

meta- Rather than *ortho*-Directed Metalations: Buttrressing Effects Prejudicing the Proton Abstraction from (2,6-Dihalophenyl)silanes

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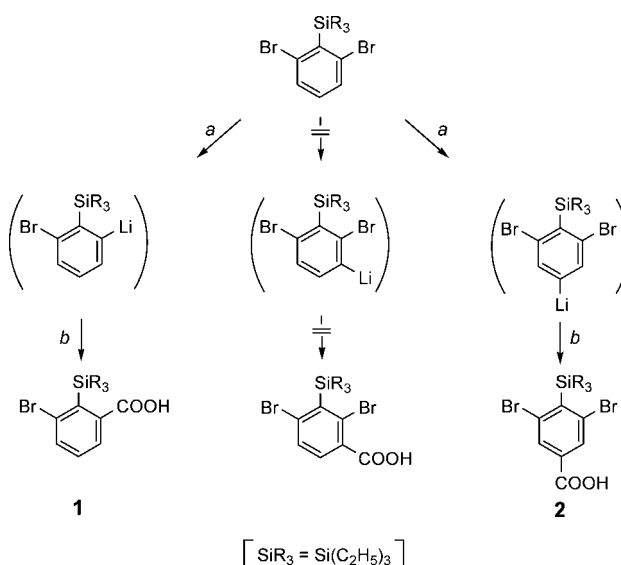
(2,6-Dichlorophenyl)trimethyl- and -triethylsilane exhibit untypical reactivity patterns toward strong bases. When treated at -100°C with lithium 2,2,6,6-tetramethylpiperidide, they give rise to two, with *sec*- or *tert*-butyllithium even three, different organometallic intermediates which can be intercepted with standard electrophiles. The trialkylsilyl group intervenes in two respects. Exerting steric pressure on the neighboring chlorine atoms, it facilitates the permutational displacement of one of them against lithium, a side reaction which occurs whenever alkylolithium compounds are employed. At the same time it impedes the attack of hydrogen

atoms by the base in the immediate vicinity of the halogens due to relay transmission of steric hindrance. As a consequence, deprotonation occurs preferentially or exclusively at the 5-(“*meta*”) rather than the 4-(“*ortho*”) position. 4-Lithiated species, generated as by-products or separately by permutational halogen/metal interconversion, eliminate lithium chloride at -75°C to set free didehydrobenzenes (“arynes”) which are trapped by their aryllithium precursors.

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When applying the “toolbox” methods^[1] to the regioexhaustive functionalization of 1,3-difluorobenzene^[2] and 1,3-dichlorobenzene^[3] we made an unexpected discovery. (2,6-Dichlorophenyl)trimethylsilane and (2,6-dichlorophenyl)triethylsilane underwent hydrogen/metal permutation (“metalation”) at the 5- rather than the 4-position or, in other words, *meta* rather than *ortho* to the activating halogen. However, the yields of the trapping products, the 3,5-dichloro-4-(trialkylsilyl)benzoic acids (60–70%), ranged far below our expectations, no matter whether *sec*-butyllithium or lithium 2,2,6,6-tetramethylpiperidide (LITMP) were employed as the base in tetrahydrofuran at -75°C . When (2,6-dibromophenyl)triethylsilane served as the substrate, 3,5-dibromo-4-(triethylsilyl)benzoic acid (**2**) was isolated in an even lower yield of only 52%. We worried whether we might have missed a regioisomer or any other by-product derived from the dichlorinated or dibrominated starting materials. The reaction was therefore repeated under systematic variation of some key parameters and the resulting mixtures were carefully examined by gas chromatography. At -100°C in tetrahydrofuran, LITMP promoted mainly a bromine/lithium permutation and only to a minor extent remote deprotonation as evidenced by the formation of 39% of 3-bromo-2-(triethylsilyl)benzoic acid (**1**) and 8% of 3,5-dibromo-4-(triethylsilyl)benzoic acid (**2**). The relative

amounts of **1** and **2** were inverted to 11% vs. 61% and 5.6% vs. 70%, respectively, when LITMP was employed in the presence of *N,N,N',N'',N'''*-pentamethyldiethylenetriamine (PMDTA) alone or in the additional presence of potassium *tert*-butoxide. The latter “Faigl mix”^[4] gave the dibromo acid **2** exclusively when the reaction was performed at -125°C in tetrahydrofuran or diethyl ether (15 and 4.1%



a: Lithium 2,2,6,6-tetramethylpiperidide (LITMP), *N,N,N',N'',N'''*-pentamethyldiethylenetriamine (PMDTA) and potassium *tert*-butoxide (KOR) in tetrahydrofuran (THF) at -100°C for 2 h. *b*: (1.) Carbon dioxide; (2.) hydrochloric acid.

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yield, respectively). In all these cases not even a trace amount of the isomeric 2,4-dibromo-3-(triethylsilyl)benzoic acid was detected.

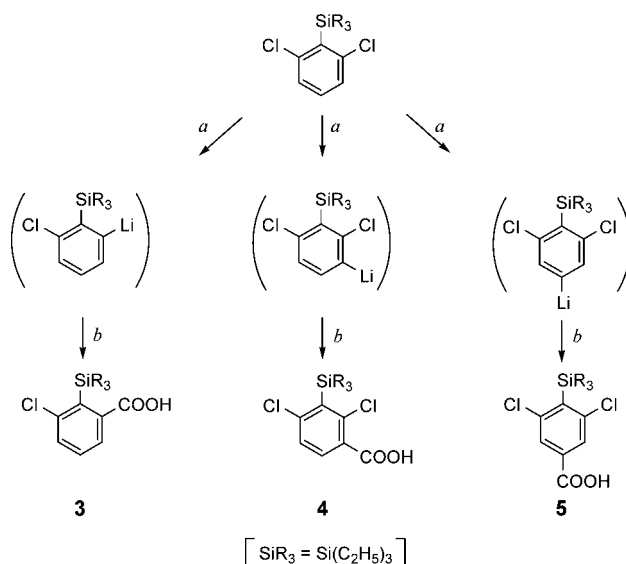
We turned then to (2,6-dichlorophenyl)triethylsilane. Its consecutive metalation and carboxylation was repeated at $-100\text{ }^{\circ}\text{C}$. Instead of the sole 3,5-dichloro-4-(triethylsilyl)benzoic acid (**5**) previously reported,^[3] this time one or two further reaction products were detected by gas chromatography (see Table 1). Lithium 2,2,6,6-tetramethylpiperidide (LITMP) gave the 2,4-dichloro-3-(triethylsilyl)benzoic acid (**4**) along with its isomer **5** in a 1:4 or 4:1 ratio, respectively, in the presence or absence of *N,N,N',N'',N'''*-pentamethyldiethylenetriamine (PMDTA). Other reagents, in particular *sec*-butyllithium in tetrahydrofuran (THF) or diethyl ether (DEE), activated or not by PMDTA, produced some 3-chloro-2-(triethylsilyl)benzoic acid (**3**) in addition to the isomers **4** and **5**, the proportions of which varied again with the reaction conditions. Only acids **5** (56–91 %) and no trace of acids **4** or **3** were isolated when the deprotonation was accomplished with polar reagents such as the “Faigl mix”^[4] (LITMP + PMDTA + potassium *tert*-butoxide), the LIC-KOR superbase^[5] and trimethylsilylmethylpotassium^[6] (Table 1). The acids obtained after carboxylation were esterified with diazomethane before being gas chromatographically identified by comparison of their retention times with that of authentic samples and quantified by determining their peak areas relative to an internal standard using calibration factors for correction.

Table 1. Consecutive metalation at $-100\text{ }^{\circ}\text{C}$ and carboxylation of (2,6-dichlorophenyl)triethylsilane: Yields and ratios of 3-chloro-2-(triethylsilyl)benzoic acid (**3**), 2,4-dichloro-3-(triethylsilyl)benzoic acid (**4**) and 3,5-dichloro-4-(triethylsilyl)benzoic acid (**5**) as a function of the basic reagent and the solvent used.

Reagent ^[a,b]	Solvent ^[a]	Yield ^[c]		Ratio ^[c] 3/4/5 ^[b]
		3	4 + 5	
$\text{LiCH}(\text{CH}_3)_2\text{C}_2\text{H}_5$	THF	91 %		7:24:69
$\text{LiCH}(\text{CH}_3)_2\text{C}_2\text{H}_5$ + PMDTA	THF	91 %		44:0:56
$\text{LiCH}(\text{CH}_3)_2\text{C}_2\text{H}_5$ + PMDTA	DEE	88 %		67:0:33
$\text{LiC}(\text{CH}_3)_3$	THF	93 %		7:11:82
$\text{LiC}(\text{CH}_3)_3$	DEE	81 %		34:9:57
LITMP	THF	65 %		0:82:18
LITMP + PMDTA	THF	83 %		0:14:86
(1.) LITMP + PMDTA (2.) KOR	THF	62 %		0:0:100
LITMP + PMDTA + KOR ^[d]	THF	66 %		0:0:100
LiC_4H_9 + KOR	THF	61 %		0:0:100
LiC_4H_9 + KOR	DEE	56 %		0:0:100
$\text{KCH}_2\text{Si}(\text{CH}_3)_3$	THF	91 %		0:0:100

[a] Abbreviations: PMDTA = *N,N,N',N'',N'''*-pentamethyldiethylenetriamine; KOR = potassium *tert*-butoxide; LITMP = lithium 2,2,6,6-tetramethylpiperidide; THF = tetrahydrofuran; DEE = diethyl ether. [b] The duration of the metalation reaction was ordinarily 45 min, but was extended to 2 h whenever LITMP was employed. When KOR was added not simultaneously with PMDTA, but later, the interval was 1 h followed by an additional hour of joint interaction. [c] Determined by gas chromatography of the product mixtures after quantitative conversion of the acids **3–5** into the methyl esters with diazomethane. [d] “Faigl mix”.^[4]

As controls have shown, all proton abstractions occur irreversibly. Thus, the strikingly divergent outcome of the metalation/carboxylation sequences depending on whether

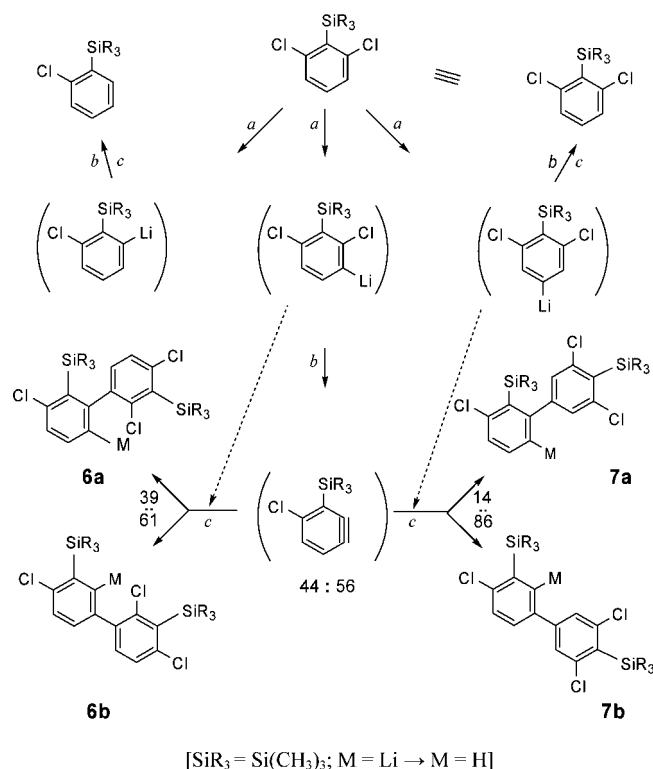


a: Metalation: for the conditions see Table 1. b: (1.) Carbon dioxide; (2.) hydrochloric acid.

alkyllithium compounds were employed in the presence or absence of potassium *tert*-butoxide and LITMP in the presence or absence of PMDTA is rigorously dictated by kinetics and is by no means the result of a subsequent isomerization step promoted by the complexand.

When the reaction mixture was stored at $-75\text{ }^{\circ}\text{C}$ for 1 h after the (2,6-dichlorophenyl)triethylsilane had been metalated at $-100\text{ }^{\circ}\text{C}$, the amount of the trapping products diminished slightly whereas the acid **4** disappeared completely from the mixture. This suggests decomposition of the corresponding organometallic precursor species by elimination of lithium chloride at the higher temperature. The dihydroarene (“aryne”) thus generated was intercepted by its own precursor, 2,4-dichloro-3-(triethylsilyl)phenyllithium, and the most abundant organometallic intermediate, 3,5-dichloro-4-(triethylsilyl)phenyllithium to afford, after neutralization, four isomers of trichloro- and bis(triethylsilyl)-substituted biphenyls.

In the correct hope to make such trichlorobiphenylbis(silanes) volatile enough for gas chromatography, we carried out all the following experiments starting from aryltrimethylsilanes. Thus, (2,6-dichlorophenyl)trimethylsilane was treated with *sec*-butyllithium in tetrahydrofuran at $-100\text{ }^{\circ}\text{C}$ for 45 min before the temperature was raised to $-75\text{ }^{\circ}\text{C}$ and, after again 45 min, the reaction was quenched with methanol. The concentrations of (2-chlorophenyl)trimethylsilane and (2,6-dichlorophenyl)trimethylsilane were determined relative to a calibrated internal standard and were found to correspond to 6.5 % and 58 %, respectively. Then all volatiles, including the two aryltrimethylsilanes were evaporated under reduced pressure. The residue left behind was composed of the four biphenylbis(silanes) **6a**, **6b**, **7a** and **7b** and represented 34 % of the starting material in an approximate 2:3:1:6 ratio.

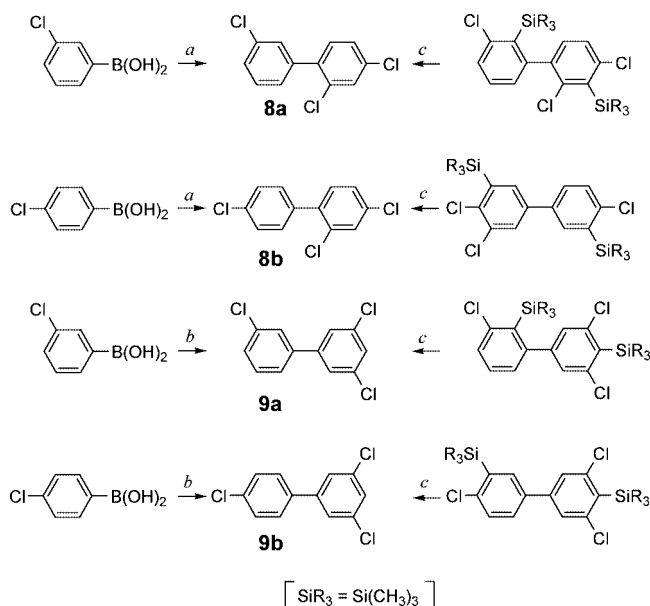


a: *sec*-Butyllithium in THF at -100°C for 45 min. b: At -75°C for 45 min. c: Methanol (excess).

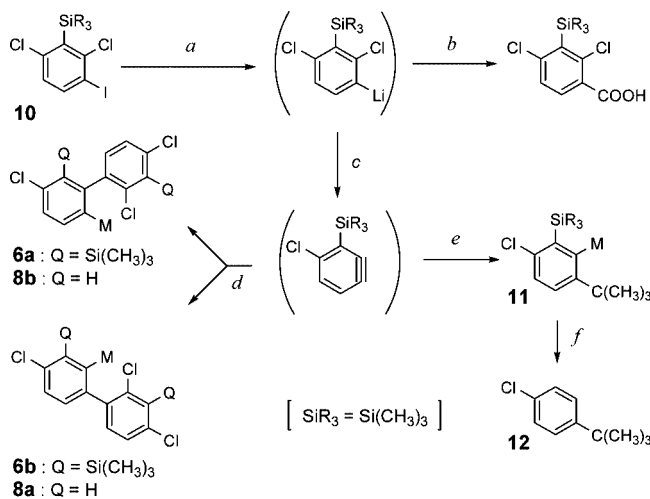
Fluoride-promoted protodesilylation converted the biarylboronic acids **6** and **7** quantitatively into the corresponding trichlorobiphenyls **8a** (2.8%), **8b** (9.4%), **9a** (4.9%) and **9b** (16.7%). Each of them were independently prepared by Suzuki–Miyaura coupling of 3- or 4-chlorophenylboronic acid with 2,4-dichloro-1-iodobenzene or 1,3-dichloro-5-iodobenzene. This enabled the unequivocal assessment of the trichlorobiphenyl mixture by gas chromatography.

The aryne precursor 2,4-dichloro-3-(trimethylsilyl)phenyllithium can be selectively generated from (2,6-dichloro-3-iodophenyl)trimethylsilane (**10**) by a permutational halogen/metal interconversion at -100°C as evidenced by its transformation to the 2,4-dichloro-3-(trimethylsilyl)benzoic acid (**6**; 93%). Raising the temperature to -75°C caused elimination of lithium chloride. The aryne was trapped by 2,4-dichloro-3-(trimethylsilyl)phenyllithium, this time the only arylmetal compound available, to furnish the two trichlorobiphenyls **8a** (27%) and **8b** (37%) after neutralization and protodesilylation. When the aryne was set free in the presence of a threefold excess of *tert*-butyllithium, nucleophilic addition of the latter occurred. Upon neutralization, (5-*tert*-butyl-2-chlorophenyl)trimethylsilane (**11**) and, upon protodesilylation, 1-*tert*-butyl-4-chlorobenzene (**12**) were both obtained in 73% yield, respectively. The latter product was separately prepared from the commercial 1-bromo-4-*tert*-butylbenzene by consecutive halogen/metal permutation and chlorination with 1,1,2-trichloro-1,2,2-trifluoroethane.

The extreme regioselectivity of the *tert*-butyllithium addition to the aryne deserves attention as it was not to be



a: 2,4-Dichloro-1-iodobenzene (1.0 equiv.) and tetrakis(triphenylphosphane)palladium (0.050 equiv.) in benzene at $+25^{\circ}\text{C}$ for 12 h. b: 1,3-Dichloro-5-iodobenzene (1.0 equiv.) and tetrakis(triphenylphosphane)palladium in benzene at $+25^{\circ}\text{C}$ for 12 h. c: Tetrabutylammonium fluoride trihydrate (2.0 equiv.) in tetrahydrofuran at $+25^{\circ}\text{C}$ for 24 h.



a: *tert*-Butyllithium (2.0 equiv.) in THF at -100°C for 15 min. b: (1.) Dry ice (excess); (2.) hydrochloric acid. c: At -75°C for 45 min. d: After 45 min., methanol (excess). e: In the presence of excess *tert*-butyllithium (3.0 equiv.). f: Tetrabutylammonium fluoride hydrate in THF at $+25^{\circ}\text{C}$ for 24 h.

expected. It is in contrast with the behavior of *tert*-butyllithium toward 1,2-didehydronaphthalene where it adds to the 1- and 2-position in the same ratio of 1:2 exactly as butyllithium, phenyllithium and lithium diethylamide do.^[7,8] High regioselectivities (e.g., 20:1 in the case of the phenyllithium addition to 1,2-didehydro-3-methoxybenzene^[9]) were so far only found with electronically biased arynes, in particular when a heterosubstituent coordinates with the lithium atom at the transition state and thus guides it to its future location.

On the other hand it remains a puzzling question why the sterically less hindered 3,5-dichloro-4-(trimethylsilyl)-phenyllithium attacks the formal triple bond of the 4-chloro-1,2-didehydro-3-(trimethylsilyl)benzene more selectively than the isomeric 2,4-dichloro-3-(trimethylsilyl)phenyllithium does, providing the adducts **7a/7b** and **6a/6b** in a 1:6 (14:86) and 4:6 (39:61) ratio, respectively (see above). On the basis of steric considerations one might have predicted the opposite outcome.

The results presented above confirm previously expressed tentative ideas. The bulky trialkylsilyl group exerts a “but-tressing”^[3] action on the neighboring chlorine atoms which substantially decreases the proton mobility at the adjacent 4-position to the extent of being surpassed by the remote 5-position. At the same time, the steric pressure exerted by the trialkylsilyl group on the chlorine atoms makes those more prone to halogen/metal permutational displacement, an unprecedented reaction mode among dichloroarenes.

Experimental Section

1. Generalities: Details concerning standard operations and abbreviations have been given in previous publications from this laboratory.^[10–12] ¹H and (¹H-decoupled) ¹³C NMR spectra were recorded at 400 and 101 MHz, respectively. If not specified otherwise, the samples were dissolved in deuteriochloroform or, if marked by an asterisk, in hexadeuterioacetone. ¹³C NMR signals being monitored as lines, their intensities cannot be exactly determined. They were only estimated by visual inspection. The stationary phases employed for gas chromatography were of the silicon rubber type (SE-30, DB-1), polyethylene glycol type (C-20M, DB-WAX) and polyether type (PFO = perfluoropolyether PFO-XR75 supplied by Apollo Scientific, Stockport, SK6 2QR, UK).

2. Derivatives of (2,6-Dibromophenyl)triethylsilane

(2,6-Dibromophenyl)triethylsilane and 3,5-dibromo-4-(triethylsilyl)-benzoic acid (**2**) have been described previously.^[3]

Methyl 3,5-Dibromo-4-(triethylsilyl)benzoate: Acid **2** (5.9 g, 15 mmol) was converted into its methyl ester by treatment with ethereal diazomethane until persistence of the yellow color; b.p. 131–133 °C/0.2 Torr; $n_D^{20} = 1.5307$; $d_4^{20} = 1.783$; yield: 5.63 g (92%). ¹H NMR: $\delta = 8.13$ (s, 2 H), 3.91 (s, 3 H), 1.1 (m, 6 H), 1.0 (m, 9 H) ppm. ¹³C NMR: $\delta = 164.4$, 145.1, 133.4, 132.4, 131.4, 52.5, 7.9 (3 C), 6.5 (3 C). C₁₄H₂₀Br₂O₂Si (408.17): calcd. C 41.19, H 4.93; found C 41.23, H 4.86.

3-Bromo-2-triethylsilylbenzoic Acid (1): (2,6-Dibromophenyl)triethylsilane^[3] (6.2 mL, 8.8 g, 25 mmol) was added to a solution of butyllithium (25 mmol) in hexanes (15 mL) and diethyl ether (35 mL) kept in a dry ice/methanol bath. After 15 min at –75 °C, the mixture was poured onto an excess of freshly crushed dry ice. At +25 °C, a 2.0 M ethereal solution of hydrogen chloride (30 mL) was added and the solvents were evaporated. The residue was extracted with hot pentanes and the filtrate distilled to afford a heavy yellowish oil; b.p. 146–148 °C/0.2 Torr; yield: 7.10 g (90%). ¹H NMR: $\delta = 7.70$ (dd, $J = 8.0$, 1.3 Hz, 1 H), 7.65 (dd, $J = 7.7$, 1.3 Hz, 1 H), 7.23 (t, $J = 8.0$ Hz, 1 H), 1.1 (m, 6 H), 1.0 (m, 9 H) ppm. ¹³C NMR: $\delta = 175.9$, 141.6, 138.8, 136.3, 132.3, 129.7, 127.4, 7.9 (3 C), 5.1 (3 C) ppm. C₁₃H₁₉BrO₂Si (315.25): calcd. C 49.52, H 6.07; found C 49.34, H 5.91. Methyl ester: Prepared from acid **1** (5.9 g, 15 mmol) with diazomethane. Immediate distillation gave a color-

less oil; b.p. 117–120 °C/3 Torr; $n_D^{20} = 1.4941$; $d_4^{20} = 1.372$; yield: 4.64 g (94%). ¹H NMR: $\delta = 7.63$ (dd, $J = 8.0$, 1.0 Hz, 1 H), 7.43 (dd, $J = 7.4$, 1.0 Hz, 1 H), 7.19 (t, $J = 8.0$ Hz, 1 H), 3.87 (s, 3 H), 0.9 (m, 15 H) ppm. ¹³C NMR: $\delta = 170.0$, 142.9, 137.5, 135.3, 132.0, 129.7, 126.9, 52.3, 7.7 (3 C), 4.6 (3 C) ppm. C₁₄H₂₁BrO₂Si (329.27): calcd. C 51.06, H 6.42; found C 51.00, H 6.47.

Reaction of (2,6-Dibromophenyl)triethylsilane with LITMP Followed by Carboxylation: 2,2,6,6-Tetramethylpiperidine (4.3 mL, 3.5 g, 25 mmol) and, where appropriate, also *N,N,N',N',N''*-pentamethyldiethylenetriamine (PMDTA; 5.2 mL, 4.3 g, 25 mmol) or potassium *tert*-butoxide (2.8 g, 25 mmol) and (2,6-dibromophenyl)triethylsilane (6.2 mL, 8.8 g, 25 mmol) were added consecutively to a solution of butyllithium (25 mmol) in hexanes (15 mL) and tetrahydrofuran (35 mL) cooled to –100 °C. After 2 h at this temperature, the reaction mixture was poured onto an excess of freshly crushed dry ice. After evaporation of the volatiles, it was acidified with 2.0 M hydrochloric acid (10 mL), extracted with ethyl acetate (3 × 50 mL) and dried. One tenth of the organic phase was treated with an ethereal solution of diazomethane until the yellow color persisted. The product composition (see Table 1) was assessed by gas chromatographic analysis (30 m DB-WAX, 250 °C; 30 m DB-1, 250 °C; calibrated internal standard: tridecane). Methyl 2,4-dibromo-3-triethylsilylbenzoate was not detected even in trace amounts in any of these runs. The bulk of the mixture resulting from the LITMP/PMDTA/KOR reaction was evaporated and the residue crystallized from hexanes to afford acid **2**; m.p. 157–159 °C (ref.^[3] 157–159 °C); yield: 6.31 g (64%).

3. Derivatives of (2,6-Dichlorophenyl)triethylsilane

(2,6-Dichlorophenyl)triethylsilane, 2,4-dichloro-3-(triethylsilyl)benzoic acid (**4**) and 3,5-dichloro-4-(triethylsilyl)benzoic acid (**5**) have been described previously.^[3] Meanwhile a simplified access to acid **4** has been found (see below). To increase their gas chromatographic volatility, all acids were converted into the methyl esters by exhaustive treatment with diazomethane.

2,4-Dichloro-3-(triethylsilyl)benzoic Acid (4): A solution of (2,6-dichloro-3-iodophenyl)triethylsilane (see following paragraph; 6.7 mL, 9.7 g, 25 mmol) and *tert*-butyllithium (50 mmol) in diethyl ether (70 mL) and pentanes (30 mL) was kept at –100 °C for 15 min. The mixture was poured onto an excess of freshly crushed dry ice before being neutralized with a 2.0 M ethereal solution of hydrogen chloride (30 mmol). The volatiles were evaporated and the residue was extracted with boiling hexanes (3 × 15 mL). Upon filtration and cooling of the combined filtrates, small needles were obtained; m.p. 87–89 °C (ref.^[3] 87–89 °C); yield: 6.87 g (90%). Methyl ester: colorless oil; b.p. 106–108 °C/0.3 Torr, $n_D^{20} = 1.4222$; $d_4^{20} = 1.208$; yield: (95%). ¹H NMR: $\delta = 7.49$ (d, $J = 8.3$ Hz, 1 H), 7.29 (d, $J = 8.0$ Hz, 1 H), 3.91 (s, 3 H), 1.1 (m, 6 H), 1.0 (m, 9 H) ppm. ¹³C NMR: $\delta = 166.0$, 144.3, 139.8, 136.9, 130.9, 130.8, 128.1, 51.9, 7.4 (3 C), 6.0 (3 C) ppm. C₁₄H₂₀Cl₂O₂Si (319.27): calcd. C 52.66, H 6.31; found C 52.70, H 6.34.

(2,6-Dichloro-3-iodophenyl)triethylsilane: Diisopropylamine (14 mL, 10 g, 0.10 mol) and 2,4-dichloro-1-iodobenzene (13 mL, 27 g, 0.10 mol) were consecutively added to a solution of butyllithium (0.10 mol) in hexanes (67 mL) and tetrahydrofuran (0.14 L) at –75 °C. After 2 h at –75 °C, chlorotriethylsilane (18 mL, 16 g, 0.10 mol) was added. Upon direct distillation, a colorless oil was obtained; b.p. 121–123 °C/0.3 Torr; $n_D^{20} = 1.5954$; $d_4^{20} = 1.440$; yield: 32.5 g (84%). ¹H NMR: $\delta = 7.75$ (d, $J = 8.5$ Hz, 1 H), 6.93 (d, $J = 8.5$ Hz, 1 H), 1.1 (m, 6 H), 1.0 (m, 9 H) ppm. ¹³C NMR: $\delta = 145.0$, 142.3, 141.3, 137.1, 129.8, 98.9, 7.9 (3 C), 6.3 (3 C) ppm. C₁₂H₁₇Cl₂ISi (387.15): calcd. C 37.23, H 4.43; found C 37.31, H 4.36.

3,5-Dichloro-4-(triethylsilyl)benzoic Acid (5):^[3] Methyl ester: colorless oil; b.p. 98–100 °C/0.3 Torr; $n_D^{20} = 1.4946$; $d_4^{20} = 1.223$; yield: (98%). ¹H NMR: $\delta = 7.86$ (s, 2 H), 3.92 (s, 3 H), 1.0 (m, 15 H) ppm. ¹³C NMR: $\delta = 164.9, 142.5, 140.9, 132.5, 129.1, 52.5, 7.7$ (3 C), 5.9 (3 C) ppm. C₁₄H₂₀Cl₂O₂Si (319.27): calcd. C 52.66, H 6.31; found C 52.64, H 6.26.

3-Chloro-2-(triethylsilyl)benzoic Acid (3): At –75 °C, (2-bromo-6-chlorophenyl)triethylsilane (see following paragraph; 4.6 g, 25 mmol) was treated with butyllithium (25 mmol) in tetrahydrofuran (40 mL) and hexanes (10 mL). After 15 min at –75 °C, the mixture was poured onto an excess of freshly crushed dry ice. After addition of a 2.0 M ethereal solution of hydrogen chloride (30 mL), the volatiles were evaporated. The residue was extracted with hot hexanes (3 × 25 mL) and the filtrate concentrated to afford colorless needles; m.p. 37–39 °C; yield: 3.80 g (94%). ¹H NMR: $\delta = 7.61$ (dd, $J = 7.3, 1.0$ Hz, 1 H), 7.48 (dd, $J = 8.0, 1.3$ Hz, 1 H), 7.32 (t, $J = 7.7$ Hz, 1 H), 1.0 (m, 15 H) ppm. ¹³C NMR: $\delta = 175.8, 142.8, 141.0, 136.5, 132.8, 129.7, 127.0, 7.8$ (3 C), 5.1 (3 C) ppm. C₁₃H₁₉ClO₂Si (270.80): calcd. C 57.66, H 7.07; found C 57.69, H 7.06. Methyl ester: colorless oil; b.p. 80–82 °C/0.3 Torr; $n_D^{20} = 1.4089$; $d_4^{20} = 1.136$; yield: 4.10 g (96%). ¹H NMR: $\delta = 7.41$ (dd, $J = 8.0, 1.3$ Hz, 1 H), 7.40 (dd, $J = 8.0, 1.2$ Hz, 1 H), 7.28 (d, $J = 8.0$ Hz, 1 H), 3.87 (s, 3 H), 0.9 (m, 15 H) ppm. ¹³C NMR: $\delta = 169.8, 142.3, 135.1, 131.6, 129.5, 126.3$ (2 C), 52.0, 7.5 (3 C), 4.5 (3 C) ppm. C₁₄H₂₁ClO₂Si (284.83): calcd. C 59.03, H 7.43; found C 59.13, H 7.39.

(2-Bromo-6-chlorophenyl)triethylsilane: 2,2,6,6-Tetramethylpiperidine (17 mL, 14 g, 0.10 mol) and 1-bromo-3-chlorobenzene (12 mL, 19 g, 0.10 mol) were added consecutively to a solution of butyllithium (0.10 mol) in hexanes (55 mL) and tetrahydrofuran (0.15 L) kept in a dry ice/methanol bath. After 2 h at –75 °C, chlorotriethylsilane (17 mL, 15 g, 0.10 mol) was added. Immediate distillation afforded a colorless oil; b.p. 80–82 °C/1 Torr; $n_D^{20} = 1.5555$; $d_4^{20} = 1.317$; yield: 26.7 g (87%). ¹H NMR: $\delta = 7.46$ (dd, $J = 8.0, 1.0$ Hz, 1 H), 7.27 (dd, $J = 8.0, 1.0$ Hz, 1 H), 7.05 (t, $J = 8.0$ Hz, 1 H), 1.1 (m, 15 H) ppm. ¹³C NMR: $\delta = 142.6, 137.3, 132.5, 131.5, 130.7, 129.3, 7.9$ (3 C), 6.3 (3 C) ppm. C₁₂H₁₈BrClSi (306.57): calcd. C 47.01, H 5.92; found C 47.18, H 5.93.

Consecutive Reaction of (2,6-Dichlorophenyl)triethylsilane with Various Strong Bases and Carbon Dioxide: At –100 °C, (2,6-dichlorophenyl)triethylsilane (5.4 mL, 6.5 g, 25 mmol) was added to a solution containing the metalating reagent (25 mmol) and, where appropriate, a complexand (PMDTA, KOR) in stoichiometric amounts in tetrahydrofuran (30 mL) and a hydrocarbon (20 mL) such as hexanes or cyclohexane. After 45 min or, when LITMP served as the base, after 2 h at –100 °C, the mixture was poured onto an excess of freshly crushed dry ice. The slurry was worked up analogously as in the case of (2,6-dibromophenyl)triethylsilane derivatives (see above) and the product compositions (see Table 1) were quantified by gas chromatography (30 m DB-Wax, 220 °C; 30 m DB-1; internal calibrated standard: tridecane).

4. Derivatives of (2,6-Dichlorophenyl)trimethylsilane

(2,6-Dichlorophenyl)trimethylsilane, 2,4-dichloro-3-(trimethylsilyl)benzoic acid and 3,5-dichloro-4-(trimethylsilyl)benzoic acid have been described previously.^[3]

2,3',4'-Trichlorobiphenyl (8a): 3-Chlorophenylboronic acid^[13] (1.6 g, 10 mmol), 2,4-dichloro-1-iodobenzene (1.3 mL, 2.7 g, 10 mmol), tetrakis(triphenylphosphane)palladium(0) (0.34 g, 0.30 mmol), benzene (20 mL) and a 2.0 M aqueous solution of sodium carbonate (10 mL) were stirred at +25 °C for 12 h. Then, 35% aqueous hydrogen peroxide solution (10 mL) was added and the stirring was

continued for 45 min at +25 °C. The aqueous phase was extracted with diethyl ether (3 × 10 mL). The combined organic layers were dried and evaporated; small needles (from methanol); m.p. 36–38 °C (ref.^[13] 37–39 °C); yield: 2.30 g (90%). ¹H NMR: $\delta = 7.50$ (d, $J = 2.2$ Hz, 1 H), 7.40 (m, 1 H), 7.37 (m, 2 H), 7.30 (td, $J = 8.5, 2.1$ Hz, 2 H), 7.24 (d, $J = 8.5$ Hz, 1 H) ppm.

2,4,4'-Trichlorobiphenyl (8b): Prepared analogously from 4-chlorophenylboronic acid^[14] (1.6 g, 10 mmol) and 2,4-dichloro-1-iodobenzene (1.3 mL, 2.7 g, 10 mmol); colorless needles from methanol; m.p. 53–55 °C (ref.^[14] 55 °C); yield: 2.45 g (95%). ¹H NMR: $\delta = 7.50$ (m, 1 H), 7.42 (d, $J = 8.5$ Hz, 2 H), 7.35 (d, $J = 8.5$ Hz, 2 H), 7.25 (d, $J = 8.5$ Hz, 2 H) ppm.

3,3',5'-Trichlorobiphenyl (9a): Prepared analogously from 3-chlorophenylboronic acid (1.6 g, 10 mmol) and 3,5-dichloro-1-iodobenzene (2.7 g, 10 mmol); colorless needles from ethanol; m.p. 78–79 °C (ref.^[13] 78–79 °C); yield: 2.44 g (96%). ¹H NMR: $\delta = 7.51$ (m, 1 H), 7.42 (d, $J = 1.9$ Hz, 2 H), 7.4 (m, 4 H) ppm.

3,4',5'-Trichlorobiphenyl (9b): Prepared analogously from 4-chlorophenylboronic acid (1.6 g, 10 mmol) and 3,5-dichloro-1-iodobenzene (2.7 g, 10 mmol); colorless needles from pentanes; m.p. 87–88 °C (ref.^[15] 88 °C); yield: 2.39 g (93%). ¹H NMR: $\delta = 7.44$ (d, $J = 8.5$ Hz, 2 H), 7.42 (d, $J = 8.5$ Hz, 2 H), 7.40 (d, $J = 2.0$ Hz, 2 H), 7.35 (t, $J = 2.0$ Hz, 1 H) ppm.

Consecutive Reaction of (2,6-Dichlorophenyl)trimethylsilane with *sec*-Butyllithium, Methanol and Tetrabutylammonium Fluoride Hydrate: At –100 °C, (2,6-dichlorophenyl)trimethylsilane (9.1 mL, 11 g, 50 mmol) was added to a solution of *sec*-butyllithium (50 mmol) in cyclohexane (40 mL) and tetrahydrofuran (60 mL). After 45 min at –100 °C and another 45 min at –75 °C, the reaction mixture was treated with methanol (2.1 mL, 1.9 g, 60 mmol). According to gas chromatographic analysis (30 m, DB-1, 80 °C; 1 m, 5% SE-30, 80 °C; nonane as an internal calibrated standard), the crude material contained 6.5% of (2-chlorophenyl)trimethylsilane and 58% of (2,6-dichlorophenyl)trimethylsilane. Evaporation and extraction with hot hexanes (3 × 50 mL) gave a yellowish oil (9.85 g) which was distilled under reduced pressure. The first fraction was essentially composed of (2-chlorophenyl)trimethylsilane (b.p. 45–47 °C/6 Torr; ref.^[16] 207–208 °C/740 Torr); yield: 0.15 g (3.4%). The second fraction consisted of (2,6-dichlorophenyl)trimethylsilane (b.p. 53–54 °C/3 Torr; ref.^[16] 79–81 °C/4 Torr); yield: 3.01 g (55%). A third fraction, a yellowish oil (b.p. 161–164 °C/0.2 Torr), contained four high molecular weight products in the ratio of 2:3:6:9 according to gas chromatographic analysis (2 m, 10% PFO, 130 °C; 1 m, 2% C-20M, 180 °C; 2,2',6,6'-tetrabromobiphenyl as an internal calibrated standard); yield: 3.22 g (32%). The third fraction (3.0 g, 7.5 mmol) was treated with an excess of tetrabutylammonium fluoride trihydrate (4.7 g, 15 mmol) in dimethylformamide (50 mL) at 25 °C during 24 h. Evaporation, extraction with hot hexanes (3 × 50 mL) and distillation (b.p. 139–145 °C/0.3 Torr) afforded a viscous oil; yield: 1.91 g (99%). According to gas chromatographic analysis (same conditions as specified above) using authentic samples for retention time comparison, it was composed of 3,3',5'-trichlorobiphenyl (9a), 2,4,4'-trichlorobiphenyl (8b), 2,3',4'-trichlorobiphenyl (8a) and 3,4',5'-trichlorobiphenyl (9b) in a 2:3:6:9 ratio. An aqueous 88% solution of formic acid (2.6 mL, 5.0 mmol) in water (2.6 mL) was added dropwise over 45 min to a refluxing solution containing the four trichlorobiphenyls (1.3 g, 5.0 mmol), sodium carbonate (5.3 g, 50 mmol) and 10% palladium on charcoal (0.5 g) in toluene (20 mL). After 15 min at 100 °C, the reaction mixture was washed with brine (3 × 10 mL). The organic phase was dried and concentrated to leave behind 0.74 g (96%) of biphenyl; m.p. 70–71 °C (ref.^[17] 70.5 °C).

5. Derivatives of (2,6-Dichloro-3-iodophenyl)trimethylsilane

2,4-Dichloro-3-(trimethylsilyl)benzoic Acid (6): At -100°C , (2,6-dichloro-3-iodophenyl)trimethylsilane (**10**; see following paragraph; 4.8 mL, 8.6 g, 25 mmol) was added to a solution of *tert*-butyllithium (50 mmol) in pentanes (35 mL) and diethyl ether (70 mL). After 15 min at -100°C , the reaction mixture was poured onto an excess of freshly crushed dry ice before being neutralized with a 2.0 M ethereal solution of hydrogen chloride (30 mmol). The volatiles were evaporated and the residue was extracted with boiling hexanes (3×15 mL). Upon cooling of the combined and concentrated filtrates, small needles were obtained; m.p. $94\text{--}96^{\circ}\text{C}$ (from hexanes); yield: 6.12 g (93%). ^1H NMR: $\delta = 7.71$ (d, $J = 8.3$ Hz, 1 H), 7.33 (d, $J = 8.3$ Hz, 1 H), 0.54 (s, 9 H) ppm. ^{13}C NMR: $\delta = 171.3$, 145.5, 140.7, 139.6, 132.4, 129.0, 128.7, 3.2 ppm. $\text{C}_{10}\text{H}_{12}\text{Cl}_2\text{O}_2\text{Si}$ (263.16): calcd. C 45.64, H 4.60, found C 45.79, H 4.54.

(2,6-Dichloro-3-iodophenyl)trimethylsilane (10): Diisopropylamine (14 mL, 10 g, 0.10 mol) and 2,4-dichloro-1-iodobenzene (13 mL, 27 g, 0.10 mol) were added consecutively to a solution of butyllithium (0.10 mol) in hexanes (67 mL) and tetrahydrofuran (0.14 L) at -75°C . After 2 h at -75°C , the mixture was treated with chlorotrimethylsilane (13 mL, 11 g, 0.10 mol). Immediate distillation afforded a colorless oil; b.p. $89\text{--}91^{\circ}\text{C}/0.8$ Torr; $n_{\text{D}}^{20} = 1.5618$; $d_4^{20} = 1.775$; yield: 30.3 g (88%) ^1H NMR: $\delta = 7.75$ (d, $J = 8.3$ Hz, 1 H), 6.94 (d, $J = 8.3$ Hz, 1 H), 0.50 (s, 9 H) ppm. ^{13}C NMR: $\delta = 144.5$, 141.6, 141.2, 138.6, 129.8, 98.9, 2.8 (3 C) ppm. $\text{C}_9\text{H}_7\text{Cl}_2\text{ISi}$ (345.07): calcd. C 31.32, H 3.21; found C 31.38, H 3.13.

1-*tert*-Butyl-4-chlorobenzene (12): 1-Bromo-4-*tert*-butylbenzene (5.3 g, 25 mmol) was added to a solution of *tert*-butyllithium (50 mmol) in pentanes (35 mL) and diethyl ether (65 mL) kept in a dry ice/methanol bath. After 15 min at -75°C , the mixture was treated with 1,1,2-trichlorotrifluoroethane (5.6 g, 30 mmol). Immediate distillation afforded a colorless oil, b.p. $51\text{--}53^{\circ}\text{C}/2$ Torr (ref.^[18] $112^{\circ}\text{C}/30$ Torr); $n_{\text{D}}^{20} = 1.5103$ (ref.^[19] 1.5106); $d_4^{20} = 1.005$ (ref.^[20] 1.005); yield: 3.83 g (91%). ^1H NMR: $\delta = 7.31$ (d, $J = 8.6$ Hz, 1 H), 7.25 (d, $J = 8.6$ Hz, 1 H), 1.29 (s, 9 H) ppm.

Consecutive Reaction of (2,6-Dichloro-3-iodophenyl)trimethylsilane with *tert*-Butyllithium and Methanol: At -100°C , (2,6-dichloro-3-iodophenyl)trimethylsilane (**10**; 4.9 mL, 8.6 g, 25 mmol) was added to a solution of *tert*-butyllithium (50 mmol) in pentanes (20 mL) and tetrahydrofuran (40 mL). After 45 min at -100°C , and another 45 min at -75°C , the reaction mixture was treated with methanol (1.0 mL, 0.9 g, 30 mmol), before being distilled. The first fraction, a colorless liquid, consisted of 1.59 g (29%) of (2,6-dichlorophenyl)trimethylsilane; b.p. $56\text{--}58^{\circ}\text{C}/2$ Torr (ref.^[3] $79\text{--}81^{\circ}\text{C}/4$ Torr). A second fraction, a viscous yellowish oil, was collected in the range of b.p. $161\text{--}163^{\circ}\text{C}/0.2$ Torr; 3.50 g (70% with respect to $\text{C}_{18}\text{H}_{23}\text{Cl}_3\text{Si}_2$). According to gas chromatography (2 m, 10% PFO, 130°C ; 1 m, 2% C-20M, 200°C ; 2,2',6,6'-tetrabromobiphenyl as an internal calibrated standard), the heavy oil was composed of two products in the ratio of 42:58. This mixture (3.0 g, 7.5 mmol) was treated with an excess of tetrabutylammonium fluoride (4.7 g, 25 mmol) in dimethylformamide (30 mL) at 25°C for 24 h. Extraction with hexanes (3×20 mL) and distillation (b.p. $138\text{--}143^{\circ}\text{C}/0.2$ Torr) afforded a viscous oil; yield: 1.93 g (100% with respect to $\text{C}_{12}\text{H}_7\text{Cl}_3$). According to gas chromatography (same conditions as above) it consisted of 2,4,4'-trichlorobiphenyl (**8a**) and 2,3',4'-trichlorobiphenyl (**8b**) in a 42:58 ratio. Catalytic hydrogenation (for the conditions, see above) of a sample (1.3 g, 5.0 mmol) of this regioisomeric mixture provided pure biphenyl (0.76 g; 98%).

Reaction of (2,6-Dichloro-3-iodophenyl)trimethylsilane with Excess *tert*-Butyllithium: At -100°C , (2,6-dichloro-3-iodophenyl)trimethyl-

silane (**10**; 4.9 mL, 8.6 g, 25 mmol) was added to a solution of *tert*-butyllithium (125 mmol) in pentanes (0.15 L) and tetrahydrofuran (0.20 L). After 45 min at -100°C and another 45 min at -75°C , the reaction mixture was treated with methanol (6.9 mL, 6.2 g, 0.20 mol). According to gas chromatography (30 m, DB-1, 80°C ; 1 m, 5% SE-30, 100°C ; nonane as an internal calibrated standard), the reaction mixture contained 8.4% of (2,6-dichlorophenyl)trimethylsilane, 0.31 g (5.7%) of which were isolated by distillation; b.p. $27\text{--}28^{\circ}\text{C}/2$ Torr (ref.^[3] $79\text{--}81^{\circ}\text{C}/4$ Torr). A second fraction was collected at $80\text{--}82^{\circ}\text{C}/2$ Torr; yield: 4.41 g (73% with respect to $\text{C}_{13}\text{H}_{21}\text{ClSi}$). Treatment of a sample (2.4 g, 10 mmol) with tetrabutylammonium fluoride trihydrate (13 g, 20 mmol) in dimethylformamide (50 mL) at 25°C for 24 h followed by distillation gave a colorless oil; b.p. $58\text{--}61^{\circ}\text{C}/3$ Torr. According to gas chromatography (conditions as specified above) it was neat 1-*tert*-butyl-4-chlorobenzene^[20] (**12**); 1.62 g (96%). A third fraction distilled in the range $141\text{--}143^{\circ}\text{C}/0.2$ Torr; 1.06 g (21% with respect to $\text{C}_{18}\text{H}_{23}\text{Cl}_3\text{Si}_2$). An aliquot thereof (1.0 g, 2.5 mmol) was treated with tetrabutylammonium fluoride trihydrate (1.6 g, 5.0 mmol) as described above. Distillation (b.p. $140\text{--}144^{\circ}\text{C}/0.3$ Torr) afforded a yellowish oil which, according to gas chromatography (2 m, 10% PFO, 130°C ; 1 m, 2% C-20M, 200°C ; 2,6,2',6'-tetrabromobiphenyl as an internal calibrated standard) consisted of 2,3',4'-trichlorobiphenyl (**8b**) and 2,4,4'-trichlorobiphenyl (**8a**) in the ratio of 56:44; yield: 0.63 g (98%).

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