Metalation and Derivatization of All Six Dichlorobenzotrifluorides: Site Selectivities

Eric Masson,[a] Elena Marzi,[a] Fabrice Cottet,[a] Carla Bobbio,[a] and Manfred Schlosser*[a,b]

Keywords: Buttressing effects / Carboxylation / Haloarenes / Metalation / Regioselectivity / Trifluoromethyl groups

The metalation of 2,3-, 2,6-, 2,4- and 3,5-dichlorobenzotrifluorides can be readily effected with standard reagents such as lithium diisopropylamide, lithium 2,2,6,6-tetramethylpiperidide, and butyllithium at the chlorine-adjacent 4- and 3-positions and the chlorine-flanked 3- and 4-positions, respectively. However, regioselectivity was secured with 2,6-dichlorobenzotrifluoride only under equilibrating conditions as the initial deprotonation occurs simultaneously at the 3- and 4-positions. 3,4-Dichlorobenzotrifluoride requires methyllithium in the presence of potassium *tert*-butoxide ("LIM-KOR" mixture) to undergo regioselective metalation at the 2-position. All the organometallic intermediates were converted into the corresponding benzoic acids by trapping with carbon dioxide, arguably the most popular electrophile for the characterization of organometallic intermediates.

Introduction

There is a discrepancy between the capacity of typical halogenated substituents to stabilize electron excess in their vicinity and their ability to promote hydrogen/metal permutation ("metalation"). For example, fluorobenzene undergoes *ortho*-lithiation with *sec*-butyllithium in tetrahydrofuran 8 and 120 times faster than chlorobenzene and benzotrifluoride [(trifluoromethyl)benzene], respectively,[1] although, as experimental gas-phase data[2–6] reveal, the proton affinity (basicity) of 2-fluorobenzenide (2-fluorophenyl anion) exceeds that of 2-chlorobenzenide by approximately 0.4 kcal/mol and that of 2-(trifluoromethyl) benzenide by at least 1.0 kcal/mol.

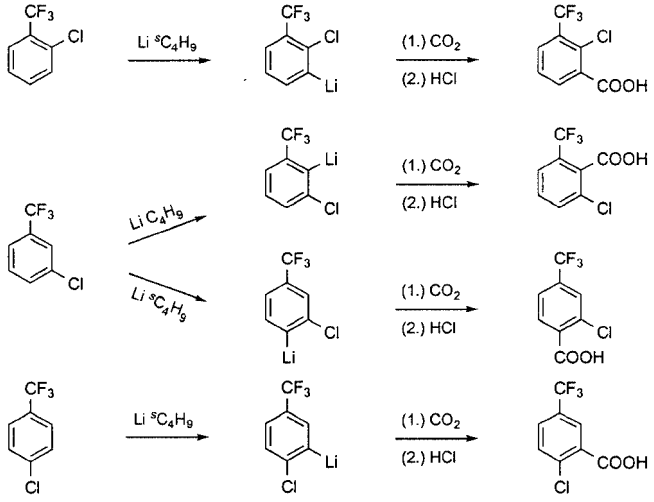
A more complete picture emerges if the quantification of energy-lowering effects exerted by halogen atoms on (het)-aromatic anions and organometallic species does not remain restricted to the directly adjacent sites but also includes the more remote, and in particular, *meta* and *para* positions. The three model substituents mentioned above again show striking differences. When the substituent is moved from the *ortho* through the *meta* to the *para* position, its charge stabilization effect levels off steeply in the fluoro series, moderately in the chloro series, and only weakly in the trifluoromethyl series.[3–7]

Thus, two coinciding reasons favor the metalation of 2- and 4-chlorobenzotrifluoride at the position next to the chlorine atom rather than next to the trifluoromethyl group. On one hand, chlorobenzene reacts with *sec*-butyllithium 15 times faster than benzotrifluoride does. On the other hand, the extra activation of the chlorine-adjacent 3-position by the *meta*-CF_3 substituent is greater than the activation of the CF_3-adjacent 6- or 2-position by the *meta*-chloro substituent. In perfect agreement with these considerations, 2- and 4-chlorobenzotrifluoride were cleanly converted into 2-chloro-3- and 2-chloro-5-(trifluoromethyl) benzoic acids when treated consecutively with *sec*-butyllithium and dry ice.[8] However, 3-chlorobenzotrifluoride featured an unexpected case of "optional site selectivity".[9] While ordinary butyllithium abstracted a proton from the 2-position flanked by the two acidifying substituents, the more reactive *sec*-butyllithium attacked, again with perfect regioselectivity, the chlorine-adjacent, but CF_3-remote 4-position.[8] Evidently, the relatively voluminous trifluoromethyl group sterically hinders the access of bulky reagents.

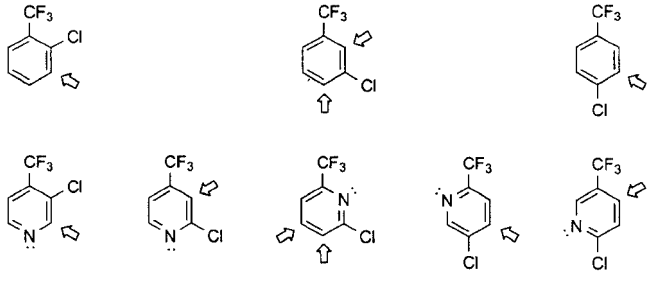
Intrigued by the cooperative and competitive interplay between the chlorine atom and the trifluoromethyl group, we turned to pyridine carrying these two substituents. 3-Chloro-4-(trifluoromethyl)pyridine, an aza analog of 2-chlorobenzotrifluoride, gave the expected 3-chloro-4-(trifluoromethyl)pyridine-2-carboxylic acid (57%) after lithiation with lithium 2,2,6,6-tetramethylpiperidide (LITMP) and subsequent carboxylation.[10] 2-Chloro-4-(trifluoromethyl)pyridine reacted with lithium diisopropylamide (LIDA), also in analogy with 3-chlorobenzotrifluoride, at the doubly activated 3-position. Carboxylation afforded 2-chloro-4-(trifluoromethyl)pyridine-3-carboxylic acid (82%).[11] However, 2-chloro-6-(trifluoromethyl)pyridine-3-carboxylic acid (79%) was obtained as the sole product only

[a] Institute of Chemical Sciences and Engineering (ISIC-BCh), Ecole Polytechnique Fédérale, 1015 Lausanne, Switzerland
[b] Faculté des Sciences, Université, BCh, 1015 Lausanne, Switzerland
E-mail: manfred.schlosser@epfl.ch

 DOI: 10.1002/ejoc.200500240



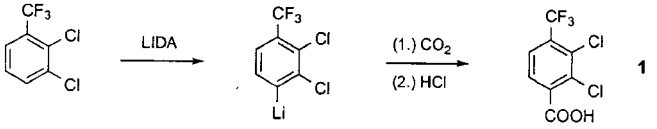
after incubation of 2-chloro-6-(trifluoromethyl)pyridine with LIDA in tetrahydrofuran at –85 °C for 4 h under conditions in which transmetalation processes can take place.[12] If the same reaction was carried out at –100 °C, a 1:1 mixture of 2-chloro-6-(trifluoromethyl)pyridine-3- and -4-carboxylic acids was formed. Apparently, the enhanced kinetic acidity of the 4-position reflects the intrinsic order of thermodynamic acidity which increases in the pyridine series with the distance from the nitrogen atom.[13,14] Presumably for the same reason 2-chloro-5-(trifluoromethyl)-pyridine was metalated by LIDA (in the presence of lithium *N*,*N*-diisopropylcarbamate and catalytic amounts of lithium bromide) exclusively at the 4- rather than the 3-position, providing 2-chloro-5-(trifluoromethyl)pyridine-4-carboxylic acid (87%) after carboxylation.[10] 5-Chloro-2-(trifluoromethyl)pyridine was deprotonated accordingly at the 4- rather than at the 3-position, thus leading to 5-chloro-2-(trifluoromethyl)pyridine-4-carboxylic acid (83%).[15]



We have now extended our systematic investigation to the dichlorobenzotrifluorides. Although they cannot be subject to any perturbation in reactivity due to the presence of a nitrogen lone-pair, the accumulation of electronegative substituents may cause other deviations from normal behavior.

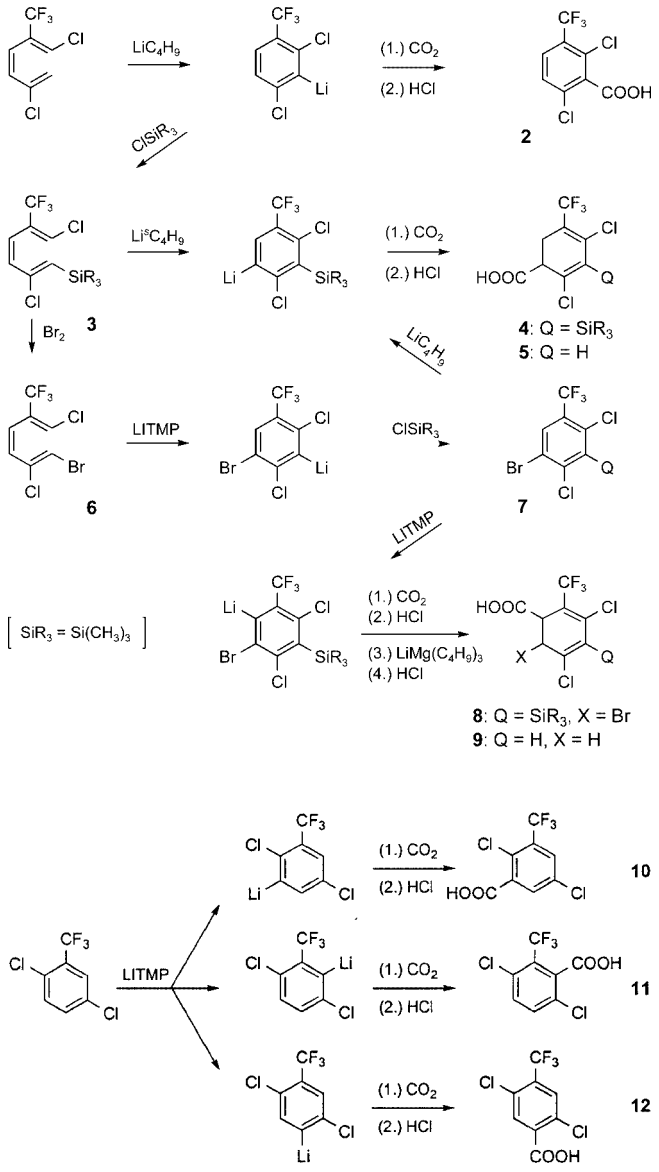
Results and Discussion

As one would have predicted, 2,3-dichlorobenzotrifluoride was cleanly metalated at the 4-position when treated with LIDA at –75 °C for 2 h. After carboxylation and neutralization, 2,3-dichloro-4-(trifluoromethyl)benzoic acid (**1**) was isolated in 76% yield.

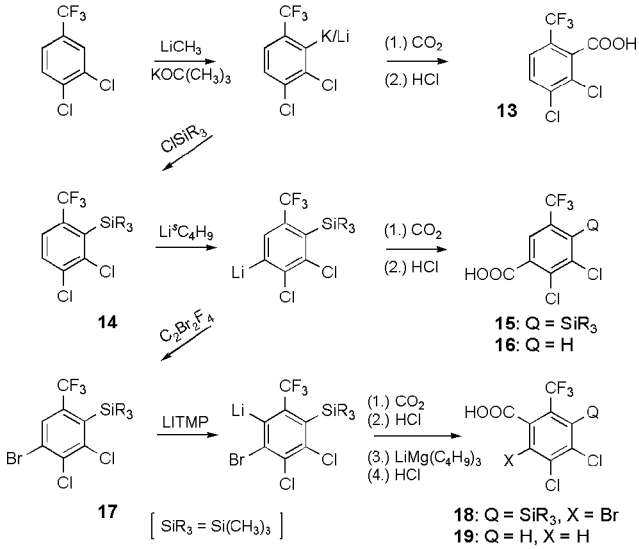


There was equally no doubt about the outcome of a similar reaction starting from 2,4-dichlorobenzotrifluoride. It afforded 2,6-dichloro-3-(trifluoromethyl)benzoic acid (**2**) in 75% yield after consecutive treatment with butyllithium and dry ice. When the organometallic intermediate was trapped with chlorotrimethylsilane instead, [2,6-dichloro-3-(trifluoromethyl)phenyl]trimethylsilane (**3**; 82%) was formed. Like other (2,6-dichlorophenyl)silanes,[16,17] silane **3** underwent deprotonation when exposed to *sec*-butyllithium in the presence of *N*,*N*,*N*′,*N*′′,*N*′′-pentamethyldiethylenetriamine (PMDTA) even at –100 °C, although only sluggishly, giving rise to 2,4-dichloro-5-trifluoromethyl-3-(trimethylsilyl)benzoic acid (**4**; 42%) in moderate yield and, after protodesilylation using tetrabutylammonium fluoride trihydrate (TBAF), 2,4-dichloro-5-(trifluoromethyl)benzoic acid (**5**; 87%; 30% overall). The latter compound was prepared more cleanly by converting silane **3** by bromodesilylation into 3-bromo-2,4-dichlorobenzotrifluoride (**6**; 75%). Subsequent LITMP-triggered heavy-halogen migration[12,18] followed by interception with chlorotrimethylsilane yielded [3-bromo-2,6-dichloro-5-(trifluoromethyl)-phenyl]silane (**7**; 57%), which eventually gave the silylated acid **4** (73%) upon consecutive reaction with butyllithium at –100 °C and dry ice. Deprotonation of the bromosilane **7** with LITMP at the sole vacant position afforded 2-bromo-3,5-dichloro-6-(trifluoromethyl)-4-(trimethylsilyl)benzoic acid (**8**; 74%). Deprotection to 3,5-dichloro-2-(trifluoromethyl)benzoic acid (**9**; 84%) was accomplished in three steps. First, bromine was replaced by magnesium using lithium tributylmagnesate,[19,20] and the resulting compound was neutralized with dilute acid before the trimethylsilyl group was removed with TBAF hydrate.

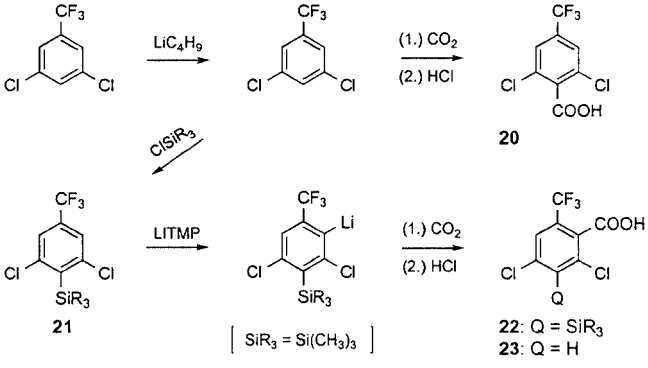
The functionalization of 2,5-dichlorobenzotrifluoride proved troublesome even though a wide variety of organolithium and mixed-metal reagents were tested. When the substrate was treated with LITMP and the intermediate trapped with dry ice, a 1:7:2 mixture (74%) of 2,5-dichloro-3-(trifluoromethyl)benzoic acid (**10**), 3,6-dichloro-2-(trifluoromethyl)benzoic acid (**11**), and 2,5-dichloro-4-(trifluoromethyl)benzoic acid (**12**) was produced. The main component **11**, isolated in 19% yield, was purified by fractional crystallization. The other isomers were identified after reductive dechlorination[11,21–23] by gas chromatographic comparison with authentic 3- and 4-(trifluoromethyl)benzoic acid. The same 1:7:2 mixture (83%) was obtained when butyllithium was employed as the base whereas *sec*-butyllithium gave a 3:2:6 mixture (57%) of the acids **10**, **11**, and **12**.



The site-selective metalation of 3,4-dichlorobenzotrifluoride and the subsequent trapping of the 2-lithio intermediate with carbon dioxide has been claimed in a Nippon Soda patent.[24] In reality, however, a careful reexamination has revealed that a 3:1 mixture (80%) of the regioisomeric 2,3-dichloro-6-(trifluoromethyl)benzoic acid (**13**) and 2,3-dichloro-5-(trifluoromethyl)benzoic acid (**16**) was formed under the given reaction conditions. With *sec*-butyllithium in tetrahydrofuran as the metalating reagent a 2:3 mixture (77%) of the acids **13** and **16** resulted. The pure isomer **13** (38%) was produced only when the metalation was carried out at –100 °C with the so-called LIM-KOR superbase, that is, with methyllithium in the presence of potassium *tert*-butoxide. The pure acid **16** was prepared in a sequence involving trimethylsilylation to the [2,3-dichloro-6-(trifluoromethyl)phenyl]trimethylsilane (**14**; 55%), metalation with *sec*-butyllithium in tetrahydrofuran at –100 °C followed by carboxylation to the acid **15** (46%), and deprotection to the 2,3-dichloro-5-(trifluoromethyl)benzoic acid (**16**; 84%). When silane **14** was lithiated and then treated with 1,2-dibromo-1,1,2,2-tetrafluoroethane, rather than with dry ice, [4-bromo-2,3-dichloro-6-(trifluoromethyl)phenyl]trimethylsilane (**17**; 59%) was obtained which furnished 2-bromo-3,4-dichloro-6-(trifluoromethyl)-5-(trimethylsilyl)benzoic acid (**18**; 38%) upon metalation with LITMP at –75 °C followed by carboxylation and 4,5-dichloro-2-(trifluoromethyl)benzoic acid (**19**; 64%) after double deprotection using lithium tributylmagnesate, hydrochloric acid, and tetrabutylammonium fluoride consecutively.

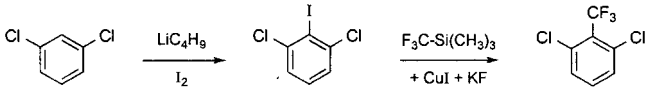


The conversion of 3,5-dichlorobenzotrifluoride into the two possible acids was straightforward. 2,6-Dichloro-4-(trifluoromethyl)benzoic acid (**20**; 78%) was prepared simply by metalation with butyllithium at –75 °C and subsequent carboxylation. Condensation of the organometallic intermediate with chlorotrimethylsilane provided [2,6-dichloro-4-(trifluoromethyl)phenyl]trimethylsilane (**21**) and, upon metalation (with LITMP at –75 °C for 15 min) and subsequent carboxylation, 2,4-dichloro-6-(trifluoromethyl)-3-(trimethylsilyl)benzoic acid (**22**), which was not isolated but immediately deprotected to afford 2,4-dichloro-6-(trifluoromethyl)benzoic acid (**23**; 52%).

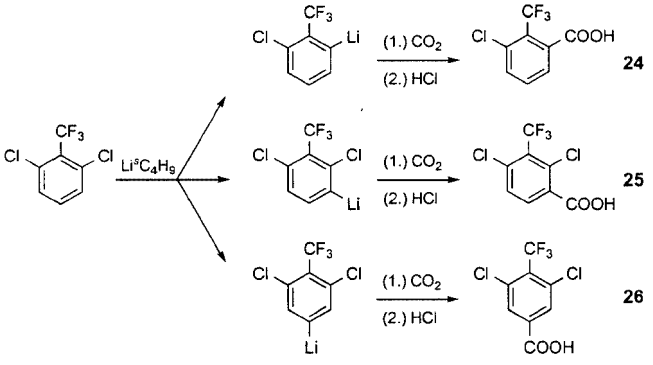


Three of the dichlorobenzotrifluorides that have served as starting materials so far can be purchased at moderate prices (30–300 EUR/mol); 2,3- and 3,5-dichlorobenzotriflu-

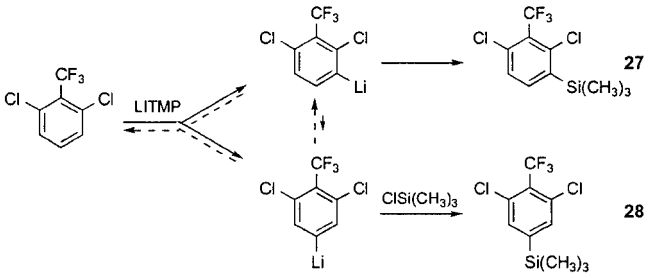
orides are also commercially available but are very expensive (5000–6000 EUR/mol). Therefore, we have carried out only a few reactions with the latter two substrates. 2,6-Dichlorobenzotrifluoride has never been available on the chemicals market and we therefore had no other choice than to design a suitable method of access. The compound was prepared in 69% yield from 1,3-dichlorobenzene via 1,3-dichloro-2-iodobenzene (98%) by condensation with in situ generated (trifluoromethyl)copper.[25]



Consecutive treatment of 2,6-dichlorobenzotrifluoride with *sec*-butyllithium at –75 °C and carbon dioxide afforded a mixture (74%) of the three acids **24**, **25**, and **26** in the approximate ratio of 8:3:1. The main product 3-chloro-2-(trifluoromethyl)benzoic acid (**24**) must have originated from a permutational chlorine/lithium interconversion. Although this is a rare process, analogies featuring several polychloroarenes (e.g. 1,2,3-trichlorobenzene,[6,26] 1,2,3,4-tetrachlorobenzene,[26] and hexachlorobenzene[27]) have been documented. 2,4-Dichloro-3-(trifluoromethyl)benzoic acid (**25**) is the expected "*ortho*-metalation" product derived from an intermediate bearing the metal atom at a chlorine-adjacent position whereas the isomeric 3,5-dichloro-4-(trifluoromethyl)benzoic acid (**26**; identified by NMR spectroscopy as a byproduct after reductive dechlorination[11,21–23] of the crude reaction mixture) is obviously the result of a "*meta*-directed metalation" reaction. Such an anomalous regioselectivity of organometallic attack has so far been observed with trialkyl(2,6-dichlorophenyl)- and trialkyl(2,6-dibromophenyl)silanes for which "*meta* metalation" was found to be the preferred if not exclusive reaction mode.[16,17] This anomalous behavior has been attributed to a buttressing effect that is exerted by the bulky substituent on the neighboring heavy halogen atoms, which, as a consequence, perturbs the proton transfer in their vicinity.[28]



By using LITMP instead of *sec*-butyllithium, the halogen/metal permutation could of course be completely avoided. After 2 h of exposure time at –75 °C, the acid **25** was isolated as the sole product in 71% yield. However, initially, the 4- and 5-lithiated species, the *ortho*- and *meta*-metalated intermediates, were concomitantly generated. Equilibration[28] brought about by perpetual deprotonation and reprotonation privileged the thermodynamically more stable, i.e. less basic, *ortho*-metalated intermediate at the expense of the *meta*-metalated species. When 2,6-dichlorobenzotrifluoride in tetrahydrofuran was simultaneously treated at –75 °C with LITMP and chlorotrimethylsilane, [2,4-dichloro-3-(trifluoromethyl)phenyl]trimethylsilane (**27**; 52%) and [3,5-dichloro-4-(trifluoromethyl)phenyl]trimethylsilane (**28**; 12%) were formed together in a 4:1 ratio.



Conclusion

In conclusion, dichlorobenzotrifluorides undergo metalation, like monochlorobenzotrifluorides, at a Cl- rather than CF_3-adjacent site. If this qualitative coincidence has been established, there are quantitative deviations. First of all, no counterpart of the optional site selectivity discovered with 3-chlorobenzotrifluoride (deprotonation either at the 2- or at the 4-position) has been found. Moreover, 2,6-dichlorobenzotrifluoride reacts simultaneously at the 3- and 4-positions and thus exhibits another case of "*meta* metalation" caused by buttressing effects. There is no reason to be afraid of artifacts due to aryne formation; electronegatively substituted 2-chloroaryllithium (and even 2-bromoaryllithium) compounds are amazingly stable at –75 °C.[8,12,29]

Experimental Section

General: For laboratory routine and abbreviations, see previous publications[30–32] from this laboratory. ^1H and ^{13}C NMR spectra were recorded at 400 and 101 MHz, respectively, all samples being dissolved in deuteriochloroform.

2,3-Dichloro-4-(trifluoromethyl)benzoic Acid (1): Diisopropylamine (1.4 mL, 1.0 g, 10 mmol) and 1,2-dichloro-3-(trifluoromethyl)benzene (1.4 mL, 2.2 g, 10 mmol) were added consecutively to a solution of butyllithium (10 mmol) in tetrahydrofuran (15 mL) and hexanes (5.0 mL) cooled in a dry ice/toluene bath. After 2 h at –75 °C, the mixture was poured onto an excess of freshly crushed dry ice covered with tetrahydrofuran (20 mL). After evaporation of the solvents, the residue was partitioned between diethyl ether (25 mL) and water (50 mL). Crystallization from hexanes afforded colorless prisms; m.p. 138–140 °C; yield: 1.97 g (76%). ^1H NMR: δ = 7.97 (dm, J = 7.8 Hz, 1 H), 7.92 (d, J = 8.4 Hz, 1 H) ppm. ^{13}C NMR: δ = 165.8 (s), 138.4 (s), 133.8 (q, J = 1 Hz), 132.7 (q, J = 1 Hz), 132.2 (q, J = 32 Hz), 129.6 (s), 127.0 (q, J = 6 Hz), 123.3 (q, J = 273 Hz) ppm. $C_8H_3Cl_2F_3O_2$ (259.01): calcd. C 37.10, H 1.17; found C 37.02, H 1.16.

2,6-Dichloro-3-(trifluoromethyl)benzoic Acid (2): A solution of 2,4-dichloro-1-(trifluoromethyl)benzene (3.6 mL, 5.4 g, 25 mmol) and butyllithium (25 mmol) in tetrahydrofuran (25 mL) and hexanes (15 mL) was kept at –75 °C for 45 min. The dark violet mixture was poured onto an excess of freshly crushed dry ice covered with tetrahydrofuran (25 mL). After evaporation of the solvents, the residue was partitioned between water (10 mL) and hexanes (10 mL). The aqueous layer was acidified with concentrated hydrochloric acid (10 mL) and extracted with diethyl ether (3×25 mL). Crystallization from hexanes afforded colorless needles; m.p. 95–97 °C; yield: 4.87 g (75%). ^{1}H NMR: δ = 7.72 (d, J = 8.6 Hz, 1 H), 7.50 (d, J = 8.6 Hz, 1 H) ppm. ^{13}C NMR: δ = 169.5 (s), 135.4 (s), 135.0 (s), 130.4 (q, J = 2 Hz), 129.1 (q, J = 5 Hz), 128.1 (s), 127.9 (q, J = 32 Hz), 122.1 (q, J = 274 Hz) ppm. $C_8H_3Cl_2F_3O_2$ (259.01): calcd. C 37.10, H 1.17; found C 37.17, H 1.18.

[2,6-Dichloro-3-(trifluoromethyl)phenyl]trimethylsilane (3): A solution of 2,4-dichloro-1-(trifluoromethyl)benzene (7.2 mL, 11 g, 50 mmol) and butyllithium (50 mmol) in tetrahydrofuran (50 mL) and hexanes (30 mL) was kept at –75 °C for 45 min. Chlorotrimethylsilane (6.3 mL, 5.4 g, 50 mmol) was poured into the violet solution. Water (5.0 mL) was added and the resulting suspension filtered. After evaporation of the solvents, distillation afforded a colorless liquid; b.p. 65–66 °C/0.6 Torr; n_D^{20} = 1.4975; yield: 11.8 g (82%). ^{1}H NMR: δ = 7.57 (d, J = 8.4 Hz, 1 H), 7.34 (d, J = 8.5 Hz, 1 H), 0.54 (s, 9 H) ppm. ^{13}C NMR: δ = 145.4 (s), 140.3 (s), 139.8 (q, J = 2 Hz), 128.8 (q, J = 6 Hz), 128.6 (s), 127.6 (q, J = 31 Hz), 122.9 (q, J = 273 Hz), 3.1 (s, 3 C) ppm. $C_{10}H_{11}Cl_2F_3Si$ (287.18): calcd. C 41.82, H 3.86; found C 42.01, H 3.80.

2,4-Dichloro-5-(trifluoromethyl)-3-(trimethylsilyl)benzoic Acid (4): *N*,*N*′,*N*′,*N*′′,*N*′′-Pentamethyldiethylenetriamine (2.1 mL, 1.7 g, 10 mmol) and [2,6-dichloro-3-(trifluoromethyl)phenyl]trimethylsilane (**3**; 2.2 mL, 2.9 g, 10 mmol) were added consecutively to a solution of *sec*-butyllithium (10 mmol) in tetrahydrofuran (20 mL) and hexanes (10 mL) cooled to –100 °C. After 15 min at –100 °C, the dark violet mixture was poured onto an excess of freshly crushed dry ice covered with tetrahydrofuran (25 mL). After evaporation of the solvents, the residue was partitioned between water (10 mL) and hexanes (10 mL). The aqueous layer was acidified with concentrated hydrochloric acid (10 mL) and extracted with diethyl ether (3×25 mL). A 76:24 ratio of isomers was determined by gas chromatography after treatment of an aliquot of the mixture with diazomethane to obtain the corresponding esters. Crystallization from hexanes afforded colorless needles; m.p. 125–126 °C; yield: 1.40 g (42%). ^{1}H NMR: δ = 8.15 (s, 1 H), 0.58 (s, 9 H) ppm. ^{13}C NMR: δ = 171.6 (s), 145.1 (s), 144.3 (s), 144.1 (s), 131.6 (q, J = 6 Hz), 129.7 (s), 128.6 (q, J = 32 Hz), 123.1 (q, J = 274 Hz), 4.3 (s) ppm. $C_{11}H_{11}Cl_2F_3O_2Si$ (331.19): calcd. C 39.89, H 3.35; found C 40.22, H 3.42. The pure acid **4** was obtained directly from a solution of [3-bromo-2,6-dichloro-5-(trifluoromethyl)phenyl]trimethylsilane (**7**; 9.2 g, 25 mmol) and butyllithium (25 mmol) in tetrahydrofuran (25 mL) and hexanes (15 mL) at –100 °C for 45 min. The mixture was poured onto an excess of freshly crushed dry ice covered with tetrahydrofuran (25 mL). After evaporation of the solvents, the residue was partitioned between water (10 mL) and hexanes (10 mL). The aqueous layer was acidified with concentrated hydrochloric acid (10 mL) and extracted with diethyl ether (3×25 mL). Crystallization from hexanes afforded colorless needles; yield: 6.03 g (73%).

2,4-Dichloro-5-(trifluoromethyl)benzoic Acid (5): A solution containing 2,4-dichloro-5-(trifluoromethyl)-3-(trimethylsilyl)benzoic acid (**4**; 1.0 g, 3.0 mmol) and tetrabutylammonium fluoride trihydrate (0.95 g, 3.0 mmol) in tetrahydrofuran (10 mL) was heated to reflux for 5 min. After evaporation of the solvent, crystallization from hexanes afforded colorless needles; m.p. 140–141 °C; yield: 0.676 g (87%). ^{1}H NMR: δ = 8.39 (s, 1 H), 7.70 (s, 1 H) ppm. ^{13}C NMR: δ = 168.6 (s), 139.6 (s), 137.6 (s), 134.3 (s), 131.6 (q, J = 5 Hz), 127.5 (q, J = 32 Hz), 126.7 (s), 122.0 (q, J = 273 Hz) ppm. $C_8H_3Cl_2F_3O_2$ (259.01): calcd. C 37.10, H 1.17; found C 37.20, H 1.50.

2-Bromo-1,3-dichloro-4-(trifluoromethyl)benzene (6): Bromine (7.0 mL, 22 g, 0.14 mol, 2.5 equiv.) and [2,6-dichloro-3-(trifluoromethyl)phenyl]trimethylsilane (**3**; 12 mL, 16 g, 55 mmol) in tetrachloromethane (55 mL) were heated to reflux for 20 h. The solution was poured into a saturated solution of sodium sulfite (50 mL), the organic layer was separated, the solvents evaporated, and the residue distilled as a colorless liquid; b.p. 47–48 °C/0.7 Torr; n_D^{20} = 1.5261; yield: 12.1 g (75%). ^{1}H NMR: δ = 7.61 (d, J = 8.3 Hz, 1 H), 7.50 (d, J = 8.6 Hz, 1 H) ppm. ^{13}C NMR: δ = 140.4 (s), 134.8 (s), 128.5 (q, J = 32 Hz), 128.0 (s), 126.8 (s), 126.4 (q, J = 5 Hz), 122.0 (q, J = 273 Hz) ppm. $C_7H_2BrCl_2F_3$ (293.90): calcd. C 28.60, H 0.68; found C 28.85, H 0.80.

[3-Bromo-2,6-dichloro-5-(trifluoromethyl)phenyl]trimethylsilane (7): 2,2,6,6-Tetramethylpiperidine (8.5 mL, 10 g, 50 mmol) and 2-bromo-1,3-dichloro-4-(trifluoromethyl)benzene (**6**; 7.9 mL, 15 g, 50 mmol) were added consecutively to a solution of butyllithium (50 mmol) in tetrahydrofuran (50 mL) and hexanes (30 mL) cooled in a dry ice/toluene bath. After 45 min at –75 °C, chlorotrimethylsilane (6.3 mL, 5.4 g, 50 mmol) was poured into the yellow mixture. The suspension was partitioned between 2.0 M hydrochloric acid (50 mL) and hexanes (50 mL), the organic layer was dried with sodium sulfate, concentrated, and the residue was distilled to afford a colorless oil that solidified in the course of 3 d; b.p. 78–79 °C/0.8 Torr; m.p. 43–45 °C; yield: 10.5 g (57%). ^{1}H NMR: δ = 7.94 (s, 1 H), 0.55 (s, 9 H) ppm. ^{13}C NMR: δ = 144.7 (s), 142.9 (s), 138.2 (q, J = 2 Hz), 132.9 (q, J = 6 Hz), 128.5 (q, J = 31 Hz), 122.7 (s), 122.0 (q, J = 274 Hz), 3.4 (s, 3 C) ppm. $C_{10}H_{10}BrCl_2F_3Si$ (366.08): calcd. C 32.81, H 2.75; found C 32.76, H 2.69.

2-Bromo-3,5-dichloro-6-(trifluoromethyl)-4-(trimethylsilyl)benzoic Acid (8): 2,2,6,6-Tetramethylpiperidine (4.0 mL, 3.3 g, 20 mmol) and [3-bromo-2,6-dichloro-5-(trifluoromethyl)phenyl]trimethylsilane (**7**; 7.3 g, 20 mmol) were added consecutively to a solution of butyllithium (20 mmol) in tetrahydrofuran (20 mL) and hexanes (15 mL) cooled in a dry ice/toluene bath. After 45 min at –75 °C, the solution was poured onto an excess of freshly crushed dry ice covered with tetrahydrofuran (20 mL). After evaporation of the solvents, the residue was partitioned between brine (20 mL) and hexanes (20 mL). The aqueous layer was acidified with concentrated hydrochloric acid (10 mL) and extracted with diethyl ether (3×20 mL). Precipitation in hexanes afforded a white powder; m.p. 195–198 °C; yield: 6.08 g (74%). ^{1}H NMR: δ = 0.57 (s) ppm. ^{13}C NMR: δ = 170.3 (s), 145.9 (s), 144.3 (s), 139.6 (s), 136.9 (q, J = 3 Hz), 124.9 (q, J = 31 Hz), 121.6 (q, J = 275 Hz), 120.6 (s), 3.4 (s, 3 C) ppm. $C_{11}H_{10}BrCl_2F_3O_2Si$ (410.09): calcd. C 32.22, H 2.46; found C 32.16, H 2.36.

3,5-Dichloro-2-(trifluoromethyl)benzoic Acid (9): At 0 °C, butylmagnesium chloride (8.0 mmol) in tetrahydrofuran (6.0 mL) was added to a solution of butyllithium (16 mmol) in hexanes (10 mL). The suspension was diluted with tetrahydrofuran (25 mL) and cooled to –75 °C. 2-Bromo-3,5-dichloro-6-(trifluoromethyl)-4-(trimethylsilyl)benzoic acid (**8**; 5.0 g, 12 mmol) was added all at once. The solution was allowed to reach 0 °C in the course of 45 min, poured into 5.0 M hydrochloric acid (10 mL), and extracted with diethyl ether (3×10 mL). A solution of tetrabutylammonium fluoride trihydrate (3.8 g, 12 mmol) in tetrahydrofuran (25 mL) was added to

the organic layer and the mixture heated to reflux for 15 min. After evaporation of the solvents, precipitation from hexanes afforded a white solid; m.p. 101–102 °C; yield: 2.62 g (84%). ^{1}H NMR: δ = 7.65 (s, 1 H), 7.50 (s, 1 H) ppm. ^{13}C NMR: δ = 171.6 (s), 138.6 (s), 135.0 (q, J = 2 Hz), 134.7 (q, J = 3 Hz), 133.5 (s), 126.8 (s), 124.3 (q, J = 33 Hz), 122.0 (q, J = 275 Hz) ppm. $C_8H_3Cl_2F_3O_2$ (259.01): calcd. C 37.10, H 1.17; found C 37.25, H 1.15.

3,6-Dichloro-2-(trifluoromethyl)benzoic Acid (11): 2,2,6,6-Tetramethylpiperidine (1.8 mL, 1.4 g, 10 mmol) and 2,5-dichloro(trifluoromethyl)benzene (1.5 mL, 2.2 g, 10 mmol) were added consecutively to a solution of butyllithium (10 mmol) in tetrahydrofuran (20 mL) and hexanes (5.0 mL) cooled in a dry ice/toluene bath. After 45 min at –75 °C, the brown mixture was poured onto an excess of freshly crushed dry ice covered with tetrahydrofuran (20 mL). After evaporation of the solvents, the residue was partitioned between water (20 mL) and hexanes (20 mL). The aqueous layer was acidified with concentrated hydrochloric acid (20 mL) and extracted with diethyl ether (3 × 20 mL). After evaporation of the solvents, 1.91 g (74%) of crude material was obtained. Two consecutive crystallizations from hexanes afforded colorless needles; m.p. 225–227 °C; yield: 0.503 g (19%). ^{1}H NMR: δ = 7.59 (d, J = 8.6 Hz, 1 H); 7.56 (d, J = 8.6 Hz, 1 H) ppm. ^{13}C NMR: δ = 170.4 (s), 133.8 (s), 133.7 (s), 132.9 (s), 132.2 (s), 130.1 (s), 126.6 (q, J = 32 Hz), 121.6 (q, J = 276 Hz) ppm. $C_8H_3Cl_2F_3O_2$ (259.01): calcd. C 37.10, H 1.17; found C 37.02, H 1.07. Palladium [10% on charcoal (0.11 g, 1.0 mmol)] was suspended in a solution of ammonium formate (1.9 g, 30 mmol) and the crude mixture of acids in ethanol (50 mL) added. After 2 h at reflux, the suspension was filtered through a pad of Celite. The solvent was evaporated and the residue partitioned between diethyl ether (20 mL) and 2.0 M hydrochloric acid (20 mL). Evaporation of the solvent afforded a white powder; yield: 1.60 g (87%). A 7:1:2 ratio of methyl 2-, 3-, and 4-(trifluoromethyl)benzoates was determined by gas chromatography after treatment of a sample with diazomethane. When 2,5-dichlorobenzotrifluoride was treated with butyllithium instead of lithium tetramethylpiperidide, a similar ratio of 1:7:2 of 2,5-dichloro-3-(trifluoromethyl)benzoic acid (**10**), 3,6-dichloro-2-(trifluoromethyl) benzoic acid (**11**), and 2,5-dichloro-4-(trifluoromethyl)benzoic acid (**12**) was obtained in 74% yield upon carboxylation. With *sec*-butyllithium, a 3:2:6 mixture of the acids **10**–**12** was obtained (83%).

2,3-Dichloro-6-(trifluoromethyl)benzoic Acid (13): Methyllithium (25 mmol) in diethyl ether (18 mL) was added dropwise to a solution of potassium *tert*-butoxide (2.9 g, 25 mmol) and 1,2-dichloro-4-(trifluoromethyl)benzene (3.6 mL, 5.4 g, 25 mmol) in tetrahydrofuran (25 mL) at –100 °C. After 2 h at –100 °C, the blue-violet mixture was poured onto an excess of freshly crushed dry ice covered with tetrahydrofuran (25 mL). After evaporation of the solvents, the residue was partitioned between water (20 mL) and hexanes (20 mL), the aqueous layer acidified with concentrated hydrochloric acid (10 mL) and extracted with diethyl ether (3 × 25 mL). Crystallization from hexanes/ethyl acetate (1:1) afforded colorless needles; m.p. 87–89 °C; yield: 2.46 g (38%). ^{1}H NMR: δ = 7.70 (dm, J = 8.6 Hz, 1 H), 7.60 (dm, J = 8.3 Hz, 1 H) ppm. ^{13}C NMR: δ = 169.5 (s), 137.8 (s), 132.7 (s), 131.6 (s), 130.8 (s), 127.3 (q, J = 33 Hz), 125.4 (q, J = 5 Hz), 122.4 (q, J = 274 Hz) ppm. $C_8H_3Cl_2F_3O_2$ (259.01): calcd. C 37.10, H 1.17; found C 37.00, H 1.12.

[2,3-Dichloro-6-(trifluoromethyl)phenyl]trimethylsilane (14): Methyllithium (0.10 mol) in diethyl ether (70 mL) was added dropwise to a solution of potassium *tert*-butoxide (11 g, 0.10 mol) and 1,2-dichloro-4-(trifluoromethyl)benzene (14 mL, 22 g, 0.10 mol) in tetrahydrofuran (0.10 L at –100 °C. After 2 h at –100 °C, chlorotrimethylsilane (13 mL, 11 g, 0.10 mol) was poured into the reaction mixture which was allowed to reach 25 °C in the course of 45 min. Water (10 mL) was added and the resulting suspension filtered. After evaporation of the solvents, distillation afforded a colorless liquid; b.p. 63–65 °C/0.8 Torr; n_D^{20} = 1.4995; yield: 15.7 g (55%). ^{1}H NMR: δ = 7.6 (m, 2 H), 0.5 (m, 9 H) ppm. ^{13}C NMR: δ = 141.3 (s), 140.6 (s), 137.5 (s), 135.0 (q, J = 32 Hz), 130.5 (s), 125.2 (q, J = 6 Hz), 123.6 (q, J = 275 Hz), 2.4 (s, 3 C) ppm. $C_{10}H_{11}Cl_2F_3Si$ (287.18): calcd. C 41.82, H 3.86; found C 41.76, H 3.68.

2,3-Dichloro-5-(trifluoromethyl)-4-(trimethylsilyl)benzoic Acid (15): A solution of [2,3-dichloro-6-(trifluoromethyl)phenyl]trimethylsilane (**14**; 4.4 mL, 5.8 g, 20 mmol) and *sec*-butyllithium (20 mmol) in tetrahydrofuran (20 mL) and hexanes (15 mL) was kept at –100 °C for 2 h. The dark violet mixture was poured onto an excess of freshly crushed dry ice covered with tetrahydrofuran (20 mL). After evaporation of the solvents, the residue was partitioned between water (10 mL) and hexanes (10 mL). The aqueous layer was acidified with concentrated hydrochloric acid (10 mL) and extracted with diethyl ether (3 × 25 mL). Crystallization from hexanes afforded colorless needles; m.p. 109–111 °C; yield: 3.05 g (46%). ^{1}H NMR: δ = 8.17 (s, 1 H), 0.5 (m, 9 H) ppm. ^{13}C NMR: δ = 170.2 (s), 146.4 (s), 143.2 (s), 136.8 (s), 134.5 (q, J = 32 Hz), 130.6 (s), 127.1 (q, J = 7 Hz), 123.1 (q, J = 274 Hz), 2.2 (q, J = 3 Hz, 3 C) ppm. $C_{11}H_{11}Cl_2F_3O_2Si$ (331.19): calcd. C 39.89, H 3.35; found C 39.79, H 3.37.

2,3-Dichloro-5-(trifluoromethyl)benzoic Acid (16): A solution containing 2,3-dichloro-5-(trifluoromethyl)-4-(trimethylsilyl)benzoic acid (**15**; 1.7 g, 5.0 mmol) and tetrabutylammonium fluoride trihydrate (1.6 g, 5.0 mmol) in tetrahydrofuran (10 mL) was heated to reflux for 5 min. After evaporation of the solvent, crystallization from hexanes afforded colorless needles; m.p. 127–129 °C; yield: 1.09 g (84%). ^{1}H NMR: δ = 8.15 (d, J = 2.2 Hz, 1 H), 7.94 (d, J = 2.2 Hz, 1 H) ppm. ^{13}C NMR: δ = 169.3 (s), 136.9 (s), 136.2 (s), 131.6 (s), 130.8 (q, J = 4 Hz), 130.0 (q, J = 34 Hz), 127.1 (q, J = 4 Hz), 122.5 (q, J = 273 Hz) ppm. $C_8H_3Cl_2F_3O_2$ (259.01): calcd. C 37.10, H 1.17; found C 37.39, H 1.20.

[4-Bromo-2,3-dichloro-6-(trifluoromethyl)phenyl]trimethylsilane (17): A solution of [2,3-dichloro-6-(trifluoromethyl)phenyl]trimethylsilane (**14**; 11 mL, 14 g, 50 mmol) and *sec*-butyllithium (50 mmol) in tetrahydrofuran (50 mL) and hexanes (40 mL) was kept at –100 °C for 2 h. 1,2-Dibromo-1,1,2,2-tetrafluoroethane (6.0 mL, 13 g, 50 mmol) was discharged into the reaction mixture which was warmed to 25 °C. Water (10 mL) was added and the suspension filtered. After evaporation of the solvents, distillation afforded a colorless liquid; b.p. 90–91 °C/0.7 Torr; n_D^{20} = 1.5326; yield: 10.8 g (59%). ^{1}H NMR: δ = 7.89 (s, 1 H), 0.5 (m, 9 H) ppm. ^{13}C NMR: δ = 141.9 (s), 140.0 (s), 138.0 (s), 135.0 (q, J = 32 Hz), 129.5 (q, J = 7 Hz), 124.4 (s), 122.9 (q, J = 274 Hz), 2.3 (s, 3 C) ppm. $C_{10}H_{10}BrCl_2F_3Si$ (366.08): calcd. C 32.81, H 2.75; found C 33.11, H 2.86.

2-Bromo-3,4-dichloro-6-(trifluoromethyl)-5-(trimethylsilyl)benzoic Acid (18): 2,2,6,6-Tetramethylpiperidine (10 mL, 8.4 g, 55 mmol) and [4-bromo-2,3-dichloro-6-(trifluoromethyl)phenyl]trimethylsilane (**17**; 13 mL, 20 g, 55 mmol) were added consecutively to a solution of butyllithium (55 mmol) in tetrahydrofuran (55 mL) and hexanes (35 mL) cooled in a dry ice/toluene bath. After 2 h at –75 °C, the solution was poured onto an excess of freshly crushed dry ice covered with tetrahydrofuran (50 mL). After evaporation of the solvents, the residue was partitioned between water (50 mL) and hexanes (50 mL). The aqueous layer was acidified with concentrated hydrochloric acid (20 mL) and extracted with diethyl ether (3 × 50 mL). Precipitation from hexanes afforded a white powder;

m.p. 170–172 °C; yield: 8.56 g (38%). ^{1}H NMR: δ = 0.5 (m) ppm. ^{13}C NMR: δ = 170.3 (s), 142.5 (s), 142.3 (q, J = 3 Hz), 138.9 (s), 133.9 (s), 132.2 (q, J = 32 Hz), 122.7 (s), 122.5 (q, J = 275 Hz), 2.6 (q, J = 3 Hz, 3 C) ppm. $C_{11}H_{10}BrCl_2F_3O_2Si$ (410.09): calcd. C 32.22, H 2.46; found C 32.12, H 2.73.

4,5-Dichloro-2-(trifluoromethyl)benzoic Acid (19): At 0 °C, butylmagnesium chloride (12 mmol) in tetrahydrofuran (9.0 mL) was added to a solution of butyllithium (24 mmol) in hexanes (16 mL). The suspension was diluted with tetrahydrofuran (25 mL) and cooled to –75 °C. 2-Bromo-3,4-dichloro-6-(trifluoromethyl)-5-(trimethylsilyl)benzoic acid (**18**; 7.4 g, 18 mmol) was added all at once. The solution was allowed to warm to 0 °C in the course of 45 min, poured into 5.0 M hydrochloric acid (10 mL), and extracted with diethyl ether (3 × 20 mL). A solution of tetrabutylammonium fluoride trihydrate (5.7 g, 18 mmol) in tetrahydrofuran (25 mL) was added to the organic layer and the solution heated to reflux for 5 min. After evaporation of the solvents, crystallization from hexanes/ethyl acetate (98:2, v/v) afforded colorless needles; m.p. 111–113 °C; yield: 2.96 g (64%). ^{1}H NMR: δ = 8.13 (s, 1 H), 7.90 (s, 1 H) ppm. ^{13}C NMR: δ = 169.3 (s), 137.5 (s), 136.8 (s), 133.6 (s), 129.5 (q, J = 6 Hz), 129.3 (q, J = 34 Hz), 128.8 (s), 122.0 (q, J = 274 Hz) ppm. $C_8H_3Cl_2F_3O_2$ (259.01): calcd. C 37.10, H 1.17; found C 37.06, H 1.19.

2,6-Dichloro-4-(trifluoromethyl)benzoic Acid (20): A solution of 1,3-dichloro-5-(trifluoromethyl)benzene (1.5 mL, 2.2 g, 10 mmol) and butyllithium (10 mmol) in tetrahydrofuran (20 mL) and hexanes (5.0 mL) was kept at –75 °C for 15 min. The reaction mixture was poured onto an excess of freshly crushed dry ice covered with tetrahydrofuran (20 mL) and partitioned between toluene (40 mL) and 6.0 M hydrochloric acid (20 mL). After evaporation of the solvents, crystallization from heptanes afforded slightly yellowish needles; m.p. 135–137 °C; yield: 2.01 g (78%). ^{1}H NMR: δ = 7.65 (s) ppm. ^{13}C NMR: δ = 168.2 (s), 135.7 (s), 134.0 (q, J = 34 Hz), 132.9 (s), 125.3 (q, J = 4 Hz), 122.2 (q, J = 274 Hz) ppm. $C_8H_3Cl_2F_3O_2$ (259.01): calcd. C 37.10, H 1.16; found C 37.18, H 1.15.

2,4-Dichloro-6-(trifluoromethyl)benzoic Acid (23): A solution of 1,3-dichloro-5-(trifluoromethyl)benzene (1.5 mL, 2.2 g, 10 mmol) and butyllithium (10 mmol) in tetrahydrofuran (20 mL) and hexanes (5.0 mL) was kept at –75 °C for 15 min. Chlorotrimethylsilane (1.3 mL, 1.1 g, 10 mmol), 2,2,6,6-tetramethylpiperidine (1.7 mL, 1.4 g, 10 mmol) and butyllithium (10 mmol) in hexanes (5.0 mL) were added consecutively to the reaction mixture. After 2 h at –75 °C, the reaction mixture was poured onto an excess of freshly crushed dry ice covered with tetrahydrofuran (20 mL) and partitioned between toluene (40 mL) and 6.0 M hydrochloric acid (20 mL). After evaporation of the solvents, tetrahydrofuran (20 mL) and tetrabutylammonium fluoride trihydrate (3.1 g, 10 mmol) were added to the residue and the mixture was refluxed for 5 min. Crystallization from heptanes afforded slightly yellowish needles; m.p. 133–135 °C; yield: 1.35 g (52%). ^{1}H NMR: δ = 7.68 (d, J = 1.9 Hz, 1 H), 7.64 (d, J = 1.9 Hz, 1 H) ppm. ^{13}C NMR: δ = 170.0 (s), 137.0 (s), 133.3 (s), 133.1 (s), 130.4 (q, J = 34 Hz), 129.3 (q, J = 2 Hz), 125.3 (q, J = 5 Hz), 122.0 (q, J = 275 Hz) ppm. $C_8H_3Cl_2F_3O_2$ (259.01): calcd. C 37.10, H 1.16; found C 37.10, H 1.14.

3-Chloro-2-(trifluoromethyl)benzoic Acid (24): A solution of 1,3-dichloro-2-(trifluoromethyl)benzene (6.7 mL, 5.4 g, 25 mmol) and *sec*-butyllithium (25 mmol) in tetrahydrofuran (32 mL) and cyclohexane (18 mL) was kept at –75 °C for 2 h. The reaction mixture was then poured onto an excess of freshly crushed dry ice covered with tetrahydrofuran (20 mL). After evaporation of the solvents, the residue was partitioned between water (10 mL) and diethyl ether (10 mL). The aqueous layer was acidified with concentrated hydrochloric acid (10 mL) and extracted with diethyl ether (3 × 25 mL). Crystallization from hexanes afforded colorless needles; m.p. 119–121 °C; yield: 1.74 g (31%. ^{1}H NMR (CD_3COCD_3): δ = 7.8 (m, 2 H), 7.61 (dm, J = 6.9 Hz, 1 H) ppm. ^{13}C NMR (CD_3COCD_3): δ = 168.5 (s), 137.1 (q, J = 3 Hz), 134.5 (s), 133.8 (s), 127.8 (s), 127.7 (s), 123.7 (q, J = 276 Hz), 124.9 (q, J = 32 Hz) ppm. $C_8H_4ClF_3O_2$ (224.55): calcd. C 42.79, H 1.80; found C 42.73, H 1.74.

2,4-Dichloro-3-(trifluoromethyl)benzoic Acid (25): 2,2,6,6-Tetramethylpiperidine (4.2 mL, 3.5 g, 25 mmol) and 1,3-dichloro-2-(trifluoromethyl)benzene (6.7 mL, 5.4 g, 25 mmol) were added consecutively to a solution of butyllithium (25 mmol) in tetrahydrofuran (35 mL) and hexanes (15 mL) cooled in a dry ice/toluene bath. After 2 h at –75 °C, the reaction mixture was poured onto an excess of freshly crushed dry ice covered with tetrahydrofuran (20 mL). After evaporation of the solvents, the residue was partitioned between water (25 mL) and diethyl ether (25 mL). The aqueous layer was acidified with concentrated hydrochloric acid (20 mL) and extracted with diethyl ether (3 × 25 mL). Crystallization from dichloromethane afforded colorless platelets; m.p. 136–138 °C; yield: 4.60 g (71%). ^{1}H NMR (CD_3COCD_3): δ = 7.98 (dd, J = 8.4, 0.6 Hz, 1 H), 7.78 (dd, J = 8.4, 0.6 Hz, 1 H) ppm. ^{13}C NMR (CD_3COCD_3): δ = 165.9 (s), 136.4 (q, J = 2 Hz), 135.4 (s), 134.0 (s), 133.9 (s), 132.7 (q, J = 2 Hz), 126.8 (q, J = 30 Hz), 123.2 (q, J = 276 Hz) ppm. $C_8H_3Cl_2F_3O_2$ (259.01): calcd. C 37.10, H 1.17; found C 36.99, H 1.12.

[2,4-Dichloro-3-(trifluoromethyl)phenyl]trimethylsilane (27): 2,2,6,6-Tetramethylpiperidine (0.84 mL, 0.71 g, 5.0 mmol), chlorotrimethylsilane (0.61 mL, 0.54 g, 5.0 mmol), and 1,3-dichloro-2-(trifluoromethyl)benzene (1.3 mL, 1.1 g, 5.0 mmol) were added consecutively to a solution of butyllithium (5.0 mL) in tetrahydrofuran (10 mL) and hexanes (5.0 mL) cooled in a dry ice/toluene bath. After 2 h at –75 °C, methanol (1.0 mL) was added to the reaction mixture. After evaporation of the solvents, the residue was partitioned between water (25 mL) and diethyl ether (25 mL). Gas chromatography revealed the presence of two isomers formed in approximate yields of 52 and 12% (as estimated by a comparison of the peak areas with the "internal standard" tridecane). [2,4-Dichloro-3-(trifluoromethyl)phenyl]trimethylsilane (**27**) and [3,5-dichloro-4-(trifluoromethyl)phenyl]trimethylsilane (**28**) were the structures tentatively assigned on the basis of spectral evidence. ^{1}H NMR (of **27**): δ = 7.48 (d, J = 7.5 Hz, 1 H), 7.39 (d, J = 7.5 Hz, 1 H), 0.41 (s, 9 H) ppm. ^{1}H NMR (of **28**): δ = 7.66 (s, 2 H), 0.56 (s, 9 H) ppm.

Acknowledgments

This work was supported by the Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung, Bern (grant 20-100′336-02).

[1] E. Castagnetti, M. Schlosser, *Chem. Eur. J.* **2002**, *8*, 799–804.
[2] P. B. M. Andrades, J. M. Riveros, *J. Mass Spectrom.* **1996**, *31*, 767–770.
[3] H. H. Büker, N. M. M. Nibbering, D. Espinosa, F. Mongin, M. Schlosser, *Tetrahedron Lett.* **1997**, *38*, 8519–8522.
[4] M. Schlosser, E. Marzi, F. Cottet, H. H. Büker, N. M. M. Nibbering, *Chem. Eur. J.* **2001**, *7*, 3511–3516.
[5] M. Schlosser, F. Mongin, J. Porwisiak, W. Dmowski, H. H. Büker, N. M. M. Nibbering, *Chem. Eur. J.* **1998**, *4*, 1281–1286.
[6] E. Marzi, M. Schlosser, *Chem. Eur. J.* **2005**, *11*, 3449–3454.
[7] J. Gorecka, M. Schlosser, manuscript in preparation.

[8] F. Mongin, O. Desponds, M. Schlosser, *Tetrahedron Lett.* **1996**, *37*, 2767–2770.
[9] M. Schlosser in *Organometallics in Synthesis: A Manual*, Wiley, Chichester, **2002**, pp. 1–352, especially pp. 253–257.
[10] F. Cottet, M. Schlosser, *Eur. J. Org. Chem.* **2004**, 3793–3798.
[11] F. Cottet, M. Marull, O. Lefebvre, M. Schlosser, *Eur. J. Org. Chem.* **2003**, 1559–1568.
[12] F. Mongin, A. Tognini, F. Cottet, M. Schlosser, *Tetrahedron Lett.* **1998**, *39*, 1749–1752.
[13] I. F. Tupitsyn, N. N. Zatsepina, A. V. Kirova, Y. L. Kaminskii, A. G. Ivanenko, *Reakts. Sposobnost Org. Soedin.* **1973**, *10*, 143–162 [*Chem. Abstr.* **1973**, *79*, 114928v].
[14] O. A. Reutov, I. P. Beletskaya, K. P. Butin, *CH-Acids*, Pergamon Press, Oxford, **1978**, pp. 111–114.
[15] F. Cottet, M. Schlosser, *Tetrahedron* **2004**, *60*, 11869–11874.
[16] C. Heiss, E. Marzi, M. Schlosser, *Eur. J. Org. Chem.* **2003**, 4625–4629.
[17] C. Heiss, F. Cottet, M. Schlosser, manuscript in preparation.
[18] T. Rausis, M. Schlosser, *Eur. J. Org. Chem.* **2002**, 3351–3358.
[19] T. Iida, T. Wada, K. Tomimoto, T. Mase, *Tetrahedron Lett.* **2001**, *42*, 4841–4844.
[20] A. Inoue, K. Kitagawa, H. Shinokubo, K. Oshima, *J. Org. Chem.* **2001**, *66*, 4333–4339.
[21] E. Marzi, J. Gorecka, M. Schlosser, *Synthesis* **2004**, 1609–1618.
[22] F. Cottet, E. Castagnetti, M. Schlosser, *Synthesis* **2005**, 798–803.
[23] C. Bobbio, M. Schlosser, *J. Org. Chem.* **2005**, *70*, 3039–3045.
[24] I. Kasahara, T. Sugiura, T. Inoue (Nippon Soda Co.), *PCT. Int. Appl.* WO 97′00′845, **1997** [*Chem. Abstr.* **1997**, *126*, 143985f].
[25] F. Cottet, M. Schlosser, *Eur. J. Org. Chem.* **2002**, 327–330.
[26] I. Haiduc, H. Gilman, *Chem. Ind. (London)* **1968**, 1278–1279.
[27] M. D. Rausch, F. E. Tibbetts, H. B. Gordon, *J. Organomet. Chem.* **1966**, *5*, 493–500.
[28] J. Gorecka, C. Heiss, R. Scopelliti, M. Schlosser, *Org. Lett.* **2004**, *6*, 4591–4593.
[29] M. Schlosser, E. Castagnetti, *Eur. J. Org. Chem.* **2001**, 3991–3997.
[30] L. Ondi, O. Lefebvre, M. Schlosser, *Eur. J. Org. Chem.* **2004**, 3714–3718.
[31] M. Schlosser, M. Marull, *Eur. J. Org. Chem.* **2003**, 1569–1575.
[32] C. Heiss, M. Schlosser, *Eur. J. Org. Chem.* **2003**, 447–451.

Received: April 4, 2005
Published Online: August 22, 2005

