

Dimetalation: The Acidity of Monometalated Arenes Towards Superbasic Reagents

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Twofold hydrogen/metal interconversions ("dimetalations") can be accomplished with "spiny" arenes (*tert*-butylbenzene, 1,4-di-*tert*-butylbenzene, 1,1,3,3-tetramethylindane and congeners) and *N,N*-crowded anilines (2,2,6,6-tetramethyl-1-phenylpiperidine and *N,N*-bis(triethylsilyl)aniline), albeit incompletely (average and optimum yields of trapping products 25% and 41%, respectively). All the evidence points at an aggregate phenomenon. Dimetalation occurs only with an excess of a highly concentrated butyllithium/potassium *tert*-

butoxide mixture in hydrocarbon media. In tetrahydrofuran, no trace of a dimetalated species is found, although such species, once generated in a different manner, are moderately stable in this solvent at -75°C . 1,4-Dimetalloarenes are favored over the 1,3-isomers; 1,2-isomers do not form at all. As found by competition kinetics, 2,2,6,6-tetramethyl-1-phenylpiperidine and *N,N*-bis(triethylsilyl)aniline undergo monometalation at roughly the same rate as *tert*-butylbenzene and much more slowly than benzene does.

Introduction

Organic dimetal and polymetal compounds^[1] continue to attract attention because of their intriguing structures and special modes of generation. They had an additional spotlight shone on them when recent computational work revealed *phenyllithium to be more acidic than benzene*.^[2] This opened not just the frivolous perspective that aryl anion-arylmatal adducts might be long-lived in the gas phase, but also that dimetalated arenes might be thermodynamically favored over monometalated ones even in condensed phases. In continuation of previous investigations,^[3] we have studied this issue experimentally. As detailed below, our findings clarify the problem in all major aspects:

Dimetalation can be achieved with a variety of aromatic substrates bearing one or two *tert*-alkyl groups or hetero-substituents. So far, dimetalation at the same aromatic ring has been reported only with benzene itself, with variable amounts (generally $< 10\%$) of isophthalic and terephthalic acid being identified after carboxylation.^[4–9]

Dimetalation of monosubstituted benzenes occurs exclusively at the *meta* positions. In this way, adverse steric and electrostatic effects are obviously minimized.

Dimetalation is only kinetically, not thermodynamically favored over monometalation. It is mediated by high-olecular aggregates, the formation of which requires high reagent concentrations and noncoordinating solvents.

To gain further insights, competition experiments were carried out. In this way, substituent effects on metalation rates were quantified.

Results and Discussions

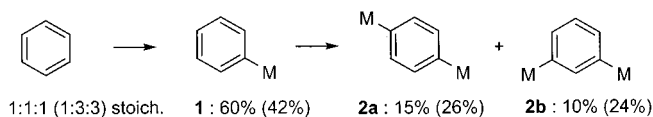
A principal objection had to be addressed first. Even if dimetal species should indeed be less basic than monometal analogs, their generation may be impeded by the notoriously poor solubility of the monometalated species in paraffin-type hydrocarbons, the standard reaction media. This argument no longer holds if one works in homogeneous solution. To date, no trace of a dimetalated benzene derivative has ever been detected in tetrahydrofuran-rich mixtures, which at a quick glance would appear to be irrefutable evidence against dimetalation in ethereal solvents. But can one really rule out the rapid generation of dimetalated species and their even more rapid destruction by solvent attack under such conditions?

To examine this possibility, we treated benzene with equimolar amounts of butyllithium and potassium *tert*-butoxide, dissolved or suspended in hexanes, as described previously.^[10] The solvent was then removed and the residue was dissolved in precooled tetrahydrofuran. After 2 h of storage at -75°C , the composition of the organometallic intermediates (as monitored by interception with chlorotrimethylsilane) had not changed much. The quantity of monometalated species had increased slightly ($51 \rightarrow 53\%$) at the expense of the 1,3- and 1,4-phenylenedimetals ($12 \rightarrow 6\%$ and $16 \rightarrow 9\%$, respectively). A major proportion of dimetalated species, had such species ever been produced in tetrahydrofuran, would obviously have survived.

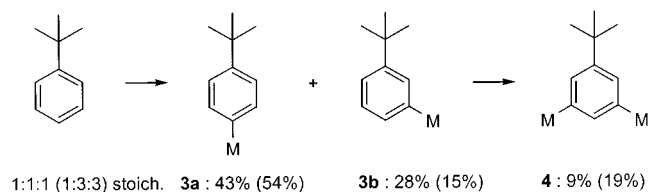
Solubility in hydrocarbon media does not appear to be a crucial factor. The amounts of monometalated, *para*-dimetalated, and *meta*-dimetalated species ($M = K + Li$), as reflected by their carboxylation products ($M = \text{COOH}$), remain constant (approximately 60%, 15%, and 10%, respectively) regardless of whether a 0.5 or 1.5 M^[3] solution of benzene is treated with equimolar quantities of butyllithium and potassium *tert*-butoxide. In contrast, the propor-

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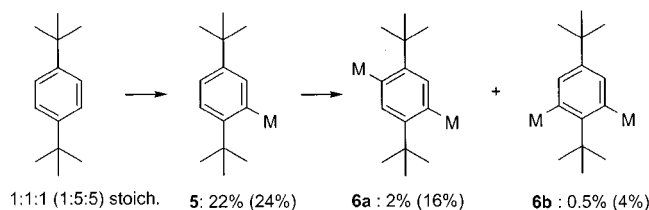
tions shift considerably when the superbasic reagent mixture is employed in threefold excess, which promotes the formation of *para*-dimetalated and *meta*-dimetalated intermediates (**26** and **24%**) at the expense of the monometalated one (**42%**).



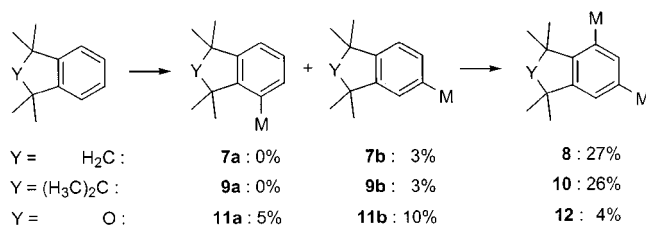
Bulky substituents should increase the solubility of organometallic intermediates in petroleum ether. If *tert*-butylbenzene is compared with benzene, however, the ratio of dimetalated species to monometalated species (**4** vs. **3a** + **3b**) diminishes from 25:60 to 9:71 and from 50:42 to 19:69 at the 1:1:1 and 1:3:3 stoichiometries, respectively.



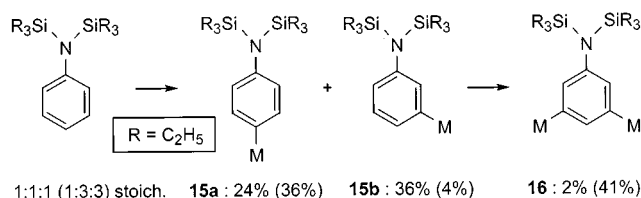
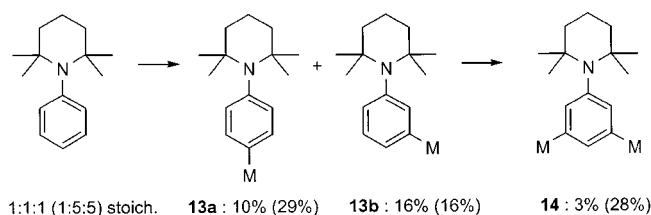
1,4-Di-*tert*-butylbenzene is particularly tough to crack, all aromatic positions suffering from massive steric hindrance. Dimetalation generating the *para*- and *meta*-isomers **6a** and **6b** in significant yields occurs only if a fivefold excess of butyllithium and potassium *tert*-butoxide is employed at elevated temperatures (e.g., +75 °C) and prolonged reaction times are used.



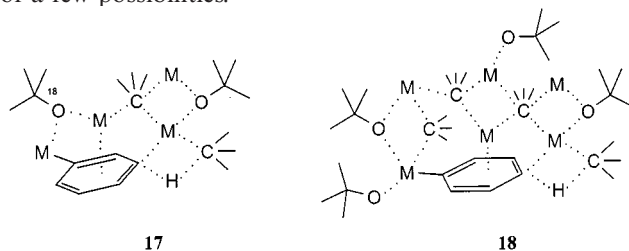
Recently the superbases-promoted monometalation of 1,1,3,3-tetramethylindane, 1,1,2,2,3,3-hexamethylindane, and 1,1,3,3-tetramethyl-1,3-dihydroisobenzofuran has been reported.^[10] These substrates can be considered as substitutes for the less readily available 1,2-(di-*tert*-butyl)benzene. Monosubstitution of an *ortho*-position does not occur with the hydrocarbons (neither **7a** nor **9a**), but does, at least to some extent, with the cyclic ether (5% of **11a**), thus suggesting the operation of a long-range inductive heteroelement effect. Dimetalation implies proton abstraction from one crowded position. This may explain why only moderate yields of derivatives **8** and **10** can be achieved even when a fivefold excess of the superbasic reagent is used. No more than traces of the species **12** have been identified. This is presumably a consequence of the fragility of the oxygen heterocycle, which tends to undergo ring scission by β -elimination.



In order to examine heteroelement effects further, the investigation was extended to two aniline derivatives. Both 2,2,6,6-tetramethyl-1-phenylpiperidine and *N,N*-bis(trimethylsilyl)aniline showed high levels of dimetalation when treated with an excess of the superbase. The former substrate afforded doubly and singly substituted products in a 28:45 ratio (**14** vs. **13a** + **13b**, at a 1:5:5 stoichiometry), the latter in a 41:40 ratio (**16** vs. **15a** + **15b**, at a 1:3:3 stoichiometry).



Despite their structural diversity, the substrates examined exhibit common reactivity features. To push dimetalation to synthetically useful levels, a threefold or fivefold excess of the metalating reagent is required in all cases. If equimolar amounts of the substrate and the superbase are allowed to react with each other, only benzene affords substantial proportions of dimetalated species (up to 15% of the *para*-isomer and 10% of the *meta*-isomer). Under the same conditions, *tert*-butylbenzene, 2,2,6,6-tetramethyl-1-phenylpiperidine, and *N,N*-bis(trimethylsilyl)aniline give only 9%, 3%, and 2%, respectively, of the sterically uncongested *meta*-dimetalated species. All this evidence suggests that the second deprotonation is accomplished within a tightly packed mixed aggregate, the depicted 1:2:2 and 1:4:4 adducts (**17** and **18**) being intended only as a nonexhaustive illustration of a few possibilities.

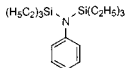


Electrostatics obviously dictate the regiochemical outcome of dimetalations. Whereas *ortho*-dimetalations are rigorously precluded, *para*-dimetalation dominates over *meta*-dimetalation whenever this is possible, as with benzene (*p/m* ratio of approximately 2.5 after statistical correction) and 1,4-di-*tert*-butylbenzene (*p/m* ratio 4.0) as the substrates.

Benzenes carrying a single bulky substituent undergo monometalation at both the *m*- and the *p*-positions, but dimetalation only at *m,m'*-positions. In other words, the dimetalated intermediate is generated exclusively at the expense of the *m*-monometalated one. As a consequence, the *p/[m+m']* ratios (all statistically corrected) do not vary excessively as a function of the substrate/reagent stoichiometry: between 1.3 and 3.2 with *tert*-butylbenzene, between 1.1 and 1.3 with 2,2,6,6-tetramethyl-1-phenylpiperidine, and between 1.3 and 1.6 with *N,N*-bis(triethylsilyl)aniline.

Regioisomeric ratios reflect the reactivity at various sites that compete with each other intramolecularly. They do not tell us anything about how rapidly or slowly a given substrate becomes metalated in comparison with a reference compound. The easiest way to collect information on relative intermolecular reactivities is to carry out competition kinetic experiments. This has already been accomplished for a series of "spiny" arenes such as *tert*-butylbenzene and di-*tert*-butylbenzenes, relative to benzene.^[3,10] This study has now been extended to the bulky aniline derivatives 2,2,6,6-tetramethyl-1-phenylpiperidine and *N,N*-bis(triethylsilyl)aniline (see Table 1).

Table 1. Metalation of *tert*-butylbenzene, 2,2,6,6-tetramethyl-1-phenylpiperidine, and *N,N*-bis(triethylsilyl)aniline with butyllithium in the presence of potassium *tert*-butoxide in hexanes at 25 °C: relative rates k_{rel} [a] and partial rate factors k_{f} [b]

Substrate	k_{rel}	k_{o}^{f}	k_{m}^{f}	k_{p}^{f}
	0.28	< 0.01	0.06	0.15
	0.15	< 0.01	0.05	0.05
	0.31	< 0.01	0.10	0.12

[a] Reaction rates relative to that of benzene = 6.0. – [b] Relative rates multiplied by the fraction of reaction occurring at the given site (*ortho*, *meta*, or *para*) and divided by the number of equivalent exchange-active positions (2 or 1).

Are dimetalations useful practically? Without doubt, if one is aiming at the preparation of a dicarboxylic acid, a dialdehyde, or a dialcohol by reaction with carbon dioxide, a formamide, or formaldehyde, respectively. Such highly polar derivatives can easily be separated and purified even in cases of moderate yields. Moreover, improvements are possible. To boost yields and to avoid the formation of regioisomers, one may first perform a permutational halogen/metal or metalloid/metal exchange to generate a specific

monometalated intermediate, 3-[*N,N*-bis(triethyl)silyl]aminophenyllithium, for example. The second metal may then be introduced separately and regioselectively by treatment with the superbase.

Experimental Section

For standard laboratory practice and abbreviations, see recent publications from this laboratory.^[11–12] ¹H NMR spectra were recorded using solutions in deuteriochloroform or, if marked with an asterisk, in perdeuterated dimethyl sulfoxide at 400 MHz.

***tert*-Butylbenzene as the Substrate:** Potassium *tert*-butoxide (1.1 g, 10 mmol) was added to a solution of *tert*-butylbenzene (1.6 mL, 1.3 g, 10 mmol) and butyllithium (10 mmol) in hexanes (35 mL). The suspension was vigorously stirred for 2 h at +25 °C before being poured on an excess of freshly crushed dry ice covered with a layer of tetrahydrofuran. The mixture was acidified with 2 M hydrochloric acid (50 mL) and extracted with diethyl ether (2 × 25 mL). One twentieth of the solution was withdrawn and treated with ethereal diazomethane until the yellow color persisted. A known amount (approx. 10 mg) of tridecane was added as an "internal standard" for the gas chromatographic analysis (2 m, 5% C-20M, 50 °C → 200 °C; 2 m, 5% Ap-L, 50 °C → 220 °C). The peaks of methyl 4-*tert*-butylbenzoate,^[13] methyl 3-*tert*-butylbenzoate,^[14] and dimethyl 5-*tert*-butylisophthalate^[15] (**3a**, **3b**, and **4**, respectively; M = COOCH₃) were identified by comparison of their retention times with those of authentic samples and their areas relative to the reference compound were corrected using separately determined calibration factors. The products **3a**, **3b**, and **4** had formed in 43%, 28%, and 9% yields. The remainder of the combined organic layers was washed with brine (2 × 25 mL), dried and evaporated to dryness. Recrystallization of the residue from acetic acid gave a small amount (3%) of 5-*tert*-butylisophthalic acid; m.p. (decomp.) 340–342 °C. – When three equivalents (30 mmol) of butyllithium and potassium *tert*-butoxide were employed under otherwise identical conditions, the methyl esters **3a**, **3b**, and **4** were found to be present in 54%, 15% and 19% yields.

1,4-Di-*tert*-butylbenzene as the Substrate: A vigorously stirred mixture containing 1,4-di-*tert*-butylbenzene (19 g, 0.10 mol), butyllithium (0.50 mol), and potassium *tert*-butoxide (0.50 mol) in hexanes (0.35 L) was heated under reflux (approx. 75 °C) for 25 h. It was cooled to –75 °C and diluted with precooled tetrahydrofuran (0.10 L) before being poured on an excess of freshly crushed dry ice covered with a layer of tetrahydrofuran (50 mL). Diethyl ether (0.25 L) was added and the products were extracted with a 10% aqueous solution (5 × 50 mL) of sodium hydroxide and, after acidification of this alkaline phase to pH 2, with dichloromethane (3 × 50 mL). After drying and evaporation of the solvent, methyl iodide (12 mL, 28 g, 0.20 mol), potassium carbonate (28 g, 0.20 mol), and acetone (0.25 L) were added and the mixture was stirred for 25 h at 25 °C.^[16] The methyl 2,5-di-*tert*-butylbenzoate^[17] (**5**; M = COOCH₃) was isolated by distillation (bp 148–150 °C/7 Torr). The residue was absorbed on silica gel (0.25 L). Elution with a 1:19 (v/v) mixture of diethyl ether and hexanes resulted in the separation of dimethyl 2,5-di-*tert*-butylterephthalate [**6a**; M = COOCH₃; m.p. 141–142 °C. – ¹H NMR: δ = 7.34 (s, 2 H), 3.91 (s, 6 H), 1.37 (s, 18 H)] and dimethyl 2,5-di-*tert*-butylisophthalate [**6b**; M = COOCH₃; m.p. 99–100 °C. – ¹H NMR: δ = 7.33 (s, 2 H), 3.90 (s, 6 H), 1.43 (s, 9 H), 1.29 (s, 9 H)]. – Hydrolysis of each component under standard conditions (acetic acid, boron trifluoride–diethyl ether, 15 h 25 °C) afforded 2,5-di-*tert*-butyl-

benzoic acid^[18,19] (**5**: R = COOH; m.p. 162–163 °C), 2,5-di-*tert*-butylterephthalic acid [**6a**: R = COOH; m.p. > 250 °C. – C₁₆H₂₂O₄ (278.35): calcd. C 69.04, H 7.97; found C 69.08, H 8.13] and 2,5-di-*tert*-butylisophthalic acid [**6b**: R = COOH; m.p. > 250 °C. – C₁₆H₂₂O₄ (278.35): calcd. C 69.04, H 7.97; found C 69.15, H 7.92]. – To determine the exact yields of the esters **5**, **6a**, and **6b** (M = COOCH₃) obtained, a suspension containing potassium *tert*-butoxide (2.8 g, 25 mmol), butyllithium (25 mmol), and 1,4-di-*tert*-butylbenzene (5.0 or 25 mmol) was vigorously stirred for 25 h at 75 °C. Treatment with carbon dioxide and diazomethane followed as described above. The product concentrations were determined by gas chromatographic analysis (30 m, DB-210, 100 → 200 °C; 30 m DB-1701, 110 → 200 °C), using 4,4'-di-*tert*-butylbiphenyl as an internal calibrated standard.

1,1,3,3-Tetramethylindane as the Substrate: A suspension containing potassium *tert*-butoxide (5.6 g, 50 mmol), butyllithium (50 mmol), and 1,1,3,3-tetramethylindane^[20–21] (1.7 g, 10 mmol) in hexanes (50 mL) was vigorously stirred for 25 h at +25 °C. The mixture was worked up as described in the preceding section to afford the esters **7b** and **8** (M = COOCH₃), which could readily be separated by elution from silica gel, using a 1:4 (v/v) mixture of ethyl acetate and hexanes. Hydrolysis gave **7b** and **8**. – **1,1,3,3-Tetramethylindane-5-carboxylic Acid (7b)**: M = COOH; m.p. 174–175 °C. – ¹H NMR*: δ = 7.79 (dd, *J* = 7.8, 1.6 Hz, 1 H), 7.72 (d, *J* = 1.6 Hz, 1 H), 7.27 (d, *J* = 7.8 Hz, 1 H), 1.91 (s, 2 H), 1.28 (s, 12 H). – C₁₄H₁₈O₂ (218.29): calcd. C 77.03, H 8.31; found C 76.92, H 8.25. – **1,1,3,3-Tetramethylindane-4,6-dicarboxylic Acid (8)**: M = COOH; m.p. > 250 °C. – ¹H NMR*: δ = 8.07 (d, *J* = 1.6 Hz, 1 H), 7.87 (d, *J* = 1.6 Hz, 1 H), 1.94 (s, 2 H), 1.45 (s, 6 H), 1.30 (s, 6 H). – C₁₅H₁₈O₄ (262.30): calcd. C 68.69, H 6.92; found C 68.53, H 7.22. –

The exact yields of esters were determined by gas chromatographic analysis (1 m, 5% SE-30, 90 °C; 30 m, DB-1701, 120 °C) using methyl *tert*-butylbenzoate as an internal and calibrated standard. When the hydrocarbon substrate and the basic reagents were employed in a stoichiometric 1:1:1 ratio, ester **7b** (M = COOCH₃) was obtained in 51% yield, but no diester **8** was formed at all.

1,1,2,2,3,3-Hexamethylindane as the Substrate: The reaction was performed with 1,1,2,2,3,3-hexamethylindane^[22] (2.0 g, 10 mL) exactly as described above for 1,1,3,3-tetramethylindane. The standard workup procedure (see the 1,4-di-*tert*-butylbenzene section) provided 1,1,2,2,3,3-hexamethylindane-5-carboxylic acid (**9b**) and 1,1,2,2,3,3-hexamethylindane-4,6-dicarboxylic acid (**10**). – **1,1,2,2,3,3-Hexamethylindane-5-carboxylic Acid (9b)**: M = COOH; m.p. 179–180 °C. – ¹H NMR: δ = 7.97 (d, *J* = 8.0 Hz, 1 H), 7.87 (s, 1 H), 7.22 (d, *J* = 8.0 Hz, 1 H), 1.25 (s, 6 H), 1.23 (s, 6 H), 0.89 (s, 6 H). – C₁₆H₂₂O₂ (246.35): calcd. C 78.01, H 9.00; found C 78.10, H 9.10]. – **1,1,2,2,3,3-Hexamethylindane-4,6-dicarboxylic Acid (10)**: M = COOH; m.p. > 250 °C. – ¹H NMR*: δ = 13.14 (s, broad, 2 H), 7.79 (d, *J* = 1.6 Hz, 1 H), 7.78 (d, *J* = 1.6 Hz, 1 H), 1.32 (s, 6 H), 1.21 (s, 6 H), 0.81 (s, 6 H). – C₁₇H₂₂O₄ (290.34): calcd. C 70.32, H 7.64; found C 70.12, H 7.64]. – Gas chromatographic analysis (1 m, 5% SE-30, 90 °C; 30 m, DB-1701, 120 °C, methyl *tert*-butylbenzoate as the internal standard) of the methyl esters (M = COOCH₃), identified **9b** and **10** in 3% and 26% yields, respectively, but **9b** appeared as the sole product in 52% yield if a 1:1:1 substrate/superbase mixture was used in place of one of 1:5:5.

1,3-Dihydro-1,1,3,3-tetramethylisobenzofuran as the Substrate: 1,3-Dihydro-1,1,3,3-tetramethylisobenzofuran^[23] (1.8 g, 10 mmol) was submitted to the same reaction and workup conditions as described for 1,4-di-*tert*-butylbenzene (see above). The three products found

were again characterized by their spectra and combustion analysis as 1,3-dihydro-1,1,3,3-tetramethyl-4-isobenzofurancarboxylic acid (**11a**) and 1,3-dihydro-1,1,3,3-tetramethyl-5-isobenzofurancarboxylic acid^[23] (**11b**) and 1,3-dihydro-1,1,3,3-tetramethyl-4,6-isobenzofurandicarboxylic acid (**12**). – **1,3-Dihydro-1,1,3,3-tetramethyl-4-isobenzofurancarboxylic Acid (11a)**: M = COOH; m.p. 185–187 °C. – ¹H NMR: δ = 8.07 (dd, *J* = 7.6, 1.3 Hz, 1 H), 7.41 (t, *J* = 7.5 Hz, 1 H), 7.34 (dd, *J* = 7.5, 1.3 Hz, 1 H), 1.76 (s, 6 H), 1.54 (s, 6 H). – C₁₃H₁₆O₃ (220.67): calcd. C 70.87, H 7.33; found C 70.68, H 7.12]. – **1,3-Dihydro-1,1,3,3-tetramethyl-5-isobenzofurancarboxylic Acid (11b)**:^[23] M = COOH; m.p. 202–204 °C. – ¹H NMR: δ = 8.08 (dd, *J* = 7.8, 1.2 Hz, 1 H), 7.65 (d, *J* = 1.2 Hz, 1 H), 7.26 (d, *J* = 7.8 Hz, 1 H), 1.58 (s, 6 H), 1.57 (s, 6 H)]. – **1,3-Dihydro-1,1,3,3-tetramethyl-4,6-isobenzofurandicarboxylic Acid (12)**: M = COOH; m.p. > 250 °C. – ¹H NMR*: δ = 8.34 (d, *J* = 1.5 Hz, 1 H), 7.97 (d, *J* = 1.5 Hz, 1 H), 1.62 (s, 6 H), 1.45 (s, 6 H). – C₁₅H₁₈O₄ (262.30): calcd. C 68.69, H 6.92; found C 68.53, H 7.22]. – Gas chromatography (1 m, 5% SE-30, 90 °C; 30 m, DB-1701, 120 °C; methyl *tert*-butylbenzoate as the internal standard), showed that the esters (M = COOCH₃) **11a**, **11b**, and **12** were formed in 5%, 10%, and 4% yields or in 12%, 23%, and 0% yields, respectively, depending on whether a 1:5:5 or a 1:1:1 substrate/bases stoichiometry was chosen. – When *tert*-butyllithium (1 equiv.) was used to replace butyllithium as a component of the superbasic reagent mixture, isomer **11b** was formed exclusively (52%).

2,2,6,6-Tetramethyl-1-phenylpiperidine as the Substrate: A suspension containing potassium *tert*-butoxide (10 mmol), butyllithium (10 mmol), and 2,2,6,6-tetramethyl-1-phenylpiperidine (0.43 g, 2.0 mmol; see below) in hexanes (10 mL) was vigorously stirred for 25 h at 25 °C. Methyl iodide (0.62 mL, 1.4 g, 10 mmol) in tetrahydrofuran (10 mL) was added at –75 °C. After having reached 25 °C, the mixture was filtered and its composition was examined by gas chromatography (1 m, 5% SE-30, 100 °C; 30 m, DB-1701, 120 °C; 1,4-di-*tert*-butylbenzene as an internal standard). The products were identified by comparison of their retention times with those of authentic samples (see below). 2,2,6,6-Tetramethyl-1-*p*-tolylpiperidine (**13a**: R = CH₃), 2,2,6,6-tetramethyl-1-*m*-tolylpiperidine (**13b**: R = CH₃) and 1-(3,5-dimethylphenyl)-2,2,6,6-tetramethylpiperidine (**14**: R = CH₃) were found to be present in concentrations corresponding to yields of 29%, 16%, and 28%. When a 1:1:1 substrate (2.2 g, 10 mmol)/bases (2 × 10 mmol) stoichiometry was applied and the metalation time was simultaneously shortened to 2 h (at 25 °C), the products **13a**, **13b**, and **14** were formed in 10%, 16%, and 3% yields. – **2,2,6,6-Tetramethyl-1-phenylpiperidine** was prepared by sequentially adding 2,2,6,6-tetramethylpiperidine (84 mL, 71 g, 0.50 mol) and bromobenzene (53 mL, 79 g, 0.50 mol) to butyllithium (0.50 mol) in tetrahydrofuran (0.50 L) and by keeping this solution for 25 h at 25 °C. The product was isolated by distillation; bp 115–117 °C/12 Torr; n_D²⁰ = 1.5236; 46%. – ¹H NMR: δ = 7.2 (m, 5 H), 1.7 (m, 2 H), 1.6 (m, 4 H), 1.01 (s, 12 H). – C₁₅H₂₃N (217.35): calcd. C 82.89, H 10.66; found C 83.01, H 10.55. – A 55:45 mixture of 1-(4-methylphenyl)- and 1-(3-methylphenyl)-2,2,6,6-tetramethylpiperidine (**13a** and **13b**: M = CH₃) was obtained analogously, using 4-bromotoluene (62 mL, 86 g, 0.50 mol) instead of bromobenzene; bp 123–125 °C/110 Torr; 47%. – C₁₆H₂₅N (231.38): calcd. C 83.06, H 10.89; found C 83.42, H 10.61. – **1-(3,5-Dimethylphenyl)-2,2,6,6-tetramethylpiperidine (14)**: (M = CH₃) was made by heating a mixture of 1-fluoro-3,5-dimethylbenzene (1.9 g, 15 mmol), 2,2,6,6-tetramethylpiperidine (5.0 mL, 4.2 g, 30 mmol), and sodium amide (2.3 g, 60 mmol) in hexamethylphosphorus triamide (30 mL) and tetrahydrofuran (10 mL) at 50 °C for 25 h. The product was collected by distillation; bp 93–94 °C/2 Torr; 21%. – ¹H NMR: δ = 7.21 (s, 2 H), 6.93 (s, 1 H), 2.37 (s,

6 H), 1.7 (m, 2 H), 1.6 (m, 4 H), 1.04 (s, 12 H). — $C_{17}H_{27}N$ (245.41): calcd. C 83.20, H 11.10, N 5.71; found C 83.21, H 10.79, N 6.05.

***N,N*-Bis(triethylsilyl)aniline as the Substrate:** A suspension containing potassium *tert*-butoxide (3.4 g, 30 mmol), butyllithium (30 mmol), and *N,N*-bis(trimethylsilyl)aniline (3.2 g, 10 mmol; see below) in hexanes (20 mL) was vigorously stirred for 2 h at 25 °C. Methyl iodide (1.9 mL, 4.3 g, 30 mmol) in tetrahydrofuran (20 mL) and a known amount (approx. 0.5 g) of octadecane (as an internal reference compound) were added at –75 °C. When it had warmed up to 25 °C, the mixture was washed with brine (5×10 mL) and analyzed by gas chromatography (30 m, DB-FFAP, 130 °C; 30 m, DB-1701, 165 °C). The new products **15a** ($M = CH_3$, 36%), **15b** ($M = CH_3$, 4%), and **16** ($M = CH_3$, 41%) were identified by comparison of their retention times with those of authentic samples (see below). When a 1:1:1 substrate stoichiometry (9.6 g, 30 mmol)/bases (2×30 mmol) was observed, the yields of **15a**, **15b**, and **16** were 24%, 36%, and 2%, respectively. — ***N,N*-Bis(triethylsilyl)aniline:** The compound was prepared by sequential addition, at –75 °C, of aniline (9.1 mL, 9.8 g, 0.10 mol) and chlorotriethylsilane (17 mL, 15 g, 0.10 mol) to butyllithium (0.10 mol) in tetrahydrofuran (0.20 L) and hexanes (60 mL). After 1 h at 25 °C, the mixture was cooled to –75 °C and again treated sequentially with butyllithium (0.10 mol) in hexanes (60 mL) and chlorotriethylsilane (17 mL, 15 g, 0.10 mol) before being allowed to stand overnight (18 h) at 25 °C. The fine precipitate was removed by filtration with suction through a pad of kieselguhr and the solvents were evaporated. Distillation of the residue under reduced pressure afforded a colorless liquid; bp 109–111 °C/0.5 Torr; $n_D^{20} = 1.5075$; 18 g (57%). — 1H NMR: $\delta = 7.17$ (t, $J = 7.9$ Hz, 2 H), 7.03 (t, $J = 7.7$ Hz, 1 H), 6.9 (m, 2 H), 0.89 (t, $J = 7.9$ Hz, 18 H), 0.54 (q, $J = 7.9$ Hz, 12 H). — $C_{18}H_{35}NSi_2$ (321.66): calcd. C 67.21, H 10.97; found C 67.14, H 10.82. — The same procedure was used to obtain **15a**, **15b** and **16**. — ***N,N*-Bis(triethylsilyl)-*p*-toluidine (**15a**):** ($M = CH_3$); bp 130–135 °C/0.3 Torr; $n_D^{20} = 1.5122$; 28 g (84%). — 1H NMR: $\delta = 7.00$ (d, $J = 8.0$ Hz, 2 H), 6.86 (d, $J = 8.0$ Hz, 2 H), 2.31 (s, 3 H), 0.92 (t, $J = 7.8$ Hz, 12 H), 0.55 (q, $J = 7.8$ Hz, 18 H). — $C_{19}H_{37}NSi_2$ (335.68): calcd. C 67.98, H 11.11; found C 67.59, H 11.14]. — ***N,N*-Bis(triethylsilyl)-*m*-toluidine (**15b**):** ($M = CH_3$); bp 148–150 °C/0.3 Torr; $n_D^{20} = 1.5850$; 27 g (84%). — 1H NMR: $\delta = 7.05$ (t, $J = 7.5$ Hz, 1 H), 6.85 (d, $J = 7.5$ Hz, 1 H), 6.76 (s, 1 H), 6.75 (d, $J = 7.2$ Hz, 1 H), 2.27 (s, 3 H), 0.89, (t, $J = 7.9$ Hz, 18 H), 0.52 (q, $J = 7.9$ Hz, 12 H). — $C_{19}H_{37}NSi_2$ (335.68): calcd. C 67.98, H 11.11; found C 68.03, H 11.25]. — ***N,N*-Bis(triethylsilyl)-3,5-dimethylaniline (**16**):** ($M = CH_3$); bp 130–137 °C/0.5 Torr; $n_D^{20} = 1.5061$; 23 g (66%). — 1H NMR: $\delta = 6.69$ (s, 1 H), 6.58 (s, 2 H), 2.25 (s, 6 H), 0.91 (t, $J = 7.8$ Hz, 18 H), 0.54 (q, $J = 7.8$ Hz,

12 H). — $C_{20}H_{39}NSi_2$ (349.70): calcd. C 68.69, H 11.24; found C 68.52, H 11.31].

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