSO_4$, filtered and concentrated *in vacuo* to give dihydro-4-tolylgermane **12** as a clear colourless oil (0.0911 g, 100%); R_f 0.71 (petrol/EtOAc, 9 : 1); ^{1}H NMR (250 MHz, $CDCl_3$) $\dot{\delta}$ 1.26 (3H, t, *J* 7.0, CH_3CH$_2$O), 1.47 (2H, m, CH$_2$CH_2Ge), 2.36 (3H, s, ArCH_3), 2.76 (2H, m, CH_2CH$_2$Ge), 3.61 (2H, q, *J* 7.0, CH$_3$CH_2O), 3.79 (2H, t, *J* 5.0, OCH_2CH$_2$OAr), 4.11 (2H, t, *J* 5.0, OCH$_2$CH_2OAr), 4.36 (2H, m, GeH_2), 6.85 (2H, d, *J* 9.0, OCC*H*CHCCH$_2$), 7.09 (2H, d, *J* 9.0, OCCHC*H*CCH$_2$), 7.17 (2H, d, *J* 8.0, GeCCHC*H*CCH$_3$), 7.38 (2H, d, *J* 8.0, GeCC*H*CHCCH$_3$); ^{13}C NMR (63 MHz, $CDCl_3$) $\dot{\delta}$ 13.8 (t), 15.2 (q), 21.4 (q), 31.8 (t), 66.9 (t), 67.5 (t), 69.0 (t), 114.6 (2d), 128.8 (2d), 129.1 (2d), 131.1 (s), 134.9 (2d), 136.2 (s), 138.6 (s), 157.1 (s); IR (neat) ν_{max} 2922, 2043, 1511, 1245, 1124, 747 cm^{-1}; MS (EI$^+$) m/z 360 (M$^+$, 18%), 260 (8%), 239 (13%), 165 (47%), 120 (55%), 91 (43%), 73 (49%), 45 (100%); HRMS calcd for $C_{19}H_{26}{}^{74}GeO_2$ 360.1145, found 360.1143, δ 0.5 ppm.

4-{2-[(4-Methoxyphenyl)germyl]ethyl}phenyl-(2-ethoxyethyl)ether 13

$LiAlH_4$ (0.101 g, 2.65 mmol) was added to a solution of dichlorogermane **7b** (0.149 g, 0.336 mmol) in THF (10 ml) at 0 °C, the solution was then warmed to RT before being heated at reflux for 17 h. The crude reaction mixture was

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cooled to 0 °C before saturated aqueous NH_4Cl solution (1 ml) was added cautiously. Once effervescence had ceased, further saturated aqueous NH_4Cl was added (25 ml) and the aqueous layer extracted with CH_2Cl_2 (2 × 25 ml). The organics were combined filtered through a hydrophobic frit, before being concentrated *in vacuo* to give dihydro-4-anisylgermane **13** as a clear colourless oil (0.115 g, 91%); R_f 0.07 (petrol/EtOAc, 9 : 1); ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.27 (3H, t, *J* 7.0, CH_3CH$_2$O), 1.43–1.52 (2H, m, CH$_2$CH_2Ge), 2.74–2.80 (2H, m, CH_2CH$_2$Ge), 3.62 (2H, q, *J* 7.0, CH$_3$CH_2O), 3.80 (2H, t, *J* 5.0, OCH_2CH$_2$OAr), 3.83 (3H, s, ArOCH_3), 4.12 (2H, t, *J* 5.0, OCH$_2$CH_2OAr), 4.37 (2H, m, GeH_2), 6.86 (2H, d, *J* 9.0, OCC*H*CHCCH$_2$), 6.92 (2H, d, *J* 9.0, GeCCHC*H*COCH$_3$), 7.11 (2H, d, *J* 9.0, OCCHC*H*CCH$_2$), 7.41 (2H, d, *J* 9.0, GeCC*H*CHCOCH$_3$); ^{13}C NMR (63 MHz, $CDCl_3$) δ 13.9 (t), 15.2 (q), 31.8 (t), 55.1 (q), 66.9 (t), 67.5 (t), 69.0 (t), 114.0 (2d), 114.5 (2d), 128.8 (2d), 136.2 (2d), 157.0 (s), 176.1 (s), two quaternary carbons not observed; IR (neat) ν_{max} 2974, 2928, 2870, 2043, 1593, 1511, 1247, 1180, 1125, 823 cm^{-1}; MS (EI$^+$) *m*/*z* 376 (M$^+$, 10%), 268 (16%), 239 (22%), 192 (35%), 181 (39%), 121 (27%), 73 (36%), 45 (100%); HRMS calcd for $C_{19}H_{26}{}^{74}GeO_3$ 376.1094, found 376.1102, δ − 2.2 ppm.

4-{2-[Dichloro-(4-methylphenyl)germyl]ethyl} phenol 6a

A solution of MSA in CH_2Cl_2 (6.03 M, 40 ml) was added to tri-(4-tolyl)germane **4a** (0.406 g, 0.869 mmol) and the mixture stirred at RT for 2.5 h. The reaction mixture was then transferred to a large conical flask and neutralized with saturated aqueous $NaHCO_3$ solution (200 ml) initially added dropwise, and then stirred for 15 min. Phases were separated and the aqueous layer extracted with CH_2Cl_2 (2 × 50 ml). The organic washings were treated with c.HCl (150 ml), the phases separated and the acid layer extracted with further CH_2Cl_2 (2 × 50 ml). The organics were combined, dried with $MgSO_4$, filtered, concentrated *in vacuo* and analysed by ^{1}H NMR to reveal the presence of dichloro-4-tolylphenol **6a** and a trace of the corresponding chlorodi-(4-tolyl)phenol. The crude mixture was partitioned between CH_2Cl_2 (30 ml) and aqueous NaOH (0.5 M, 60 ml). The layers were separated and the basic layer extracted with CH_2Cl_2 (2 × 15 ml). The organic washings were combined and extracted with further NaOH (0.5 M, 50 ml). The basic aqueous layers were combined, filtered, and then cautiously treated with aqueous HCl (1 M, 50 ml), before being further acidified with conc. HCl (100 ml). The now acidic layer was then extracted with CH_2Cl_2 (3 × 50 ml), the organic washings were combined, dried with $MgSO_4$, filtered and concentrated *in vacuo* to give dichloro-4-tolylphenol **6a** as a pale brown oil (0.252 g, 82%). ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.07 (2H, m, CH$_2$CH_2Ge), 2.39 (3H, s, ArCH_3), 2.94 (2H, m, CH_2CH$_2$Ge), 4.82 (1H, bs, O*H*), 6.74 (2H, d, *J* 8.5, HOCC*H*CHC), 7.07 (2H, d, *J* 8.5, HOCCHC*H*C), 7.27 (2H, d, *J* 8.0, GeCCHC*H*CCH$_3$), 7.46 (2H, d, *J* 8.0, GeCC*H*CHCCH$_3$); ^{13}C NMR (63 MHz, $CDCl_3$) δ 21.6 (q), 27.6 (t), 28.5 (t), 115.5 (2d), 129.3 (2d), 129.6 (2d), 132.0 (2d), 132.1 (s), 133.8 (s), 142.0 (s), 154.1 (s); IR (neat) ν_{max} 3350, 2921, 1597, 1514, 1235, 1090, 799, 695 cm^{-1}; MS (EI$^+$) *m*/*z* 356 (M$^+$, 5%), 235 (8%), 165 (2%), 120 (100%), 107 (31%), 91 (59%), 65 (32%); HRMS calcd for $C_{15}H_{16}Cl_2{}^{74}GeO$ 355.9790, found 355.9802, δ − 3.3 ppm.

4-{2-[Di-(2-furyl)-(4-methylphenyl)germyl] ethyl}phenol 14a

n-Butyl lithium (2.5 M, 2.2 ml, 5.5 mmol) was added dropwise with stirring to a solution of furan (0.45 ml, 0.412 g, 6.19 mmol) in THF (10 ml) at 0 °C and stirred for 30 min. A solution of dichloro-4-tolylphenol **6a** (0.502 g, 1.41 mmol) in THF (5 ml) was then added dropwise to the solution of furyl lithium at 0 °C, the ice bath removed and the resulting mixture allowed to warm to RT over 90 min. The mixture was then heated at reflux for 17 h. Distilled water was cautiously added to destroy any excess organometallic species before the crude reaction mixture was partitioned between distilled water (30 ml) and Et_2O (3 × 20 ml). Organic washings were combined, dried with $MgSO_4$, filtered and concentrated *in vacuo*. Purification with a Silica gel SPE cartridge (10 g, cyclohexane → cyclohexane/EtOAc, 19:1 → cyclohexane/EtOAc, 9:1 → cyclohexane/EtOAc, 8 : 2) gave difuryl-4-tolylphenol **14a** as a pale brown oil (0.230 g, 39%). R_f 0.63 (petrol/EtOAc, 8 : 2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.82 (2H, m, CH$_2$CH_2Ge), 2.39 (3H, s, ArCH_3), 2.83 (2H, m, CH_2CH$_2$Ge), 5.93 (1H, s, O*H*), 6.48 (2H, m, furyl CH's), 6.73–6.74 (2H, m, furyl CH's), 6.76 (2H, d, *J* 9.0, HOCC*H*CHCC), 7.07 (2H, d, *J* 9.0, HOCCHC*H*C), 7.23 (2H, d, *J* 8.0, GeCCHC*H*CCH$_3$), 7.48 (2H, d, *J* 8.0, GeCC*H*CHCCH$_3$), 7.76–7.77 (2H, m, furyl CH's); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.9 (t), 20.8 (t), 29.2 (q), 109.0 (2d), 114.5 (2d), 120.3 (2d), 128.3 (2d), 128.5 (2d), 130.6 (s), 133.5 (2d), 135.8 (s), 138.7 (s), 146.6 (2d), 152.8 (2s), 154.1 (s); IR (neat) ν_{max} 3418, 2923, 2853, 1513, 1461, 1377, 1199, 1000, 800 cm^{-1}; MS (ESI$^+$) *m*/*z* 443 [(M + Na)$^+$, 100%]; HRMS calcd for $C_{23}H_{22}O_3{}^{74}GeNa$ 443.0678, found 443.0690, δ 2.7 ppm.

4-{2-[Di-(2-furyl)-(4-methylphenyl)germyl] ethyl}phenyl-(2-ethoxyethyl)ether 14b

Caesium carbonate (0.163 g, 0.501 mmol), TBAI (0.0173 g, 0.0468 mmol) and 2-chloroethyl ethyl ether (0.23 ml, 0.227 g, 2.10 mmol) were added to a solution of difuryl-4-tolylphenol **14a** (0.190 g, 0.454 mmol) dissolved in MeCN (20 ml), and the resulting mixture heated at 80 °C for 18 h. The crude reaction mixture was partitioned between distilled water (20 ml) and Et_2O (2 × 20 ml). The organic washings were combined, dried with $MgSO_4$, filtered and concentrated *in vacuo*. Purification with a Silica gel SPE cartridge (5 g, cyclohexane/EtOAc, 8 : 2) gave difuryl-4-tolylgermane **14b** as a pale brown oil (0.197 g, 88%). R_f 0.48 (petrol/EtOAc, 8 : 2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (3H, t, J 7.0, CH$_3$CH$_2$O), 1.79 (2H, m, CH$_2$CH$_2$Ge), 2.35 (3H, s, ArCH$_3$), 2.80 (2H, m, CH_2CH$_2$Ge), 3.59 (2H, q, *J* 7.0, CH$_3$CH_2O), 3.77 (2H, t, *J* 5.0, OCH_2CH$_2$OAr), 4.08 (3H, t, *J* 5.0, OCH$_2$CH_2OAr), 6.44–6.46 (2H, m, furyl CH's), 6.69–6.70 (2H, m, Furyl CH's), 6.81 (2H, d, *J* 9.0, OCC*H*CHCCH$_2$), 7.08 (2H, d, *J* 9.0, OCCHC*H*CCH$_2$), 7.19 (2H, d, *J* 8.0, GeCCHC*H*CCH$_3$), 7.43 (2H, d, *J* 8.0, GeCC*H*CHCCH$_3$), 7.71 (2H, m, furyl CH's);

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^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9 (t), 15.2 (q), 20.2 (q), 28.5 (t), 65.5 (t), 66.2 (t), 67.7 (t), 108.3 (2d), 113.2 (2d), 119.6 (2d), 127.4 (2d), 127.9 (2d), 129.9 (s), 132.9 (2d), 135.2 (s), 138.0 (s), 145.9 (2d), 153.5 (2s), 155.7 (s); IR (neat) ν_{max} 2924, 2868, 1610, 1510, 1245, 1124, 1002, 800 cm^{-1}; MS (ESI$^+$) m/z 515 [$(M + Na)^+$, 100%]; HRMS calcd for $C_{27}H_{30}O_4{}^{74}GeNa$ 515.1254, found 515.1240, $\delta - 2.6$ ppm.

4-{2-[Diallyl-(4-methoxyphenyl)germyl] ethyl}phenol 15a

To a solution of dichloro-4-anisylphenol **7a**[64] (0.600 g, 1.62 mmol) in toluene (40.0 ml) at 0 °C was added a solution of allylmagnesium chloride in THF (3.28 ml, 6.45 mmol, 2.0 M) dropwise. The mixture turned grey and was allowed to warm up to RT and was stirred for 12 h before being quenched with water (10 ml). The resulting solution was diluted with toluene (20 ml) and the aqueous layer was extracted with toluene (3 × 20 ml) and combined organic layers were dried with $MgSO_4$. The solvent was removed *in vacuo* and the residue was purified by FC (petrol/EtOAc 90:10 → 70:30) to give diallylgermane **15a** as a yellow oil (0.600 g, 73%). R_f 0.35 (petrol/EtOAc, 80 : 20); ^{1}H NMR (270 MHz; $CDCl_3$): δ 1.33 (2H, m, CH_2CH_2Ge), 1.93 (4H, d, J 9.0, 2 × CH_2Ge), 2.65 (2H, m, CH_2CH_2Ge), 3.82 (3H, s, ArOCH_3), 4.64 (1H, bs, ArOH), 4.82 (2H, d, J 10.0, 2 × CH_{cis}CHCH$_2$Ge), 4.88 (2H, d, J 17.0, 2 × CH_{trans}CHCH$_2$Ge), 5.76 (2H, ddt, J 17.0, 10.0, and 9.0, 2 × CHCH$_2$Ge), 6.72 (2H, d, J 8.5, OCCHCHCCH$_2$), 6.91 (2H, d, J 8.5, GeCCHCHCOCH$_3$), 7.01 (2H, d, J 8.5, OCCHCHCCH$_2$) 7.37 (2H, d, J 8.5, GeCCHCHCOCH$_3$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 14.8 (t), 20.1 (2t), 30.0 (t), 55.1 (q), 113.3 (2t), 113.9 (2d), 115.2 (2d), 128.9 (2d), 135.1 (2d), 135.2 (2d), 136.7 (s), 153.7 (s), 160.0 (s), one quaternary carbon not observed; IR (neat) ν_{max} 3410 (OH), 3076–2972 (CH), 1628, 1592 (C═C), 1246 cm^{-1}; MS (EI$^+$) m/z 343 [$(M - 41)^+$, 57%], 301 (49%), 223 (5%), 181 (100%); HRMS calcd for $C_{18}H_{21}{}^{74}GeO_2$ 343.0753, found 343.0759, Δ 1.6 ppm; analysis for $C_{21}H_{26}GeO_2$ expected C 65.85%, H 6.84%, found C 65.93%, H 6.81%.

Diallyl-{2-[4-(2-ethoxyethoxy)phenyl]ethyl}-(4-methoxyphenyl)germane 15b

Potassium carbonate (0.720 g, 5.22 mmol), TBAI (0.097 g, 0.261 mmol) and 2-chloroethyl ethyl ether (0.867 ml, 0.850 g, 7.83 mmol) were added to a solution of phenol **15a** (0.500 g, 1.305 mmol) in DMF (10.0 ml), and the resulting mixture heated at 80 °C for 17 h. The crude reaction mixture was then diluted with Et_2O (25.0 ml) and washed with saturated NaCl (aq) (3 × 30.0 ml). The organic layer was then dried with $MgSO_4$, filtered and concentrated *in vacuo*. Purification by FC (petrol/EtOAc 95:5 → 80:20) gave ethoxyethylether **15b** as a colourless oil (0.620 g, 70%). R_f 0.37 (petrol/EtOAc, 90 : 10); ^{1}H NMR (270 MHz; $CDCl_3$): δ 1.23 (3H, t, J 7.0, CH_3CH_2O), 1.34 (2H, m, CH_2CH_2Ge), 1.94 (4H, d, J 9.0, 2 × CH_2Ge), 2.66 (2H, m, CH_2CH_2Ge), 3.58 (2H, q, J 7.0, CH_3CH_2O), 3.77 (2H, t, J 5.0, OCH_2CH_2OAr), 3.82 (3H, s, ArOCH_3), 4.10 (2H, t, J 5.0, OCH$_2CH_2$OAr), 4.84 (2H, d, J 10.0, 2 × CH_{cis}CHCH$_2$Ge), 4.90 (2H, d, J 17.0, 2 × CH_{trans}CHCH$_2$Ge), 5.80 (2H, ddt, J 17.0, 10.0, 9.0, 2 × CHCH$_2$Ge), 6.82 (2H, d, J 8.5, OCCHCHCCH$_2$), 6.92 (2H, d, J 8.5, GeCCHCHCOCH$_3$), 7.06 (2H, d, J 8.5, OCCHCHCCH$_2$), 7.37 (2H, d, J 8.5, GeCCHCHCOCH$_3$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 14.8 (t), 15.2 (q), 20.0 (2t), 29.4 (t), 55.1 (q), 66.8 (t), 67.5 (t), 69.0 (t), 113.3 (2t), 113.8 (2d), 114.5 (2d), 128.6 (2d), 128.8 (s), 135.0 (2d), 135.2 (2d), 136.9 (s), 157.7 (s), 160.0 (s); IR (neat) ν_{max} 2972 (CH), 1629, 1592 (C═C), 1510, 1247 cm^{-1}; MS (CI$^+$) m/z. 474 ($MNH_4{}^+$, 21%), 432 (24%), 415 (9%), 366 (16%), 193 (100%); HRMS calcd for $C_{25}H_{38}N^{74}GeO_3$ 474.2063, found 474.2068, Δ 1.0 ppm; analysis for $C_{25}H_{34}GeO_3$ expected C 65.97%, H 7.53%, found C 65.85%, H 7.41%.

4-{2-[(4-Methoxyphenyl)dipyridin-2-ylgermyl] ethyl}phenol 16a

2-Bromopyridine (0.211 g, 0.130 ml, 1.34 mmol) was added to a suspension of magnesium turnings (0.033 g, 1.34 mmol) in THF (13.0 ml). The reaction mixture was then refluxed for 3 h to initiate Grignard reagent formation. To this red coloured reaction was added a solution of dichloro-4-anisylphenol **7a** (0.050 g, 0.134 mmol) in THF (2.00 ml) dropwise and the resulting mixture was stirred for 12 h at RT. Water was added to the reaction mixture until no effervescence occurred and the solvent was then removed *in vacuo*. The residue taken up in Et_2O (40.0 ml) and was extracted with water (2 × 10.0 ml) and then dried with $MgSO_4$. The solvent was concentrated *in vacuo* and the residue was purified by rapid FC on basic alumina (EtOAc→IPA/EtOAc 5 : 95) and then dried under high vacuum to give dipyridylgermane **16a** as a brown oil (0.010 g, 20%). R_f 0.25 (5 : 95 IPA/EtOAc); ^{1}H NMR (270 MHz; $CDCl_3$): δ 1.94 (2H, m, CH_2CH_2Ge), 2.75 (2H, m, CH_2CH_2Ge), 3.80 (3H, s, ArOCH_3), 6.60 (2H, d, J 8.5, OCCHCHCCH$_2$), 6.85 (2H, d, J 8.5, GeCCHCHCOCH$_3$), 6.92 (2H, d, J 9.0, OCCHCHCCH$_2$), 7.24 (2H, m, GeCCHCHCHCHCN), 7.49 (2H, d, J 9.0, OCCHCHCCH$_2$), 7.55–7.62 (4H, m, GeC$CHCH$CHCHCN), 8.79 (2H, d, J 5.0, GeCCHCHCHCHCN), OH absent; ^{13}C NMR (100 MHz; $CDCl_3$) δ 15.6 (t), 29.9 (t), 55.1 (q), 114.2 (2d), 115.3 (2d), 123.2 (2d), 126.3 (s), 128.7 (2d), 131.1 (2d), 134.8 (2d), 135.6 (s), 136.2 (2d), 150.3 (2d), 154.4 (s), 160.5 (s), 165.8 (2s); IR (neat) ν_{max} 3061–2946 (CH), 1591 (C═C), 1500, 1247, 752 cm^{-1}; IR (EI$^+$) m/z 457 (M^+, 37%), 383 (50%), 338 (100%), 230 (88%), 152 (66%); HRMS calcd for $C_{25}H_{24}{}^{74}GeO_2N_2$ 458.1050, found 458.1043, Δ 1.4 ppm; analysis for $C_{25}H_{24}GeN_2O_2$ expected C 65.69%, H 5.29%, N 6.13, found 63.15%, H 8.57%, N 2.83%.

{2-[4-(2-Ethoxyethoxy)phenyl]ethyl}-(4-methoxyphenyl)dipyridin-2-ylgermane 16b

Potassium carbonate (0.061 g, 0.440 mmol), TBAI (0.008 g, 0.022 mmol) and 2-chloroethyl ethyl ether (0.621 ml, 0.614 g, 0.943 mmol) were added to a solution of phenol **16a** (0.120 g, 0.220 mmol) in DMF (5.00 ml), and the resulting mixture heated at 80 °C for 12 h. The crude reaction mixture was then diluted with Et_2O (30.0 ml) and washed with sat. NaCl (aq) (5 × 10.0 ml). The organic layer was then dried with $MgSO_4$, filtered and concentrated *in vacuo*. Purification by rapid FC on basic alumina (petrol/EtOAc 80:20 → 30:70) gave ethoxyethyl ether **16b** as a purple

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oil (0.030g, 25%). R_f 0.40 (petrol/EtOAc, 50:50); ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.20 (3H, t, *J* 7.0, CH_3CH_2O), 2.01 (2H, m, CH_2CH_2Ge), 2.84 (2H, m, CH_2CH_2Ge), 3.54 (2H, q, *J* 7.0, CH_3CH_2O), 3.73 (2H, t, *J* 5.0, OCH_2CH_2OAr), 3.79 (3H, s, $ArOCH_3$), 4.03 (2H, t, *J* 5.0, OCH_2CH_2OAr), 6.77 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 6.94 (2H, d, *J* 8.5, $GeCCHCHCOCH_3$), 7.05 (2H, d, *J* 9.0, $OCCHCHCCH_2$), 7.24 (1H, m, GeCCHCHCHCHCN), 7.50 (2H, d, *J* 9.0, $GeCCHCHCOCH_3$), 7.55–7.62 (5H, m, $GeCCHCHCHCN$), 8.84 (2H, d, *J* 5.0, $GeCCHCHCHCHCN$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.1 (q), 15.9 (t), 30.0 (t), 55.1 (q), 66.8 (t), 67.5 (t), 69.0 (t), 114.2 (2d), 114.5 (2d), 123.0 (2d), 128.8 (2d), 131.0 (2d), 134.8 (s), 136.2 (4d), 150.2 (2d), 156.9 (s), 160.5 (s), three quaternary carbons not observed; IR (neat) ν_{max} 3017–2929 (CH), 1592 (C═C), 1574, 1232, 1182, 1093, 752 cm^{-1}; MS (CI^+) *m/z* 531 (MH^+, 100%), 439 (31%), 338 (19%), 193 (62%), 80 (100%); HRMS calcd for $C_{29}H_{33}{}^{74}GeO_3N_2$ 531.1730, found 531.1715, Δ 2.82 ppm; analysis for $C_{29}H_{33}GeO_3N_2$ expected C 65.82%, H 6.10%, N 5.29% found C 63.65%, H 7.10%, N 2.26%.

4-{2-[Dibenzyl-(4-methoxyphenyl)germyl] ethyl}phenol 17a

Benzyl chloride (6.19 ml, 6.81 g, 53.76 mmol) was added to magnesium turnings (1.306 g, 53.765 mmol) in THF (25.0 ml). A single crystal of iodine was then added to initiate Grignard reagent formation and the reaction mixture stirred for 3 h. The resulting brown solution was added to a solution of dichloro-4-anisylphenol **7a** (2.00 g, 5.376 mmol) in THF (2.00 ml) dropwise before stirring for 12 h. Water was added to the reaction mixture until no effervescence occurred. The solvent was then removed *in vacuo* and the residue taken up in Et_2O (30.0 ml) washed with water (2 × 20.0 ml) and dried with $MgSO_4$. Purification by FC (petrol/EtOAc, 90:10 → 50:50) and drying under high vacuum for 24 h gave dibenzylgermane **17a** as a brown foam (2.113 g, 81%). R_f 0.26 (petrol/EtOAc, 80:20); ^{1}H NMR (270 MHz; $CDCl_3$): δ 1.16 (2H, m, CH_2CH_2Ge), 2.42 (2H, m, CH_2CH_2Ge), 2.48 (4H, s, 2 × $ArCH_2Ge$) 3.83 (3H, s, $ArOCH_3$), 4.64 (1H, bs, $ArOH$), 6.69 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 6.87–6.95 (7H, m, ArH), 7.05–7.09 (3H, m, ArH) 7.16–7.30 (6H, m, ArH); ^{13}C NMR (100 MHz; $CDCl_3$) δ 14.8 (t), 22.6 (2t), 30.0 (t), 55.0 (q), 113.8 (2d), 115.1 (2d), 124.3 (2d), 128.3 (8d), 128.9 (2d), 135.2 (2d), 137.0 (s), 140.0 (2s), 154.1 (s), 160.1 (s), one quaternary carbon not observed; IR (neat) ν_{max} 3408 (OH), 3100-2837 (CH), 1597 (C═C), 1568, 1312 cm^{-1}; MS (EI^+) *m/z* 393 [$(M-91)^+$, 100%), 273 (100%), 181 (92%), 91 (94%); HRMS calcd for $C_{22}H_{23}{}^{74}GeO_2$ 393.0909, found 393.0929, Δ 5.0 ppm; analysis for $C_{29}H_{30}GeO_2$ expected C 72.09%, H 6.26%, found C 46.60%, H 3.47%.

Dibenzyl-{2-[4-(2-ethoxyethoxy)phenyl]ethyl}-(4-methoxyphenyl)germane 17b

Potassium carbonate (1.027 g, 7.442 mmol), TBAI (0.138 g, 0.373 mmol) and 2-chloroethyl ethyl ether (1.240 ml, 1.270 g, 11.694 mmol) were added to a solution of phenol **17a** (0.900 g, 1.860 mmol) in DMF (5.00 ml), and the resulting mixture heated at 80 °C for 17 h. The crude reaction mixture was then diluted with Et_2O (22.0 ml) and washed with sat. NaCl (aq) (3 × 15.0 ml). The organic layer was then dried with $MgSO_4$, filtered and concentrated *in vacuo*. Purification by FC (petrol/EtOAc 98:2 → 70:30) gave ethoxyethyl ether **17b** as a yellow oil (0.69 g, 68%). R_f 0.36 (petrol/EtOAc 90:10); ^{1}H NMR (270 MHz; $CDCl_3$): δ 1.19 (2H, m, CH_2CH_2Ge), 1.25 (3H, t, *J* 7.0, CH_3CH_2O), 2.42 (2H, m, CH_2CH_2Ge), 2.46 (4H, s, 2 × $ArCH_2Ge$) 3.55 (2H, q, *J* 7.0, CH_3CH_2O), 3.75 (2H, t, *J* 5.0, OCH_2CH_2OAr), 3.82 (3H, s, $ArOCH_3$), 4.10 (2H, t, *J* 5.0, OCH_2CH_2OAr), 6.78 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 6.86–6.95 (7H, m, ArH), 7.03–7.08 (3H, m, ArH) 7.14–7.26 (6H, m, ArH); ^{13}C NMR (100 MHz; $CDCl_3$) δ 14.7 (t), 15.1 (q), 22.5 (2t), 30.0 (t), 55.0 (q), 66.8 (t), 67.4 (t), 69.0 (t), 113.7 (2d), 114.5 (2d), 124.2 (2d), 128.2 (8d), 128.6 (2d), 135.2 (2d), 137.0 (s), 140.0 (2s), 156.9 (s), 160.1 (s), one quaternary carbon not observed; UV ν_{max} (MeOH) 223, 275 nm; IR (neat) ν_{max} 3100–2905 (CH), 1593 (C═C), 1506, 1279 cm^{-1}; MS (CI^+) *m/z* 574 ($MNH_4{}^+$, 63%), 466 (100%), 449 (19%), 274 (11%); HRMS calcd for $C_{33}H_{42}{}^{74}GeNO_3$ 574.2376, found 574.2373, Δ 0.5 ppm; analysis for $C_{33}H_{38}GeO_3$ expected C 71.38%, H 6.90%, found C 71.29%, H 6.81%.

4-{2-[(4-Methoxyphenyl)bis(naphthalen-2-ylmethyl)germyl]ethyl}phenol 18a

2-Bromomethyl naphthalene (4.754 g, 21.5 mmol) was added to a suspension of magnesium turnings (0.522 g, 21.5 mmol) in Et_2O (25.0 ml). The reaction mixture was then stirred for 1.5 h to initiate Grignard reagent formation. To the resulting yellow coloured reaction mixture was added a solution of dichloro-4-anisylphenol **7a** (0.800 g, 2.15 mmol) in Et_2O (2 ml) dropwise and the resulting mixture was stirred for 12 h. Water was added to the reaction mixture until no effervescence occurred. The organic layer was dried with $MgSO_4$ and solvent was removed *in vacuo*. Purification by FC (petrol/EtOAc 95:5 → 50:50) gave bis(2-naphthylmethyl)germane **18a** as a yellow foam (0.730 g, 74%). R_f 0.32 (petrol/EtOAc, 85:15); ^{1}H NMR (400 MHz; $CDCl_3$): δ 1.19 (2H, m, CH_2CH_2Ge), 2.49 (2H, m, CH_2CH_2Ge), 2.62 (4H, s, 2 × CH_2Ge), 3.81 (3H, s, $ArOCH_3$), 5.05 (1H, bs, $ArOH$), 6.62 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 6.78 (2H, d, *J* 8.5, $GeCCHCHCOCH_3$), 6.86 (2H, d, *J* 8.5, 2H, $OCCHCHCCH_2$), 7.03 (2H, dd, *J* 8.5 2.0, $GeCH_2CCHCHCCH$), 7.27 (2H, d, *J* 8.5, $GeCCHCHCOCH_3$), 7.37–7.47 (6H, m, ArH) 7.69 (2H, d, *J* 8.0, $GeCH_2CCHCHCCH$), 7.72 (2H, d, *J* 8.5, $GeCH_2CCHCHCCH$), 7.85 (2H, d, *J* 8.0, $GeCH_2CCHCCHCH$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.8 (t), 22.9 (2t), 29.7 (t), 55.0 (q), 113.8 (2d), 115.1 (2d), 124.5 (2d), 125.6 (2d), 125.8 (2d), 127.0 (2d), 127.5 (2d), 127.8 (2d), 128.6 (2d), 128.8 (2d), 131.1 (2s), 133.7 (2s), 135.3 (2d), 136.5 (s), 137.5 (3s), 153.5 (s), 160.1 (s); IR (neat) ν_{max} 3333 (OH), 3053-2930 (CH), 1593 (C═C), 1506, 1246, 1126 cm^{-1}; MS *m/z* (FAB$^+$) 443 [$(M-141)^+$, 13%], 335 (15%), 301 (19%), 141 (100%); HRMS calcd for $C_{26}H_{25}{}^{74}GeO_2$ 443.1066, found 443.1086, Δ 4.3 ppm; Analysis for $C_{37}H_{34}GeO_2$ expected C 76.19%, H 5.88%, found C 76.10%, H 5.73%.

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{2-[4-(2-Ethoxyethoxy)phenyl]ethyl}-(4-methoxyphenyl)bis(naphthalen-2-ylmethyl) germane 18b

Potassium carbonate (0.850 g, 6.162 mmol), TBAI (0.076 g, 0.254 mmol) and 2-chloroethyl ethyl ether (0.430 ml, 0.442 g, 4.108 mmol) were added to a solution of phenol **18a** (0.600 g, 1.027 mmol) in DMF (5.00 ml), and the resulting mixture heated at 80 °C for 12 h. The crude reaction mixture was then diluted with Et_2O (25.0 ml) and washed with sat. NaCl (aq) (3 × 15.0 ml). The organic layer was then dried with $MgSO_4$, filtered and concentrated *in vacuo*. Purification by FC (petrol/EtOAc 95:5 → 50:50) gave ethoxyethyl ether**18b** as a yellow oil (0.500 g, 80%). R_f 0.30 (petrol/EtOAc, 90 : 10); ^{1}H NMR (270 MHz; $CDCl_3$): δ 1.17 (2H, m, CH_2CH_2Ge), 1.20 (3H, t, *J* 7.0, CH_3CH_2O), 2.49 (2H, m, CH_2CH_2Ge), 2.64 (4H, s, 2 × CH_2Ge), 3.54 (2H, q, *J* 7.0, CH_3CH_2O), 3.74 (2H, t, *J* 5.0, OCH_2CH_2OAr), 3.83 (3H, s, $ArOCH_3$), 4.04 (2H, t, *J* 5.0, OCH_2CH_2OAr), 6.74 (2H, d, *J* 8.5, $OCCHCHCCH_2$), 6.84–6.90 (4H, m, ArH), 7.03 (2H, dd, *J* 8.5 2.0, $GeCH_2CCHCHCCH$), 7.27 (2H, d, *J* 8.5, $GeCCHCHCOCH_3$), 7.37–7.47 (6H, m, ArH), 7.63 (2H, d, *J* 8.0, $GeCH_2CCHCHCCH$), 7.68 (2H, d, *J* 8.5, $GeCH_2CCHCHC$), 7.77 (2H, d, *J* 8.0, $GeCH_2CCHCCHCH$); ^{13}C NMR (100 MHz; $CDCl_3$) δ 14.8 (t), 15.2 (q), 23.0 (2t), 30.0 (t), 55.1 (q), 66.8 (t), 67.5 (t), 69.0 (t), 113.8 (2d), 114.5 (2d), 124.4 (2d), 125.7 (2d), 125.9 (2d), 127.0 (2d), 127.6 (2d), 127.7 (2d), 127.8 (2d), 128.7 (2d), 131.1 (2s), 133.7 (2s), 135.3 (2d), 136.8 (s), 137.7 (3s), 157.2 (s), 160.2 (s); UV ν_{max} (MeOH) 230, 280, 340 nm; IR (neat) ν_{max} 3054–2930 (CH), 1593 (C═C), 1506, 1280, 1126 cm^{-1}; MS (EI$^+$) *m/z* 515 [(M − 141)$^+$, 36%], 373 (52%), 323 (7%), 181 (48%), 141 (100%); HRMS calcd for $C_{30}H_{33}{}^{74}GeO_3$ 515.1641, found 515.1652, Δ 2.1 ppm; analysis for $C_{41}H_{42}GeO_3$ expected C 75.14%, H 6.46%, found C 75.06%, H 6.57%.

{2-[4-(2-Ethoxyethoxy)phenyl]ethyl}dimethyl (naphthalen-2-ylmethyl)germane 19

2-Bromomethylnaphthalene (1.259 g, 5.70 mmol) was added to a suspension of magnesium turnings (0.139 g, 5.75 mmol) in Et_2O (25.0 ml). The reaction mixture was then stirred for 1.5 h to initiate Grignard reagent formation. To the resulting yellow coloured solution was added a solution of 4-{[2-chlorodimethylgermyl]ethyl}phenyl (2-ethoxyethyl) ether[61] (**2**, 0.501 g, 1.51 mmol) in Et_2O (2.00 ml) dropwise before stirring for 12 h. Water was added to the reaction mixture until no effervescence occurred and the reaction mixture was partitioned between Et_2O (40.0 ml) and water (20.0 ml). The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by FC (petrol/CH_2Cl_2 95 : 5 → 50:50) and then dried under high vacuum for 12 h to give 2-naphthylmethylgermane **19** as a brown foam (0.347 g, 56%). R_f 0.30 (petrol/CH_2Cl_2, 90 : 10); ^{1}H NMR (270 MHz; $CDCl_3$): δ 0.0 ṡ (6H, s, $Ge(CH_3)_2$), 1.05 (2H, m, CH_2CH_2Ge), 1.24 (3H, t, *J* 7.0, CH_3CH_2O), 2.36 (2H, ṡ, CH_2Ge), 2.59 (2H, m, CH_2CH_2Ge), 3.56 (2H, q, *J* 7.0, CH_3CH_2O), 3.77 (2H, t, *J* 5.0, OCH_2CH_2OAr), 4.09 (2H, t, *J* 5.0, OCH_2CH_2OAr), 6.81 (2H, d, *J* 9.0, $OCCHCHCCH_2$), 7.03 (2H, d, *J* 9.0, $OCCHCHCCH_2$), 7.12, (1H, dd, *J* 8.5, and 2.0, $GeCH_2CCHCHCCH$), 7.32–7.44 (3H, m, ArH), 7.68 (1H, d, *J* 8.0, $GeCH_2CCHCHCCH$), 7.70 (1H, d, *J* 8.5, $GeCH_2CCHCHCCH$), 7.75 (1H, d, *J* 8.0, $GeCH_2CCHCCHCH$); ^{13}C NMR (100 MHz; $CDCl_3$) δ − 4.2 (2q), 15.2 (q), 17.3 (t), 25.3 (t), 30.1 (t), 66.8 (t), 67.4 (t), 69.0 (t), 114.5 (2d), 124.3 (d), 124.6 (d), 125.8 (d), 126.9 (d), 127.5 (2d), 127.6 (d), 128.6 (2d), 130.9 (s), 134.0 (s), 137.0 (s), 139.0 (s), 156.8 (s); UV ν_{max} (MeOH) 230, 280, 346 nm; IR (CH_2Cl_2) ν_{max} 3025–2850 (CH), 1610 (C═C), 1509, 1242, 826 cm^{-1}; MS (EI$^+$) *m/z* 438 (M$^+$, 16%), 423 (27%), 297 (100%), 141 (78%), 73 (96%); HRMS calcd for $C_{25}H_{32}{}^{74}GeO_2$ 438.1614, found 438.1619, Δ 1.0 ppm; analysis for $C_{25}H_{32}GeO_2$ expected C 66.69%, H 7.38% found 66.78%, H 7.15%.

{2-[4-(2-Ethoxyethoxy)phenyl]ethyl} dimethylfluorogermane 20

To a solution of 2-naphthylmethylgermane **19** (0.024 g, 0.076 mmol) in MeCN/MeOH (3 : 1, 20 ml) in a Pyrex Schlenk tube (1 mm thick) was added powdered $Cu(BF_4)_2 \cdot nH_2O$ (0.042 g, ∼0.15 mmol). The resulting mixture was purged with argon for 30 min before irradiating using a 125 W high pressure Hg lamp for 30 min. After this time, the solvent was removed *in vacuo*, the residue was taken up in CH_2Cl_2 (20.0 ml), and washed with water (2 × 8.00 ml) and dried with $MgSO_4$. The solvent was then removed *in vacuo* and the 2-naphthylmethyl methyl ether **21** removed under high vacuum to leave the crude germyl fluoride **20** as a brown oil (15.0 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.47 (6H, d, *J* 6.3, $Ge(CH_3)_2$) 1.24 (3H, t, *J* 7.0, CH_3CH_2O), 1.44 (2H, m, CH_2CH_2Ge), 2.79 (2H, m, CH_2CH_2Ge), 3.60 (2H, q, *J* 7.0, CH_3CH_2O), 3.78 (2H, t, *J* 4.5, OCH_2CH_2OAr), 4.09 (2H, t, *J* 4.5, OCH_2CH_2OAr), 6.85 (2H, d, *J* 8.0, $OCCHCHCCH_2$), 7.10 (2H, d, *J* 8.0, $OCCHCHCCH_2$); ^{19}F NMR (376 MHz, $CDCl_3$): δ 196.0 (1F, app septet, *J* 7.0, GeF); MS (EI$^+$) *m/z* 316 (M$^+$, 35%), 281 (16%), 224 (14%), 73 (60%), 45 (100%).

Photolytic activation and cross-coupling of bis(2-naphthylmethyl)germane 18b with 3,5-bis(trifluoromethyl)bromobenzene: *4-Methoxy-3′,5′-bis(trifluoromethyl)biphenyl* ***11f***

To a solution of bis(2-naphthylmethyl)germane **18b** (104 mg, 0.158 mmol) in MeCN/MeOH (3/1, 20 mL) in a Pyrex Schlenk tube (1 mm thick) was added powdered $Cu(BF_4)_2 \cdot nH_2O$ (0.150 g, ∼ 0.43 mmol). The resulting mixture was purged with argon for 30 min before irradiating using a 125 W high pressure Hg lamp for 1 h. A further portion of $Cu(BF_4)_2 \cdot nH_2O$ (0.150 g, ∼ 0.43 mmol) was added and the solution irradiated for a further 1 h. After this time, the solvent was removed *in vacuo*, the residue was taken up in CH_2Cl_2 (20.0 mL), washed with water (2 × 8.00 mL) and dried with $MgSO_4$. The solvent was then removed *in vacuo* and the resulting crude difluorogermane derivative and TBAF (150 mg, 0.32 mmol) were dissolved in degassed DMF (3 mL) and stirred for 30 min. $PdCl_2(MeCN)_2$ (4.1 mg, 0.016 mmol) and P(2-Tol)$_3$ (7.3 mg, 0.024 mmol) were also dissolved separately in degased DMF (2 mL) for 30 min to

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give the active Pd(0) catalyst. The active catalyst solution was added to the difluoroarylgermane solution followed by addition of 3,5-bis(trifluoromethyl)bromobenzene (93 mg, 0.318 mmol, 55 μL) and CuI (31.6 mg, 0.16 mmol). The resulting mixture was heated at 120 °C for 16 h under a nitrogen atmosphere. The crude reaction mixture was diluted with Et_2O (20.0 mL), washed with water (3 × 10.0 mL), and the organic layer dried over $MgSO_4$ and evaporated *in vacuo*. Purification by FC (hexane/EtOAc, 97/3) gave 4-methoxy-3′,5′-bis(trifluoromethyl)biphenyl **11f** (43.6 mg, 86%). Analytical data as above.

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