Enhancement of Benzylic Basicity by a Fluorine Substituent at the *para*-Position: A Case of Lone Pair/Lone Pair Repulsion

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Abstract: The introduction of a halogen atom at any aromatic position of toluene considerably accelerates the base-promoted deprotonation of the methyl group. *p*-Fluorotoluene is the only exception; proton abstraction from its benzylic site occurs approximately at one tenth of the rate found with toluene (at $-75\,^{\circ}C$). Lone-pair repulsion appears to be at the origin of the decrease in acidity. Chloro- and bromotoluenes instantaneously exchange benzylic hydrogen against metal when treated with solution of lithium 2,2,6,6-tetramethylpiperidide (LITMP) in diethyl ether in the presence of potassium *tert*-butoxide and N,N,N',N'',N''-pentamethyldiethylenetriamine at $-100\,^{\circ}C$. Due to extensive side reactions ("aryne" formation as a consequence of concomitant deprotonation of aromatic sites adjacent to the halogen atom), products can be isolated only in moderate yield (10–35 %), but they are regioisomerically pure.

Keywords: acidity · electron–electron repulsion · fluorine · lithiation · substituent effects

Introduction

The basicity changes within a series of organometallic compounds have been postulated to be proportional to those of the corresponding counterion-free ("naked") carbanions as long as differences in aggregation or solvation aptitudes remain negligibly small.[1] On the basis of this plausible assumption one might predict *p*-fluorobenzyllithium to be thermodynamically more stable (that is less basic) than benzyllithium, since the *p*-fluorobenzyl anion has been reported to exhibit a smaller proton affinity in the gas phase than benzyl anion itself (372.4 vs. 373.7 kcal mol^{-1}).[2] However, this expectation is at variance with acidity measurements in the condensed phase (acetonitrile) which have revealed a higher pK value for *p*-fluorotoluene (52.2) than for toluene (51.1).[3]

If the *p*-fluoro substituent really diminishes the acidity of a benzylic site, this could explain why *p*-fluorotoluene, unlike its *o*- and *m*-isomers, undergoes preferential deprotonation at a halogen-adjacent aromatic position rather than at the methyl group.[4] To gain deeper insight, we have decided to determine the rates of proton abstraction from all fluoro, chloro- and bromotoluene isomers relative to toluene.

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Results and Discussion

Mixtures of the respective halotoluene and toluene were dissolved in tetrahydrofuran and incubated with lithium 2,2,6,6-tetramethylpiperidide/potassium *tert*-butoxide ("LITMP-KOR") in the presence of N,N,N',N'',N''-pentamethyldiethylenetriamine ("PMDTA"). Samples were withdrawn at fixed intervals, quenched with dry ice, and treated with diazomethane. The concentrations of the initial substrates and of the reaction products were analyzed by gas chromatography as a function of time (see Figure 1).

All fluorotoluenes, not only the *p*-isomer, were found to undergo concomitant deprotonation at the methyl group and at a fluorine-adjacent aromatic position to afford, after carboxylation and neutralization, the acetic acids **1a–3a** and the benzoic acids **4a–6a**, respectively. The ratios of α-versus *o*-attack vary in the range of 0.1 and 10 (Table 1). In contrast, no chlorotoluene and bromotoluene derivatives were identified other than the arylacetic acids (**1b–3b** and **1c–3c**) formed by electrophilic substitution at the benzylic position. This does not mean that proton abstraction from aromatic positions does not occur at all. However, the *o*-haloaryllithiums thus generated appear to eliminate lithium halide instantaneously. In this way they set free dehydroarenes ("arynes"), which may undergo a variety of subsequent transformations, in particular nucleophilic additions of organolithiums and lithium amides.

The disappearance of toluene and its halogenated congeners was monitored and relative substrate reactivities k_X/k_H were calculated according to the standard equation of competition kinetics.[5, 6] The proportion of deprotonation at
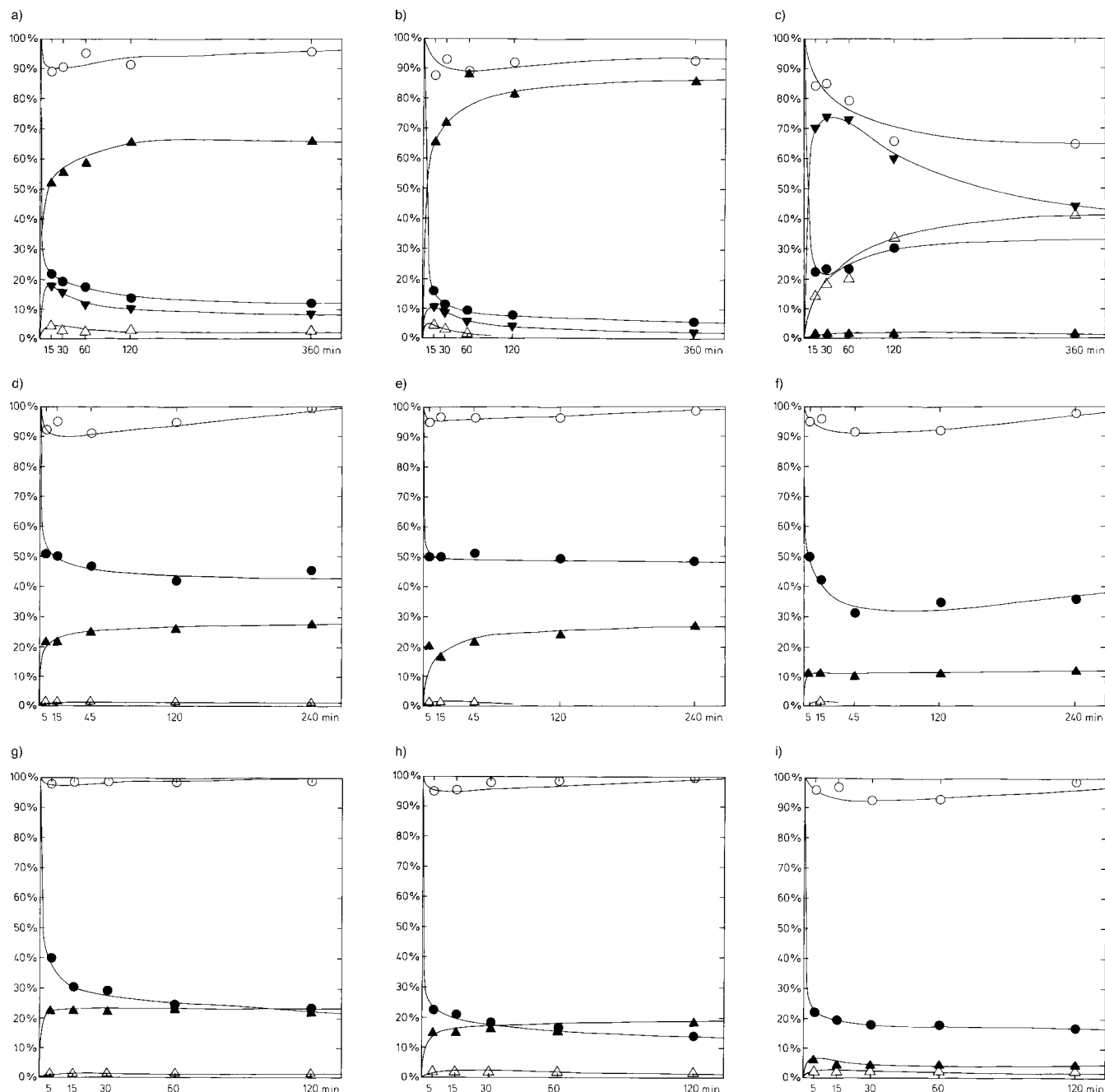
Figure 1. Top: Competitive metalation of toluene and fluorotoluenes (at −75 °C). Middle: Competitive metalation of toluene and chlorotoluenes (at −100 °C). Bottom: Competitive metalation of toluene and bromotoluenes (at −100 °C). Graphs show the consumption of the starting materials and the formation of the trapped products (see Experimental Section) as a function of the metalation time. In all graphs ○ toluene, △ methyl phenylacetate; a) ● 2-fluorotoluene, ▲ methyl (2-fluorophenyl)acetate, ▼ methyl 2-fluoro-(3-methyl)benzoate; b) ● 3-fluorotoluene, ▲ methyl (3-fluorophenyl)acetate, ▼ methyl 2-fluoro-(4-methyl)benzoate c) ● 4-fluorotoluene, ▲ methyl (4-fluorophenyl)acetate, ▼ methyl 2-fluoro-(5-methyl)benzoate; d) ● 2-chlorotoluene, ▲ methyl (2-chlorophenyl)acetate; e) ● 3-chlorotoluene, ▲ methyl (3-chlorophenyl)acetate; f) ● 4-chlorotoluene, ▲ methyl (4-chlorophenyl)acetate; g) ● 2-bromotoluene, ▲ methyl (2-bromophenyl)acetate; h) ● 3-bromotoluene, ▲ methyl (3-bromophenyl)acetate; i) ● 4-bromotoluene, ▲ methyl (4-bromophenyl)acetate.

aromatic chlorotoluene or bromotoluene positions (see above) was approximated as the difference between the total consumption of such halotoluenes and their conversion into (halophenyl)acetic acids. The numbers thus obtained are only reliable within orders of magnitudes (see Table 1), since extensive side reactions, in particular halide elimination, inevitably produce large error deviations. One unequivocal conclusion can nevertheless be drawn. The reactivity of all

halogenated substrates except one is enhanced when compared with toluene. In the case of *p*-fluorotoluene only the hydrogen/metal exchange at the halogen-adjacent position was found to be accelerated. Proton abstraction from the benzylic site of *p*-fluorotoluene proved to be retarded by one power of ten relative to toluene. This is a striking exception when compared with the behavior of the other fluorotoluene isomers and of all chlorotoluenes and bromotoluenes.
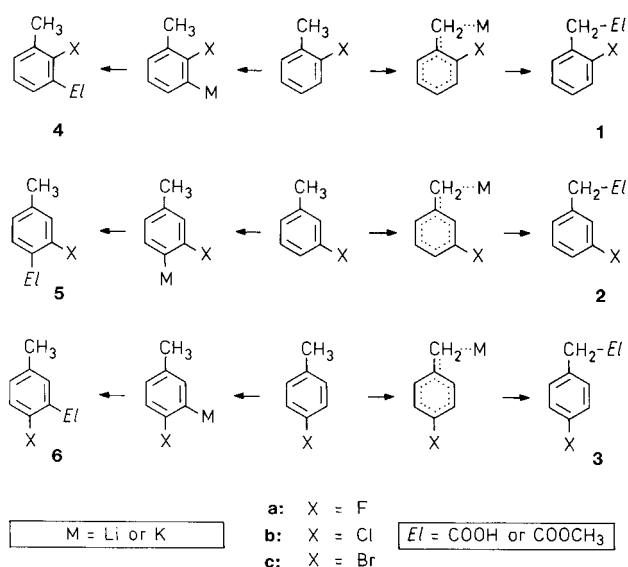
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M = Li or K		a: X = F
		b: X = Cl El = COOH or COOCH₃
		c: X = Br

Table 1. Deprotonation rates k_x^Σ (α- and *ortho*-positions summed up) and k_x^α (exclusively at the benzylic α-position) of halotoluenes relative to toluene (k_H).[a,b]

X	k_{rel}	CH₃ / X (ortho)	CH₃ / X (meta)	CH₃ / X (para)
F	k_F^Σ/k_H^Σ	10^1	10^1	10^1
	k_F^α/k_F^o	3×10^0	3×10^0	10^{-2}
	k_F^α/k_H^α	10^1	10^1	10^{-1}
Cl	k_{Cl}^Σ/k_H^Σ	10^1	10^1	10^1
	k_{Cl}^α/k_{Cl}^o	10^0	10^0	10^{-1}
	k_{Cl}^α/k_H^α	3×10^0	3×10^0	3×10^0
Br	k_{Br}^Σ/k_H^Σ	10^1	10^1	10^1
	k_{Br}^α/k_{Br}^o	10^0	10^0	10^{-1}
	k_{Br}^α/k_H^α	10^0	3×10^0	3×10^0

[a] $k_x^\Sigma = k_x^\alpha + k_x^o$. [b] With toluene, $k^\Sigma = k^\alpha$.

From a kinetic point of view only the disappearance of the substrates matters. Of course, the starting materials consumed should quantitatively reemerge as new products. Only then can the rate factors be considered accurate. A satisfactory mass balance was only found with the fluorotoluene reactions in which the substrates and their derivatives (carboxylic acids or the corresponding methyl esters) add up to 90–94% (Figure 1a–c, Tables 2–4 in the Experimental Section). When chlorotoluenes are consecutively treated with the mixed metal base (LITMP-KOR and PMDTA, during 2 h) and dry ice, only 46–74% of chlorine containing compounds were monitored (Figure 1d–f, Tables 5–7 in the Experimental Section). With bromotoluenes this number drops to 23–48% (Figure 1g–i, Tables 8–10 in the Experimental Section). As already suggested above, the remainder is lost by halide elimination generating dehydroarenes ("arynes"). Attempts to trap these products by adding furan as co-solvent failed. Cycloaddition reactions involving a short-lived intermediate are known to work well only in the absence of strong nucleophiles, which themselves readily combine with transient species such as dehydroarenes. A model reaction enabled us indeed to isolate three products that must have been formed by nucleophilic addition to 2,3-dehydrotoluene generated by the exposure of *o*-bromotoluene to LITMP-KOR/

PMDTA: 3-*tert*-butoxytoluene (9%), 2-bromophenyl-3-tolyl-methane (**7a**; 1%), and phenyl-3-tolylmethane (**7b**; 2%). The additional presence of regioisomers, of polycondensed second-generation products and of 2,2,6,6-tetramethyl-1-(3-tol-yl)piperidine is highly probable though not yet unambigu-

7a: X = Br
7b: X = H
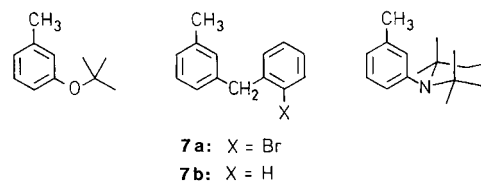
ously proven. The amount of these by-products tripled approximately when the reaction was carried out in the absence of PMDTA.

Because of such side reactions, the yields of chlorotoluene and bromotoluene derivatives are inevitably poor. The simplicity of execution and the absence of any contaminating isomer makes the α-deprotonation/electrophilic substitution nevertheless an attractive option. The one-pot preparation of (2-bromobenzyl)trimethylsilane (**8**; 32% of isolated pure product, Scheme 1) may serve as an illustration.
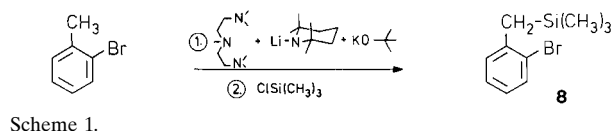
Scheme 1.

The time-resolved evolution of halotoluene deprotonation reveals further remarkable details (Figure 1). One striking feature is the extraordinary ease with which the deprotonation of the halotoluenes occurs. When fluoro-, chloro- or bromotoluenes are treated with the LITMP-KOR-PMDTA mixture, the hydrogen/metal exchange is virtually finished after some 15 min at $-100\,^\circ$C. Noteworthy are also shifts in the product compositions. Thus, during the competitive metalation of toluene and *p*-fluorotoluene, the concentration of benzylpotassium(lithium) grows continuously at the expense of 2-fluoro-4-methylphenylpotassium(lithium), which is the initially predominant intermediate (Figure 1c). This raises the general question of whether kinetic and thermodynamic acidities of halotoluenes diverge or parallel each other.

This issue is particularly relevant in the case of *p*-fluorotoluene. An unequivocal answer can be given. *p*-Fluorobenzyllithium or -potassium not only form more slowly, but are also thermodynamically less stable (that is, they are more basic) than the corresponding benzylmetal. We have demonstrated this by equilibrating, although only imperfectly, the two acid-base pairs involved. *p*-Fluorobenzyllithium was generated from tributyl(*p*-fluorobenzyl)tin (**9**) by metalloid/metal exchange with butyllithium in tetrahydrofuran at $-75\,^\circ$C (Scheme 2). Potassium *tert*-butoxide, and toluene were simultaneously added to the solution. The organometallic concentration diminished rapidly even at dry-ice temperature (94% and 34% of *p*-fluorophenylacetic acid by carboxylation after 45 min and 24 h). The principal modes of decomposition appear to be fluoride elimination, setting free a transient dehydroarene ("aryne"), and proton abstrac-
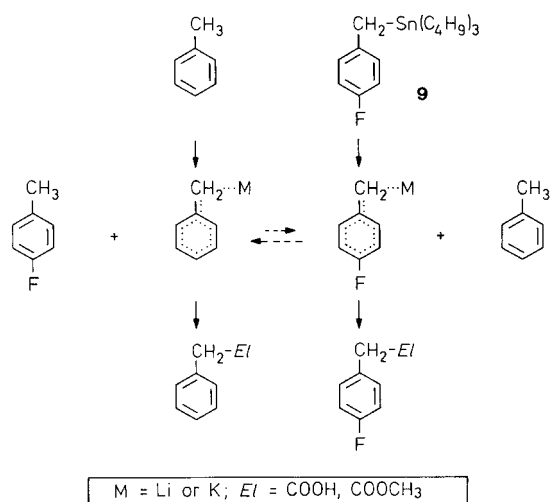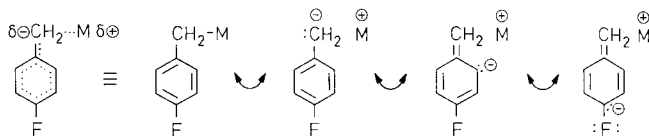
Scheme 2.

Scheme 3.

tion from the solvent, affording *p*-fluorotoluene (3% and 15% after 45 min and 24 h). As expected,[7] the permutational hydrogen/metal exchange proceeded slowly but measurably as evidenced by 0.2% and 3.8% of phenylacetic acid isolated upon trapping after 45 min and 24 h (Scheme 2). On the other hand, transmetalation was found to occur not at all when *p*-fluorotoluene was incubated with benzyllithium and very sluggishly with benzylpotassium (upon carboxylation after 45 min and 24 h: < 0.1% and 0.8% *p*-fluorophenylacetic acid (**3a**); about 98% and 81% of phenylacetic acid; 100% and 92% of *p*-fluorotoluene and 1.5% and 13% of toluene).

The introduction of a fluorine substituent into the *para*-position of toluene lowers both the kinetic and thermodynamic acidity. This relationship is in agreement with previous findings in solution[3] (see the Introduction), but in conflict with a study of the gas-phase acidities of *p*-fluorotoluene (ΔG_{deprot} 372.4 kcal mol^{-1} [2]) relative to toluene (ΔG_{deprot} 373.7 kcal mol^{-1} [8]). These numbers, obtained by equilibrating separately *p*-fluorotoluene/*p*-fluorophenylmethanide and toluene/phenylmethanide with methanol/methoxide look absolutely reliable.[9] How can one solve the apparent contradiction between gas-phase and condensed-phase data? We wondered whether a specific interaction between fluorine and the metal (lithium, sodium, potassium) ions might produce an artefact. Therefore, we decided to probe the effect of a *p*-fluoro substituent on the basicity of metal-ion free, but charge-attenuated, benzylic anions in the condensed phase, using tetrahydrofuran as a solvent of low polarity. We have generated a series of (triphenylphosphonio)arylmethanides (**10**) and determined their benzylic resonance energy by NMR spectroscopy at variable temperature.[10] The barrier to rotation E_{tors} around the C^α–C^{aryl} axis (**10a** ⇔ **10b**; Scheme 3) is a measure for the benzylic resonance.[11] While an activation energy of 8.5 kcal mol^{-1} was found with the unsubstituted parent compound (X = H), this number was lowered upon the introduction of a *p*-fluoro substituent (X = F) to 7.7 kcal mol^{-1} and raised upon the introduction of a *p*-chloro substituent (X = Cl) to 8.9 kcal mol^{-1}.[10] In other words, a fluorine atom attached to a benzylic *para*-position impedes and a chlorine atom facilitates the accumulation of electron density in its vicinity.
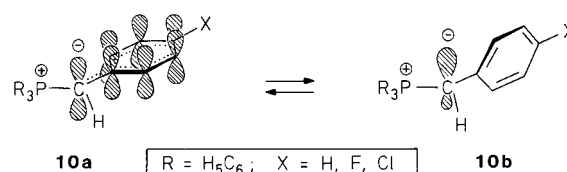
The apparent inconsistency with which fluorine stabilizes or destabilizes a benzyl anion or a related derivative must be related to its dual electronic character. If an integral negative charge, as present in the "naked" gas-phase species, is to be better accommodated by delocalization, the inductive electron-withdrawing effect of the halogen becomes predominant and makes it to a net attractor. In contrast, when the electron excess is attenuated by a metal or another counterion, only the remaining fractional charge will to some extent spread out into the aromatic ring. There it encounters resistance in form of π-electron/n-electron repulsion,[12] which this time overrides the inductive effect. In other words, fluorine acts as a net donor towards a weak donor and as an attractor towards a strong donor. To express the latter situation in the valence bond language, the resonance structure carrying the negative charge at the *para*-position does not contribute much to the electronic delocalization (Scheme 4).

Scheme 4.

A fluorine substituent placed at the *ortho*-position will, of course, perturb the resonance delocalization in the same manner. This time, however, the electron withdrawing effect is more powerful due to the short-range distance and overcompensates the destabilizing action. The lone pair/lone pair repulsion vanishes when fluorine is replaced by chlorine or bromine. The heavier halogens have lost almost all of their donor capacity, because of their increased bond length (and hence poor π–n overlap), while their polarizability ("d-orbital resonance") qualifies them as excellent electron attractors.

Fluorine is a particularly sensitive electronic probe, but it is not the only element that exhibits the donor/attractor dualism.[13] Whereas 3-methoxytoluene is deprotonated faster at the benzylic position than toluene itself, 2- and 4-methoxytoluene react, respectively, 10 and 100 times more slowly.[14] *N,N*,4-Trimethylaniline undergoes superbase-promoted metalation only very sluggishly (50 h at −75 °C!) to afford *p*-(dimethylamino)benzylpotassium.[15, 16] 1,4-Phenylenediamine (ammonium salt pK_a 6.2[17]) is considerably more basic than any of its isomers or aniline itself (pK_a 4.6 – 5.0[17]). No one has ever succeeded in generating an α,α'-dimetalated *p*-xylene although the α,α'-disodio[18, 19] and α,α'-dilithio[20] derivatives of *o*-xylene and *m*-xylene and even α,α',α''-trilithiomesitylene[20] are known. Thus we are dealing with a universal phenomenon.

Experimental Section

For practical routine and technical details, see other articles[21–23] recently published by this laboratory.

Products: The esters were prepared by treatment of the corresponding acids with diazomethane in diethyl ether until the solution turned yellow; they were isolated by distillation.

Fluorotoluene derivatives: The metalation and subsequent carboxylation was carried out as previously described.[4]

2-Fluoro-3-methylbenzoic acid (4a): M.p. 117–118 °C (ref. [4]: M.p. 113–114 °C); 78%, methyl ester.[4]

(2-Fluorophenyl)acetic acid (1a): M.p. 66–67 °C (ref. [24]: M.p. 63–65 °C); 58%; methyl ester.[25]

2-Fluoro-4-methylbenzoic acid (5a): M.p. 183–185 °C (ref. [4]: M.p. 182–183 °C); 40%; methyl ester.[4]

(3-Fluorophenyl)acetic acid (2a): M.p. 42–44 °C (ref. [4]: M.p. 47–48 °C); 40%; methyl ester.[26]

2-Fluoro-5-methylbenzoic acid (6a): M.p. 160–161 °C (ref. [4]: M.p. 154–155 °C); 82%; methyl ester.[4]

(4-Fluorophenyl)acetic acid (3a): not isolated as such (ref. [27]: M.p. 94 °C); ≈5%; methyl ester.[28, 29]

Tributyl(4-fluorobenzyl)stannane (9): A solution of 4-fluorobenzylmagnesium bromide (prepared from 25 mmol of 4-fluorobenzyl bromide) in tetrahydrofuran (30 mL) was rapidly added to tributylchlorostannane (6.7 mL, 8.1 g, 25 mmol) in tetrahydrofuran (20 mL). After 4 h at 25 °C, the mixture was neutralized. The product was isolated by extraction with diethyl ether (87%) and purified by two-fold distillation; b.p. 104–108 °C/0.1 mm Hg (Ref. [30]: b.p. 105–108 °C/0.5 mm Hg); $[n]_D^{20}$ 1.5104; 40%. This material (5.0 mmol) was used to generate 4-fluorobenzyllithium by treatment with butyllithium (5.0 mmol) for 2 h at −75 °C in a 5:1 mixture (v/v; 18 mL) of tetrahydrofuran and hexanes, before potassium tert-butoxide (5.0 mmol) and toluene (7.4 mmol) were added to start the transmetalation reaction at −75 °C.

Chlorotoluene derivatives: At −75 °C and under vigorous stirring, potassium tert-butoxide (1.12 g, 10.0 mmol), 2,2,6,6-tetramethylpiperidine (1.70 mL, 1.41 g, 10.0 mmol), N,N,N′,N″,N″-pentamethyldiethylenetriamine ("PMDTA"; 2.10 mL, 1.73 g, 10.0 mmol) and chlorotoluene (1.17 or 1.18 mL, 1.27 g, 10.0 mmol) were consecutively added to a solution of butyllithium (10.0 mmol) in a 4:1 (v/v) mixture (33 mL) of tetrahydrofuran and hexanes. After 15 min at −75 °C, the mixture was poured on an excess of freshly crushed dry ice and evaporated. The residue was dissolved in water (30 mL). The aqueous phase was washed with diethyl ether (3 × 10 mL), acidified with hydrochloric acid (2 M), and extracted with diethyl ether (3 × 25 mL). The combined organic layers were washed with brine (2 × 10 mL), dried, and evaporated. The solid residue was recrystallized from hexanes.

(2-Chlorophenyl)acetic acid (1b): M.p. 95–97 °C (ref. [31]: M.p. 93–95 °C); 27%; methyl ester.[32]

(3-Chlorophenyl)acetic acid (2b): M.p. 77–78 °C (ref. [31]: M.p. 76–77 °C); 16%; methyl ester.[33]

(4-Chlorophenyl)acetic acid (3b): M.p. 102–104 °C (ref. [31]: M.p. 104–106 °C); 5% (crude product: 7%); methyl ester.[34]

Bromotoluene derivatives: The same procedure as described above for the chlorotoluene derivatives was applied, by replacing the chlorotoluene with bromotoluene (1.20–1.23 mL, 1.71 g, 10.0 mmol).

(2-Bromophenyl)acetic acid (1c): M.p. 105–106 °C (ref. [31]: M.p. 104–105 °C); 23% (crude product: 41%); methyl ester.[35]

(3-Bromophenyl)acetic acid (2c): M.p. 101.0–101.5 °C (ref. [31]: M.p. 102–103 °C); 20% (crude product: 32%); methyl ester.[36]

(4-Bromophenyl)acetic acid (3c): M.p. 117–118 °C (ref. [31]: M.p. 113–115 °C); 13% (crude product :19%); methyl ester.[28, 37, 38].

(2-Bromobenzyl)trimethylsilane (8): This was isolated in 32% yield when the reaction mixture was treated with an excess of chlorotrimethylsilane (3.5 mL, 3.0 g, 28 mmol) rather than with dry ice. It was kept 1 h at −75 °C before being concentrated, diluted with diethyl ether (30 mL), and washed with hydrochloric acid (2 M, 3 × 25 mL), a saturated aqueous solution of sodium hydrogen carbonate (2 × 25 mL), and brine (25 mL). Distillation

afforded a pure product; b.p. 102–103 °C/13 mm Hg (Ref. [39]: b.p. 80–81 °C/3.5 mm Hg); $[n]_D^{20}$ 1.5283; 32%.

Competitive deprotonation experiments

Reactions involving fluorotoluenes: The fluorotoluene (5.00 mmol) and toluene (5.00 mmol), both precooled, were simultaneously added to a cold solution (−75 °C) containing lithium 2,2,6,6-tetramethylpiperidide (prepared from butyllithium and 2,2,6,6-tetramethylpiperidine, 5.0 mmol each), potassium tert-butoxide (0.56 g, 5.0 mmol), and decane (0.144 g, 1.00 mmol) in tetrahydrofuran (20 mL) and hexanes (3.1 mL). Samples (of approximtely 2 mL) were withdrawn at fixed intervals, treated with an excess of dry ice covered with anhydrous diethyl ether, acidified (to pH 1–3) with hydrochloric acid (2 M), and treated with diazomethane in diethyl ether until the yellow color of the latter reagent persisted. Unconsumed starting materials and the esters formed were identified by gas chromatography (30 m, DB-1, 45 °C [5 min] →85 °C [2 °C min⁻¹] →220 °C [10 °C min⁻¹]; 2 m, 5% C-20M, 200 °C) by comparing their retention times with those of authentic materials and their concentrations (see Tables 2–4) were determined by monitoring their peak areas relative to that of the "internal standard" decane and by using calibration factors to correct the ratios thus obtained.

Table 2. Competitive deprotonation of 2-fluorotoluene and toluene with LITMP-KOR: concentrations [%] of starting materials and trapped products as a function of time.
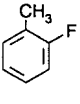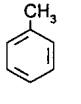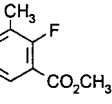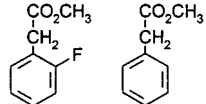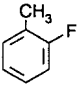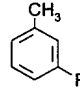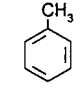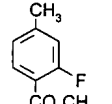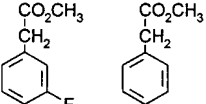
Reaction time [h]	CH₃ / F (ring)	CH₃ (ring)	CH₃ / F / CO₂CH₃ (ring)	CH₂ / CO₂CH₃ / F (ring)	CH₂ / CO₂CH₃ (ring)
0.00	100	100	–	–	–
0.25	22	89	18	52	4.8
0.50	20	91	15	55	3.0
1.0	18	95	12	59	2.6
2.0	14	91	11	65	3.2
6.0	12	96	8.4	66	3.2

Table 3. Competitive deprotonation of 3-fluorotoluene and toluene with LITMP-KOR: concentrations [%] of starting materials and trapped products as a function of time.
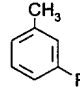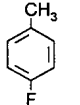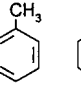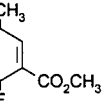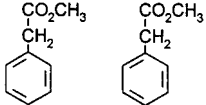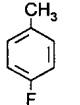
Reaction time [h]	CH₃ / F (ring)	CH₃ (ring)	CH₃ / F / CO₂CH₃ (ring)	CO₂CH₃ / CH₂ / F (ring)	CO₂CH₃ / CH₂ (ring)
0.00	100	100	–	–	
0.25	16	87	10	66	4.8
0.50	13	93	8.6	74	3.0
1.0	9.5	89	5.6	88	1.8
2.0	8.2	94	4.0	82	–
6.0	5.8	95	2.2	86	–

Table 4. Competitive deprotonation of 4-fluorotoluene and toluene with LITMP-KOR: concentrations [%] of starting materials and trapped products as a function of time.

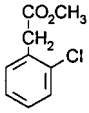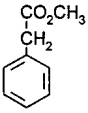| Reaction time [h]	CH₃ / F (ring)	CH₃ (ring)	CH₃ / F / CO₂CH₃ (ring)	CO₂CH₃ / CH₂ / F (ring)	CO₂CH₃ / CH₂ (ring)
0.00	100	100	–	–	–
0.25	22	84	70	1.0	15
0.50	24	85	74	1.2	19
1.0	24	80	73	1.3	20
2.0	30	66	60	1.1	34
6.0	32	65	44	1.3	42

Reactions involving chlorotoluenes: In addition to all the other ingredients specified above, *N,N,N′,N″,N″*-pentamethyldiethylenetriamine ("PMDTA"; 5.0 mmol) was present and the reaction was performed at −100°C. The reaction mixtures were analyzed by gas chromatography (2 m, 5% SE-30, 65°C [15 min]→210°C [10°Cmin⁻¹]; 2 m, 5% Ap-L, 220°C) to determine the concentrations of starting materials and products at given intervals (see Tables 5–7).

Table 5. Competitive deprotonation of 2-chlorotoluene and toluene with LITMP-KOR-PMDTA: concentrations [%] of starting materials and trapped products as a function of time.
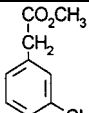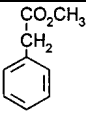
Reaction time [h]	CH_3, Cl (2-chlorotoluene)	CH_3 (toluene)	CO_2CH_3, CH_2, Cl	CO_2CH_3, CH_2
0.00	100	100	–	–
0.10	51	93	22	1.0
0.25	50	95	22	1.0
0.45	47	91	25	0.9
2.0	42	95	26	0.4
4.0	46	106	28	0.4

Table 6. Competitive deprotonation of 3-chlorotoluene and toluene with LITMP-KOR-PMDTA: concentrations [%] of starting materials and trapped products as a function of time.
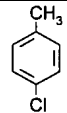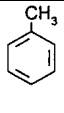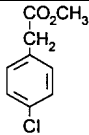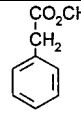
Reaction time [h]	CH_3, Cl (3-chlorotoluene)	CH_3 (toluene)	CO_2CH_3, CH_2, Cl	CO_2CH_3, CH_2
0.00	100	100	–	–
0.10	50	95	20	1.0
0.25	50	96	16	1.2
0.45	51	97	21	0.8
2.0	50	96	24	0.1
4.0	48	102	27	–

Table 7. Competitive deprotonation of 4-chlorotoluene and toluene with LITMP-KOR-PMDTA: concentrations [%] of starting materials and trapped products as a function of time.

Reaction time [h]	CH_3, Cl (4-chlorotoluene)	CH_3 (toluene)	CO_2CH_3, CH_2, Cl	CO_2CH_3, CH_2
0.00	100	100	–	–
0.10	45	95	11	0.5
0.25	43	96	11	–
0.45	32	92	10	–
2.0	35	92	11	–
4.0	36	99	12	–

Reactions involving bromotoluenes: The execution followed exactly the procedure given for chlorotoluenes above. Gas chromatography (2 m, 5% SE-30, 70°C [15 min]→220°C [10°Cmin⁻¹]; 2 m, 5% C-20M, 220°C) was again the method of choice for analyzing the composition of the reaction mixtures (see Tables 8–10).

Further kinetic competition experiments were performed in the same way as described in the preceding paragraphs but by using three different halotoluenes simultaneously as the starting materials. These "triplets" were: *o*-, *m*- and *p*-chlorotoluene; *o*-, *m*- and *p*-bromotoluene; the *ortho* isomers of fluoro-, chloro- and bromotoluene; the *meta* isomers of fluoro-, chloro- and bromotoluene; and the *para* isomers of fluoro-, chloro- and

Table 8. Competitive deprotonation of 2-bromotoluene and toluene with LITMP-KOR-PMDTA: concentrations [%] of starting materials and trapped products as a function of time.
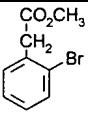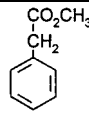
Reaction time [h]	CH_3, Br (2-bromotoluene)	CH_3 (toluene)	CO_2CH_3, CH_2, Br	CO_2CH_3, CH_2
0.00	100	100	–	–
0.10	40	99	23	0.8
0.25	30	103	23	1.2
0.45	30	102	22	1.4
2.0	25	106	23	1.1
4.0	24	109	22	1.5

Table 9. Competitive deprotonation of 3-bromotoluene and toluene with LITMP-KOR-PMDTA: concentrations [%] of starting materials and trapped products as a function of time.
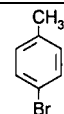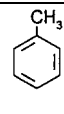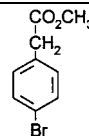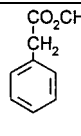
Reaction time [h]	CH_3, Br (3-bromotoluene)	CH_3 (toluene)	CO_2CH_3, CH_2, Br	CO_2CH_3, CH_2
0.00	100	100	–	–
0.10	23	96	15	1.6
0.25	21	96	15	2.0
0.45	19	99	17	1.2
2.0	16	99	17	1.4
4.0	14	102	19	1.6

Table 10. Competitive deprotonation of 4-bromotoluene and toluene with LITMP-KOR-PMDTA: concentrations [%] of starting materials and trapped products as a function of time.
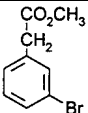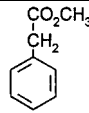
Reaction time [h]	CH_3, Br (4-bromotoluene)	CH_3 (toluene)	CO_2CH_3, CH_2, Br	CO_2CH_3, CH_2
0.00	100	100	–	–
0.10	22	96	6.0	2.2
0.25	20	97	4.3	2.2
0.45	18	93	4.4	2.2
2.0	18	93	4.8	2.4
4.0	17	103	4.6	2.4

bromotoluene. The relative reactivities observed agreed well with the numbers anticipated on the basis of the previous results (see above).

Interception of dehydroarenes: At −75°C, 2,2,6,6-tetramethylpiperidine (4.2 mL, 3.5 g, 25 mmol), potassium *tert*-butoxide (2.8 g, 25 mmol), *N,N,N′,N″,N″*-pentamethyldiethylenetriamine ("PMDTA", 5.2 mL, 4.3 g, 25 mmol) and 2-bromotoluene (3.0 mL, 4.3 g, 25 mmol) were consecutively added to butyllithium (25 mmol) in hexanes (15 mL) and tetrahydrofuran (40 mL). After 2 h at −75°C, the reaction mixture was poured on an excess of freshly crushed dry ice. Water (50 mL) and diethyl ether (50 mL) were added, and the products were partitioned between the two phases. The organic layer was dried, concentrated, and submitted to gas-chromatographic analysis (2 m, 5% Carbowax-20M, 70°C→[10°Cmin⁻¹]→200°C [15 min]; 2m, 5% Apiezon L, 80°C → [10°Cmin⁻¹]→220°C [15 min]; nonane as an internal standard). Three products, 3-*tert*-butoxytoluene[40] (9%), 2-bromophenyl-3-tolylmethane[41] (1%) and phenyl-3-tolylmethane[42] (2%), were unambiguously identified by comparison of their retention times with those of authentic samples and their yields were determined by comparison of their peak areas with that of an "internal standard" (nonane) and by correction of the ratios using calibration factors.

The aqueous alkali phase contained, in form of its salt, (2-bromophenyl)-acetic acid,[31] which was isolated after acidification (23%; M.p. 103–104°C).

Acknowledgements

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