A Tuneable Ge-based Linker that Enables Application-led Solid Phase Synthesis Optimisation – Towards a Robust Iterative Synthesis of Oligothiophenes

Alan C. Spivey,*[1] David J. Turner,[a] Michael L. Turner,[a] Stephen Yeates[b]

[a] Department of Chemistry, University of Sheffield, Brook Hill, Sheffield S3 7HF, UK
E-mail: a.c.spivey@imperial.ac.uk

[b] Avecia Ltd, Hexagon House, Blackley, Manchester M9 8ZS, UK

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Abstract: A convenient synthesis of a new dichlorogermanium-based linker-precursor for solid phase synthesis is described that allows facile introduction of a range of 'spectator' substituents (R) onto germanium. Variation of these R groups allows modulation of the stability of the key germanium–carbon bond between the linker and the aryl library. The tuning process is exemplified by application to the optimisation of a linker for the iterative solid-phase synthesis (SPS) of oligothiophenes.

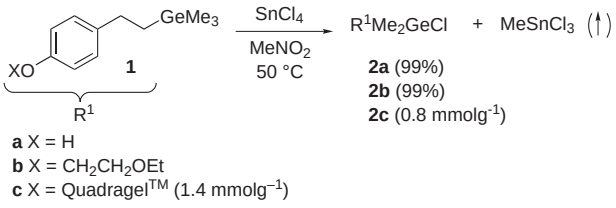
Key words: solid-phase synthesis, electrophilic aromatic substitutions, heterocycles, cross-coupling, combinatorial chemistry

Solid Phase Synthesis (SPS) using parallel or split/mix techniques constitutes an attractive method for the rapid preparation of large libraries of molecules for property screening.[2] Central to the success of the method is the compatibility of the chosen linker with the chemistry required for library construction and diversification.[3] The time required to achieve this compatibility impacts significantly on the overall efficiency of the strategy. Indeed, reservations over potentially long development times probably constitute the most significant impediment to more widespread exploitation of SPS.[4]

As no single linker constitutes a panacea for immobilisation via a given functional group, linker selection for SPS usually involves choosing from the growing repertoire of available linkers then experimentation.[5] The process has close analogy with protecting group (PG) selection for solution synthesis except that the choice is currently more limited. Moreover, PG selection is greatly aided by the availability of suites of graded PGs that allow fine-tuning vis-à-vis compatibility for a given application (such as silyl ethers with varying degrees of acid and fluoride stability for alcohol protection e.g. TMS, TES, TBDMS, TIPS, TBDPS etc.). Clearly, the ready availability of similar suites of linkers would be highly advantageous for streamlining the development of SPS programs.

We recently described solution phase studies directed towards the development of an iterative SPS of oligothiophenes using a dimethylgermanium-based linker.[6] Our approach exploited the orthogonal susceptibility of α-silyl and α-germyl substituted thiophenes towards nucleophilic *ipso*-protodemetalation to facilitate 'double-coupling' after each iteration. This double-coupling tactic was designed to minimise deletion sequences and so aid the preparation of high purity materials with interesting electronic properties.[7] In order to optimise the efficiency of the process and render it sufficiently robust for large-scale automated preparations it was desirable to be able to tune the two spectator substituents on the germanium linker (vide infra). The ability to make subtle variations to the ease of electrophilic and nucleophilic *ipso*-degermylation by such a tuning process was also expected to accelerate the deployment of this strategy for iterative synthesis of other conjugated oligomers incorporating alternative monomers and aid linker selection for other library applications.

The preparation of dimethylgermanium linkers **2a**–**c** relied on the 'activation' of trimethylgermanium linker-precursors **1a**–**c** by chemoselective mono-chlorodemethylation using excess tin(IV) chloride in nitromethane as the key step. We have previously reported the use of this reaction prior to attachment to the resin (**1a** → **2a**), in a solution phase model system (**1b** → **2b**), and 'on-resin' (**1c** → **2c**, Scheme 1).[8]



Scheme 1

The chemoselectivity of this transformation however precludes its adaptation to the preparation of analogues having spectator substituents other than methyl. Moreover, the stoichiometric co-formation of toxic methyltintrichloride and the fact that the on-resin variant of this reaction fails on tentagel-type resins[8c] detract from the attractiveness of this route.

To circumvent these issues a new more flexible route to dimethylgermanium linker **2a** and its analogues was devised. The new synthesis (Scheme 2) began with the selective formation of dichlorogermane **4a** from trichlorogermane **3a**.[8b] This was achieved by arylation with an excess of 4-anisylmagnesium bromide to provide

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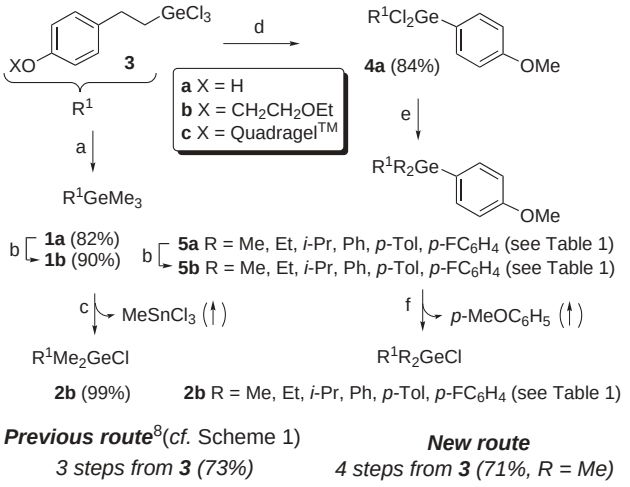
a crude mixture of di- and triarylgermanes which on work-up with concentrated HCl afforded dichlorogermane **4a** as the exclusive product (84%). The selectivity of this process arises from the stepwise attenuation of the rate of cleavage of the anisyl-Ge bonds as successive chlorides are introduced onto germanium.[9]



Scheme 2 (a) MeMgBr, toluene, 110 °C. (b) $EtOCH_2CH_2Cl$, *n*-Bu_4NI, Cs_2CO_3, MeCN, 85 °C. (c) $SnCl_4$, $MeNO_2$, 50 °C. (d) i) *p*-$MeOC_6H_4MgBr$, THF, r.t. ii) Concd HCl, CH_2Cl_2, r.t.[10] (e) RMgBr, THF, 70 °C.[11] (f) 1.0 M HCl in Et_2O, r.t.

Bis-methylation of dichlororgermane **4a** with MeMgBr gave dimethylgermane **5a** (R = Me) which, following Williamson etherification[8b] to give the ethoxyethyl linker-precursor **5b** (R = Me), underwent activation[12] with excess HCl in Et_2O to give dimethylgermane linker **2b** (R = Me). After removal of the volatile anisole by-product and excess HCl in vacuo, this material was identical to that prepared by the tin(IV) chloride route (Scheme 2).

This new route proved to be highly efficient for the preparation a series of ethoxyethyl solution phase model linkers **2b** having a variety of both alkyl and aryl spectator groups attached to germanium (Table 1).

Table 1 Preparation of Ethoxyethyl Solution Phase Model Linkers **2b** for Stability Studies

R	Isolated yields (%)		
	5a	**5b**	**2b**
Me	95	90	99
Et	74	70	Not isolated
i-Pr	53	77	Not isolated
Ph	92	80	98
p-Tol	92	70	98
p-FC_6H_4	92	72	97

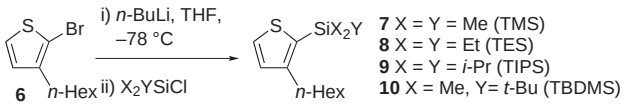
It is noteworthy that even for the three linkers having aryl substituents the HCl activation step (**5b** → **2b**) is completely selective for cleavage of anisole (vs. benzene, toluene or fluorobenzene). In all cases this step was complete within 24 hours at ambient temperature except for the *para*-fluorophenyl case for which 48 hours were required. With the aromatic substituents there is also potential for a second cleavage event to give a dichloride: this was not observed.

The utility of this new suite of sterically and electronically differentiated solution phase model linkers (**2b**) for facilitating the selection of a linker with an optimal stability profile for iterative SPS of oligothiophenes employing double-coupling was investigated next. Initial studies had employed the dimethylgermanium linker model (**2b**, R = Me) in conjunction with a TMS temporary 'blocking' group to protect the α-position of the growing oligomer.[6] For oligothiophenes greater than the tetramer, the TMS group proved to be susceptible to partial cleavage by traces of adventitious acid during analysis (e.g. during NMR spectroscopy in $CDCl_3$).[13] This finding indicated that a new silyl blocking group/germanium linker combination was needed which retained the orthogonal stability of the α-silyl vs α-germyl linkages towards CsF but for which the two partners had enhanced stability towards acid. Specifically, the following characteristics were required:

Silyl blocking group: This needed to be significantly more stable towards acid than TMS (to ensure a robust automatable process) and sufficiently labile towards fluoride to allow quantitative desilylation in the presence of the germanium linker (to allow double-coupling).

Germanium linker: This also needed to be stable towards acid (to ensure a robust automatable process), completely stable towards CsF (to allow double-coupling) and yet sufficiently labile to allow for cleavage of the final oligomer from the resin with a range of electrophiles.

Three silyl blocking groups were selected for evaluation: TES, TIPS and TBDMS. To this end, silylthiophenes **7**–**10** were prepared from bromothiophene **6** (Scheme 3).



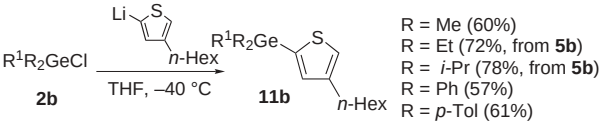
Scheme 3

As the TIPS thiophene **9** readily desilylated during chromatography on flash silica, presumably by *ipso*-protodesilylation promoted by relief of strain with the adjacent hexyl group,[14] only the TES and TBDMS derivatives **8** and **10** were taken forward for screening for their stability towards acid and fluoride. Screening consisted of monitoring the ^1H NMR spectrum of *ipso*-protodesilylation on exposure to a 1:1 mixture of HOAc in CH_2Cl_2 or a ca 0.3 M solution of CsF in DMF while the temperature was stepped up from 25 °C to 60 °C to 110 °C over 72 hours (Table 2).

Table 2 Acid and Fluoride Induced *ipso*-Desilylation of Silyl-Thiophenes **7**, **8** and **10**

Substrate	Cleavage conditions	
	HOAc	CsF
7 (TMS)	Cleavage at 25 °C	Cleavage at 25 °C
8 (TES)	Partial cleavage at 25 °C, complete at 60 °C	Cleavage at 25 °C
10 (TBDMS)	No cleavage to 110 °C	Cleavage at 60 °C

As expected the TES and TBDMS groups proved to be more resistant than TMS to *ipso*-protodesilylation by acid. The TBDMS group was most promising as it was the most acid stable. However, as this group also showed noticeably greater stability towards fluoride than the TMS or TES groups it required matching with an appropriately fluoride stable germanium linker. This was achieved by preparing hexyl thiophene derivatives of the suite of linker models **2b**[15] and subjecting these compounds to the above-described screening conditions (Scheme 4 and Table 3).



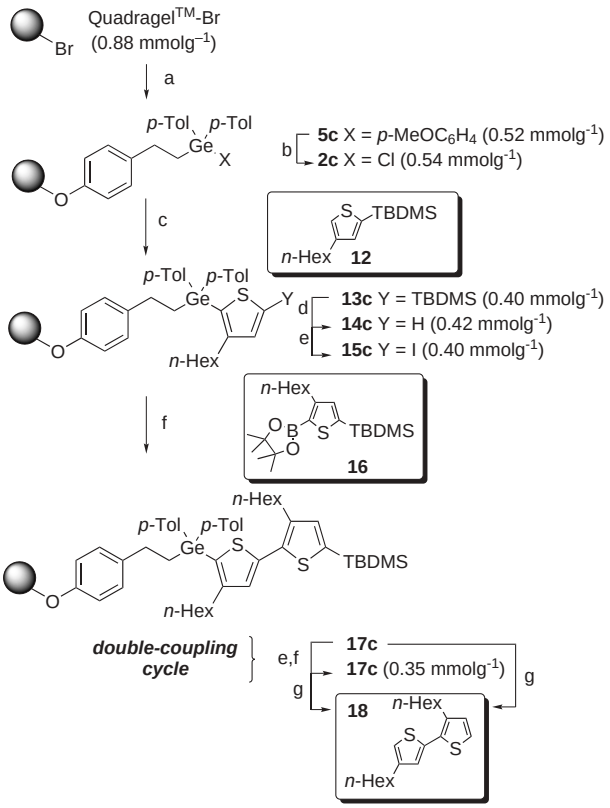
Scheme 4

Table 3 Acid and Fluoride Induced *ipso*-Protodegermylation of Germyl-Thiophenes **11b**

Substrate	Cleavage conditions	
	HOAc	CsF
11b (R = Me)	Partial cleavage at 25 °C, complete at 60 °C	No cleavage to 110 °C
11b (R = Et)	Partial cleavage at 25 °C, complete at 60 °C	No cleavage to 110 °C
11b (R = *i*-Pr)	Partial cleavage at 25 °C, complete at 60 °C	No cleavage to 110 °C
11b (R = Ph)	No cleavage to 110 °C	No cleavage to 110 °C
11b (R = *p*-Tol)	No cleavage to 110 °C	No cleavage to 110 °C

It can be seen from Table 3 that all the germanium linkers examined displayed significantly greater stability towards *ipso*-protodemetalation by CsF than the TBDMS blocked thiophene **10** and so in principle were suitable for double-coupling. Moreover, it is interesting to note that, in contrast to the situation with silicon, increasing the steric bulk around germanium (i.e. R = Me → Et → *i*-Pr) had no discernable effect on the rate of cleavage by HOAc (within the limits of our screen).[16] However, the linkers having aryl spectator substituents (i.e. R = Ph and *p*-Tol) were markedly more stable towards acid than those with alkyl substituents and therefore looked the most promising candidates for oligothiophene synthesis. To ensure that *ipso*-degermylation with strong electrophiles would still be possible for final oligomer cleavage from the resin both of these model systems (**11b**, R = Ph and *p*-Tol) were treated with a 1% solution of TFA in CH_2Cl_2 and it was found that they both underwent complete cleavage within ca 20 min.

As tolyl methyl groups provide a convenient marker for NMR reaction monitoring, the di-*p*-tolyl linker was selected for progression to SPS evaluation in conjunction with the TBDMS blocking group. Thus, di-*p*-tolylanisyl linker precursor **5a** was introduced onto Quadragel^{TM}-Br resin[17] by Williamson etherification and the resulting resin (**5c**) activated with HCl in Et_2O (→**2c**). The initial monomer, α-TBDMS-blocked hexylthiophene **12**, was then efficiently introduced, as its α-lithiated derivative. As required, TBDMS removal from the resulting resin bound thiophene proceeded selectively using CsF in DMF at 110 °C (**13c**→**14c**) without detectable cleavage of the arylgermane. Sequential α-iodination (→**15c**) and Suzuki cross-coupling with α-TBDMS-blocked thiophene boronic ester **16** also proceeded smoothly to give the resin bound bithiophene **17c** with high efficiency. The key double-coupling cycle also proceeded uneventfully (Scheme 5). HPLC analysis of cleaved (TFA) samples of bithiophene **18**[18] before and after double coupling had purities of 94% and 96% respectively, demonstrating the utility of this tactic for enhancing iteration efficiency.



Scheme 5 (a) **5a**, *n*-Bu_4NI, Cs_2CO_3, MeCN, 85 °C.[19] (b) 1.0 M HCl in Et_2O, r.t.[20] (c) **12**, LDA, THF, –40 °C.[21] (d) CsF, DMF, 110 °C.[22] (e) (i) LDA, THF, –40 °C, (ii) ICH_2CH_2I, dark, –40 °C.[23] (f) **16**, K_3PO_4, $Pd(PPh_3)_4$, DMF, 60 °C.[24] (g) TFA, CH_2Cl_2, r.t.[25]

In summary, a convenient route for the preparation of a new dichlorogermanium linker precursor **4a** has been developed and it has been shown that this compound can serve as a pivotal intermediate for the preparation of a range of di-alkyl and di-aryl germanium linkers for SPS. This new route allows activation of resin-bound linker-precursors (e.g. **5c**) simply by treatment with HCl in Et_2O. The ability to rapidly access a suite of germanium linkers displaying a range of stabilities towards electrophiles whilst retaining good stability towards nucleophiles offers exciting opportunities for tuning a linker to suit a specific library or other SPS application. This has been illustrated by the development of an iterative double-coupling approach to SPS of oligothiophenes wherein the combination of a TBDMS blocking group and a di-*p*-tolylgermanium linker was found to be optimal.

An account of the use of the optimised strategy for the SPS of high purity oligothiophenes will be disclosed shortly.

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(10) Dichlorogermane **4a**. To oven dried Mg turnings (1.01 g, 42.1 mmol) in THF (25 mL) was added 4-bromoanisole (5.21 mL, 41.6 mmol) dropwise. The resulting mixture was heated briefly, stirred for 1 h and then added dropwise to a solution of germyl trichloride **3a**[8b] (1.25 g, 4.17 mmol) in THF (10 mL) at r.t. before heating to 70 °C. After stirring for 16 h the reaction mixture was quenched by dropwise addition of water, concentrated to dryness in vacuo, and the residue dissolved in CH_2Cl_2 (30 mL). HCl (1 N, 5mL) and then concd HCl (60 mL) were added successively with stirring and the resultant mixture was stirred vigorously for 40 min. The aq layer was extracted with CH_2Cl_2 (3 × 50mL), the combined organic extracts dried ($MgSO_4$) and the solvent removed in vacuo. The residue was dissolved in CH_2Cl_2 (50 mL), extracted with 0.5 M NaOH(aq) (100 mL) and the aq layer washed with CH_2Cl_2 (3 × 50 mL). To the aq layer was added 1 N HCl (15 mL) and then concd HCl (100mL) with shaking, before extracting with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo to give dichlorogermane **4a** as an orange oil (1.30 g, 84%). IR (neat): 3019 (broad, OH), 2935–2835 (CH), 2361, 1591, 1514, 1442, 1403, 1290, 1254 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.96–2.02 (2 H), 2.83–2.90 (2 H), 3.75 (s, 3 H), 4.84 (br s, 1 H), 6.65 (d, *J* = 8.5 Hz, 2 H), 6.88 (d, *J* = 9.0 Hz, 2 H), 6.99 (d, *J* = 8.5 Hz, 2 H), 7.40 (d, *J* = 9.0 Hz, 2 H). ^{13}C NMR (63 MHz, $CDCl_3$): δ = 27.8 (t), 28.6 (t), 55.4 (q), 114.6 (2 × d), 115.5 (2 × d), 126.7 (s), 129.4 (2 × d), 133.8 (2 × d, s), 154.1 (s), 162.1 (s). MS (EI+): *m*/*z* = 372 [M^+]. HRMS: *m*/*z* [M^+] calcd for $C_{15}H_{16}Cl_2Ge^{74}O_2$: 371.9739; found: 371.9749.
(11) Di-*para*-tolylgermane **5a** (R = *p*-Tol). To oven dried Mg turnings (120 mg, 5.00 mmol) in THF (3 mL) was added 4-bromotoluene (855 mg, 5.00 mmol) dropwise. The resulting mixture was heated briefly, stirred for 1 h and then added dropwise to a solution of dichlorogermane **4a** (186 mg, 0.50 mmol) in THF (3mL) at r.t. After heating at 110 °C for 16 h the reaction mixture was quenched with sat. NH_4Cl (aq) (100 mL) and extracted with Et_2O (3 × 100 mL). The combined organic extracts were dried ($MgSO_4$), concentrated in vacuo and the residue purified by flash chromatography (SiO_2, petroleum ether–EtOAc, 3:1) to give ditolylgermane **5a** (R = *p*-Tol) as a yellow oil (231 mg, 92%); R_f 0.4 (petroleum ether–EtOAc, 3:1). IR (neat): 3409 (broad), 3012, 2921, 2861, 1593, 1568, 1512, 1442, 1392, 1281, 1247, 1180, 1089, 1031 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.72–1.80 (2 H), 2.36 (s, 6 H), 2.70–2.77 (2 H), 3.81 (s, 3 H), 4.64 (s, 1 H), 6.71 (d, *J* = 8.5 Hz, 2 H), 6.92 (d, *J* = 8.5 Hz, 2 H), 7.04 (d, *J* = 8.5 Hz, 2 H), 7.19 (d, *J* = 8.0 Hz, 4 H), 7.38 (d, *J* = 8.0 Hz, 4 H), 7.40 (d, *J* = 8.5 Hz, 2 H). ^{13}C NMR (63 MHz, $CDCl_3$): δ = 16.6 (t), 21.6 (2 × q), 30.4 (t), 55.2 (q), 114.2 (2 × d), 115.3 (2 × d), 128.2 (s), 129.0 (2 × d), 129.2 (4 × d), 133.8 (2 × s), 135.0 (4 × d), 136.3 (2 × d), 137.1 (s), 138.8 (2 × s), 153.6 (s), 160.3 (s). MS (EI+): *m*/*z* = 484 [M^+]. HRMS (EI+): *m*/*z* [M^+] calcd for $C_{29}H_{30}Ge^{74}O_2$: 484.1458; found: 484.1446.
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(19) Resin **5c**. To Quadragel™-Br (20.0 g, 18.6 mmol, from Quadragel™-OH[18] 0.93 mmol g^{-1} by treatment with CBr_4 and PPh_3 in CH_2Cl_2) swollen in a minimum of MeCN (200mL) were added germane **5a** (R = *p*-Tol, 19.4 g, 81.2 mmol), tetra-*n*-butylammonium iodide (740 mg, 2.00 mmol) and Cs_2CO_3 (26.2 g, 74.3 mmol) and the resulting mixture heated at 85 °C for 20 h. The reaction mixture was cooled and the resin was washed successively with MeCN (3 × 350 mL), DMF (3 × 350 mL), THF–water (1:1, 3 × 350 mL), THF (3 × 350 mL) and MeOH (3 × 350 mL) and then dried in vacuo to give resin **5c** as light brown granules (13.4 g, 74% conversion by the weight increase of the resin and the amount of phenol returned, LL = 0.52 mmolg^{-1}). IR (neat): 3030–2865 (CH), 1593, 1510, 1494, 1453, 1281, 1245, 698 (strong) cm^{-1}. ^{1}H MAS–NMR (400 MHz, $CDCl_3$): δ = 1.15–1.65 [CH(Ar)CH_2], 1.65–2.10 [ArCH_2, CH(Ar)CH_2], 2.37 (s, ArCH_3), 2.70–2.80 (GeCH_2), 3.50–4.15 (OCH_3, OCH_2), 6.10–6.70 (ArH), 6.70–7.30 (m, ArH), 7.41 (d, *J* = 4.5 Hz, ArH). ^{13}C MAS–NMR (100 MHz, $CDCl_3$): δ = 17.6, 21.8, 24.9, 25.2, 25.5, 25.7, 26.0, 31.7, 37.4, 41.6, 67.0, 67.3, 67.6, 67.9, 68.2, 71.7, 72.2, 128.9.

(20) Resin **2c**. To germylanisole resin **5c** (13.1 g, LL = 0.52 mmolg^{-1}, 6.8 mmol) swelled in CH_2Cl_2 (50 mL) was added HCl (65 mL, 1.0 M, 65 mmol) in Et_2O and the reaction mixture left to stir for 16 h. The solvent was then removed by filtration to give resin **2c** as brown granules (11.7 g, 100% conversion by ^{1}H NMR, LL = 0.54 mmol g^{-1}). IR(neat): 3030–2865 (CH), 1601, 1509, 1493, 1452, 1243, 697(strong) cm^{-1}. ^{1}H MAS–NMR (400 MHz, $CDCl_3$): δ = 1.00–2.30 [ArCH_2, CH(Ar)CH_2], 2.47 (s, ArCH_3), 2.85–2.95 (GeCH_2), 3.60–4.20 (OCH_2), 6.10–6.70 (ArH), 6.70–7.30 (ArH), 7.56 (d, *J* = 4.5 Hz, ArH).

(21) Resin **13c**. A solution of LDA (1.11 mL, 2.0 M, 2.21 mmol) in hexanes–THF–ethylbenzene (6:5:3) was added dropwise to a degassed solution of silylthiophene **12** (616 mg, 2.18 mmol) in THF (4 mL) at –50 °C. This solution was warmed to –40 °C, stirred for 40 min at this temperature and recooled to –50 °C. The solution was then transferred by cannula to a degassed suspension of germylchloride resin **2c** (777 mg, LL = 0.54 mmolg^{-1}, 0.42 mmol) in THF (10 mL) at –50 °C. The reaction mixture was stirred for 1 h at –40 °C, warmed to r.t. and stirred for a further 1 h. After quenching with sat. NH_4Cl (aq) (50 mL), the solvent was removed by filtration and the resin washed with DMF (3 × 50 mL), THF–water (1:1, 3 × 50 mL), THF (3 × 50 mL) and MeOH (3 × 50 mL). The resin was then dried in vacuo at 60 °C to give resin **13c** as yellow/orange granules (876 mg, 83% conversion by weight increase of resin, LL = 0.40 mmolg^{-1}). IR (neat): 3030–2865 (CH), 1601, 1509, 1492, 1451, 1244, 697 (strong) cm^{-1}. ^{1}H MAS–NMR (400 MHz, $CDCl_3$): δ = 0.41 [s, Si$(CH_3)_2$], 0.91 (t, *J* = 4.5 Hz, CH_2CH_3), 0.95–2.30 [C$(CH_3)_3$, $(CH_2)_4CH_3$, ArCH_2CH_2Ge, CH(Ar)CH_2], 2.47 (s, ArCH_3), 2.54 [t, *J* = 5.0 Hz, $CH_2(CH_2)_4CH_3$], 2.80–2.95 (GeCH_2), 3.60–4.25 (OCH_2), 6.10–6.80 (ArH), 6.80–7.30 (ArH), 7.53 (d, *J* = 4.5 Hz, ArH).

(22) Resin **14c**. To germylthiophene resin **13c** (642 mg, LL = 0.40 mmolg^{-1}, 0.26 mmol) swelled in DMF (8 mL) was added CsF (341 mg, 2.24 mmol) and the mixture left to stir for 72 h at 110 °C. The solvent was then removed by filtration and the resin washed with DMF (2 × 75 mL), THF–water (1:1, 3 × 75 mL), THF (3 × 75 mL) and MeOH (3 × 75 mL). The resin was then dried in vacuo at 60 °C to give resin **14c** as brown granules (560 mg, 100% conversion by ^{1}H NMR, LL = 0.42 mmol g^{-1}). IR (neat): 3030–2865 (CH), 1601, 1508, 1492, 1451, 1242, 697 (strong) cm^{-1}. ^{1}H MAS–NMR (400 MHz, $CDCl_3$): δ = 0.82 (t, *J* = 4.5 Hz, CH_2CH_3), 0.85–2.20 [$(CH_2)_4CH_3$, ArCH_2CH_2Ge, CH(Ar)CH_2], 2.37 (s, ArCH_3), 2.45–2.50 [$CH_2(CH_2)_4CH_3$], 2.70–2.85 (GeCH_2), 3.60–4.15 (OCH_2), 6.10–7.30 (ArH), 7.44 (d, *J* = 4.5 Hz, ArH), 7.50–7.55 (SCH).

(23) Resin **15c**. A solution of LDA (315 μL, 2.0 M, 0.63 mmol) in hexanes–THF–ethylbenzene (6:5:3) was added dropwise to a suspension of germylthiophene resin **14c** (526 mg, LL = 0.42 mmolg^{-1}, 0.22 mmol) in THF (4 mL) at –50 °C. After stirring for 2 h at –30 °C, a solution of degassed 1,2-diiodoethane (296 mg, 1.05 mmol) in THF (2 mL) was added by cannula at –50 °C. The resulting mixture was stirred in the dark for 2 h at –30 °C, warmed to r.t. and stirred for a further 1 h. The solvent was then removed by filtration and the resin washed with $Na_2S_2O_3$ (aq) (3 × 75 mL), THF–water (1:1, 3 × 75 mL), THF (3 × 75 mL) and MeOH (3 × 75 mL). The resin was then dried in vacuo at 60 °C to give resin **15c** as orange granules (533 mg, 100% conversion by ^{1}H NMR, LL = 0.40 mmol g^{-1}). IR(neat): 3030–2865 (CH), 1601, 1509, 1493, 1452, 1243, 697(strong) cm^{-1}. ^{1}H MAS–NMR (400 MHz, $CDCl_3$): δ = 0.82 (t, *J* = 4.5 Hz, CH_2CH_3), 0.85–2.20 [$(CH_2)_5CH_3$, ArCH_2CH_2Ge, C*H*(Ar)CH_2, ArCH_3], 2.70–2.85 (GeCH_2), 3.60–4.15 (OCH_2), 6.10–7.30 (ArH), 7.42 (d, *J* = 4.5 Hz, ArH).

(24) Resin **17c**. To a degassed solution of boronic ester **16** (242 mg, 0.59 mmol) and iodide resin **15c** (493 mg, LL = 0.40 mmolg^{-1}, 0.20 mmol) swelled in DMF (4 mL) was added $Pd(PPh_3)_4$ (11.6 mg, 10.0 μmol) and the resulting mixture stirred at 60 °C for 48 h. The solvent was then removed by filtration and the resin washed with DMF (2 × 50mL), THF–water (1:1, 3 × 50 mL), THF (3 × 50 mL) and MeOH (3 × 50 mL). The resin was then dried in vacuo at 60 °C to give resin **17c** as dark brown granules (508 mg, 87% conversion by the amount of bithiophene **18**[18] cleaved from the resin, *cf.* below, LL = 0.35 mmolg^{-1}). IR (neat): 3030–2865 (CH), 1601, 1509, 1492, 1451, 1244, 697 (strong) cm^{-1}. ^{1}H MAS–NMR (400 MHz, $CDCl_3$): δ = 0.31 [s, Si$(CH_3)_2$], 0.75–2.50 [C$(CH_3)_3$, $(CH_2)_5CH_3$, ArCH_2CH_2Ge, CH(Ar)CH_2, ArCH_3], 2.70–2.90 (GeCH_2), 3.50–4.20 (OCH_2), 6.10–7.60 (ArH). ^{13}C MAS–NMR (100 MHz, $CDCl_3$): δ = 14.5, 17.3, 18.6, 21.9, 22.9, 23.0, 26.8, 29.6, 29.7, 30.0, 31.1, 31.7, 32.0, 32.2, 40.9, 44.3, 67.9, 70.2, 71.1, 71.2, 114.6, 115.0, 126.1, 128.4, 128.8, 129.1, 129.5, 129.6, 130.5, 133.6, 134.2, 135.0, 135.1, 135.5, 137.4, 138.7, 139.2, 139.5, 140.1, 140.6, 141.6, 145.7, 151.4, 157.3.

(25) Bithiophene **18**.[18] To resin **17c** (after double-coupling, 40.4 mg, 16.2 μmol) was added a 33% solution of TFA in CH_2Cl_2 (750 μL) and the mixture left to stir at r.t. for 2 h. The solvent was then removed by filtration and the resin washed with CH_2Cl_2 (3 × 50 mL). These washings were then passed through a plug of silica and concentrated in vacuo to afford bithiophene **18** as an orange oil (4.7 mg, 96% pure by HPLC: Phenomenex Jupiter ODS C-18 column, UV 254 nm detection, 1 mL/min, 5–100% MeCN in H_2O + 0.1% formic acid, R_t 22.4 min). Spectroscopic data identical to that previously reported.[18]