

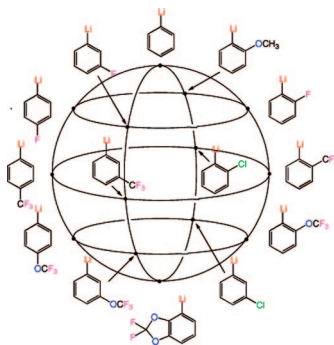
Relative Basicities of *ortho*-, *meta*-, and *para*-Substituted Aryllithiums

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The relative basicities of aryllithiums bearing methoxy, chlorine, fluorine, trifluoromethyl and trifluoromethoxy substituents at the *ortho*, *meta*, and *para* positions have been assessed. To this end, two aryllithiums of comparable basicity were equilibrated together with the corresponding bromo- or iodoarenes in a 1: 2 mixture of pentanes with tetrahydrofuran at -50 , -75 , or -100 °C. The “basicity” (protodelithiation) increments $\Delta\Delta G$ derived from the equilibrium constants are linearly correlated with the relative protonation enthalpies of the corresponding aryl anions in the gas phase. However, the correlation factor proves to be position-dependent. Compared with “naked” aryl anions, the basicity of aryllithiums mirrors the effects of *ortho*, *meta*, and *para* substituents to the extent of 36%, 30%, and 25%, respectively.

Introduction

An amazingly good free energy relationship was found to exist between the gas-phase acidity of fluorobenzene, the three difluoro-, three trifluoro-, and three tetrafluorobenzenes, and pentafluorobenzene on the one hand and their rates of metalation by *sec*-butyllithium in tetrahydrofuran at -75 ¹ or -100 °C² on the other hand. The same relationship holds between the gas-phase acidity of oligochlorobenzenes and their reactivity toward *sec*-butyllithium at -100 °C.³ Obviously, the stabilization resulting from electrostatic and polarizing interactions with the substituents is proportional at the level of the “naked” haloaryl anions and of the transition states that mediate the countercurrent transfer of a proton and the metal, although the kinetics (i.e., the free energies of activation) mirror the thermodynamics (i.e.,

the relative basicities of the benzenides corresponding to the haloaryllithiums generated) only to the extent of approximately 12%.^{2,3}

The free energy relationship between gas-phase acidities and reactivities toward metalation reactivities within the oligofluorobenzene and oligochlorobenzene series was by no means foreseeable. It would be unreasonable to expect such a relationship to cover also the comparison between substituted arenes that belong to different structural families. In fact, although fluorobenzene is slightly less acidic than chlorobenzene in the gas phase,⁴ the former substrate reacts in tetrahydrofuran 7.9 times more rapidly with *sec*-butyllithium at -100 °C and more than 20 times more rapidly with lithium 2,2,6-tetramethylpiperidide (LITMP).^{2,3} More generally speaking, there is no simple

(1) Büker, H. H.; Nibbering, N. M. M.; Espinosa, D.; Mongin, F.; Schlosser, M. *Tetrahedron Lett.* **1997**, *38*, 8519–8522.


(2) Schlosser, M.; Marzi, E. *Chem. Eur. J.* **2005**, *11*, 3449–3454.

(3) Schlosser, M.; Marzi, E.; Cottet, F.; Büker, H. H.; Nibbering, N. M. M. *Chem. Eur. J.* **2001**, *7*, 3511–3516.

(4) Andrade, P. B. M.; Riveros, J. M. *J. Mass Spectrom.* **1996**, *31*, 767–770; *Chem. Abstr.* **1996**, *125*, 247111.

(5) Davico, G. E.; Bierbaum, V. M.; DePuy, C. H.; Ellison, C. B.; Squires, R. R. *J. Am. Chem. Soc.* **1995**, *117*, 2590–2599.

TABLE 1. Absolute (ΔH_g) and Relative ($\Delta\Delta H_g$) Deprotonation Enthalpies (in Parentheses) of Heterosubstituted Benzenes and Their Statistically Corrected Rates (k_{rel}) of *sec*-Butyllithium Promoted Metalation Relative to Benzene

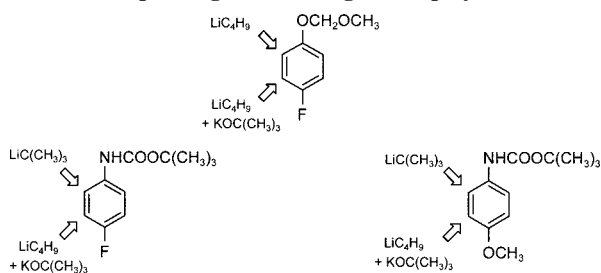
	ΔH_g	$\Delta\Delta H_g$	k_{rel}
X = H	402 ^a	0	1×10^0 ^b
X = CF ₃	389 ^c	-13	6×10^2 ^d
X = OCH ₃	393 ^{e,f}	-9	3×10^3 ^{d,g}
X = Cl	387 ^h	-15	1×10^4 ^h
X = OCF ₃	385 ⁱ	-17	3×10^4 ^j
X = F	387 ^h	-15	7×10^4 ^{d,k}

^a Reference 5. ^b This number is considerably error-afflicted. ^c Computed at an MP2 level of theory: 378 kcal/mol relative to 391 for benzene. ^d Reference 1. ^e Computed at an MP2 level of theory: 390.8 kcal/mol relative to 399.8 for benzene. ^f See also the experimental data of 391 kcal/mol rel. to the identical value of water. ^g See also ref 9. ^h Reference 3. ⁱ Computed at an MP2 level of theory: 383.2 kcal/mol relative to 399.8 for benzene. ^j Reference 10. ^k See also refs 3 and 10.

correlation between the thermodynamic acidity of a substituted benzene and its rate of metalation (Table 1).

This lack of agreement between thermodynamic and kinetic acidities was to be expected. In this context it suffices to recall the influence of the reagent on the regioselectivity of metalation. The optional attack of the organometallic base at a site adjacent to the more electronegative or the better coordinating substituent in *O*-methoxymethoxy protected 4-fluorophenol and the *N*-*tert*-butoxycarbonyl protected 4-fluoroaniline and 4-anisidine (4-methoxyaniline) offers a striking illustration of this fact (Scheme 1).^{11,12}

SCHEME 1. Optionally Site-Selective Metalation of *O*- or *N*-Protected 4-Fluorophenol, 4-Fluoroaniline, and 4-Anisidine Depending on the Reagent Employed



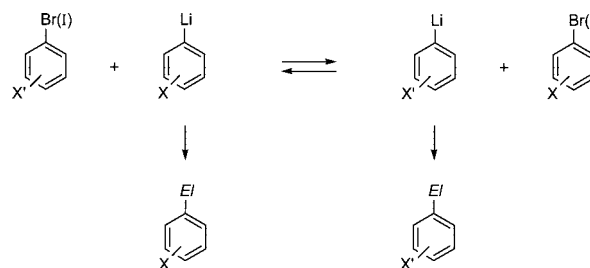
Thus one definitively cannot expect to find any far reaching interdependence of the gas-phase acidity of electronegatively substituted arenes and the rates with which they react with organometallic bases. However, a correlation may be possible between the relative stabilities (basicities) of the naked carban-

ions and the corresponding aryllithiums (generated by metalation of the aromatic substrates) as this time only ground-state species are compared with each other. We decided to embark on such a study.

Results

The acid–base equilibration involving two simple arenes and the corresponding aryllithiums is not feasible. The *ortho*-lithiation of anisole by phenyllithium requires long reaction times at 100 °C,¹³ in other words, conditions causing extensive decomposition of the reagent by solvent attack. The “uphill” reverse reaction between benzene and 2-anisyllithium would be even a hundred to a thousand times slower. Moreover, no *meta*- or *para*-substituted aryllithiums would become accessible by this transmetalation method. To assess the relative basicities of typical aryllithiums, we have therefore established the equilibrium between selected pairs of aryllithiums and the corresponding bromo- or iodoarenes by permutational halogen/metal interconversion (Scheme 2). If we assume the aryl-Br and

SCHEME 2. Assessment of Relative Aryllithium Basicities^a



^a By their halogen/metal permutational equilibration with the corresponding bromo- or iodoarenes followed by trapping with a suitable electrophile *EI* (e.g., *EI* = I).

aryl-I bond strengths to be substituent-invariant, the equilibrium constants can be directly translated into differential basicities (i.e., thermodynamic stabilities). The postulated approximate stability invariance of bromoarenes and iodoarenes is arguable. Although at variance with some experimental findings,¹⁴ a DFT study¹⁵ has revealed *o*-dihalobenzenes to be significantly less stable (up to 2.6 kcal/mol in typical cases) than their *meta*- and *para*-isomers. On the other hand, if the energies of all of our *ortho*-substituted bromoarenes and iodoarenes were raised to some extent, the relative aryllithium stabilities would be only marginally affected. In view of other ambiguities, we consider an error of ± 1 kcal/mol to be tolerable for any *o*-aryllithium data and likewise ± 0.5 kcal/mol for *m*- and *p*-aryllithiums.

The equilibrations were carried out in tetrahydrofuran or diethyl ether at -50 , -75 , or -100 °C approaching from both sides the final mixture of four components. Analogous equilibration reactions have been reported previously.^{16,17} However, they cover not more than a total of three examples and are numerically unreliable as a result of inadequate reaction conditions and analytical procedures.

(6) Schlosser, M.; Mongin, F.; Porwisiak, J.; Dmowski, W.; Bükler, H. H.; Nibbering, N. M. M. *Chem. Eur. J.* **1998**, *7*, 1281–1286.

(7) Kovačević, B.; Maksić, Z. B.; Primorac, M. *Eur. J. Org. Chem.* **2003**, 3777–3783.

(8) Dahlke, G. D.; Kass, S. R. *Int. J. Mass Spectrom. Ion Proc.* **1992**, *117*, 633–645.

(9) Maggi, R.; Schlosser, M. *Tetrahedron Lett.* **1999**, *40*, 8797–8800.

(10) Castagnetti, E.; Schlosser, M. *Chem. Eur. J.* **2002**, *8*, 799–804.

(11) Mongin, F.; Maggi, R.; Schlosser, M. *Chimia* **1996**, *50*, 650–652.

(12) Marzi, E.; Mongin, F.; Spitaleri, A.; Schlosser, M. *Eur. J. Org. Chem.* **2001**, 2911–2915.

(13) Wittig, G.; Pockels, U.; Dröge, H. *Ber. Dtsch. Chem. Ges.* **1938**, *71*, 1903–1912.

(14) (a) Hubbard, W. N.; Knowlton, J. W.; Huffman, H. M. *J. Phys. Chem.* **1954**, *58*, 396–402. (b) Platonov, V. A.; Simulin, Y. N. *Zh. Fiz. Khim.* **1984**, *58*, 2682–2686; *Russ. J. Phys. Chem. (Engl. Transl.)* **1984**, *58*, 1630–1632; *Chem. Abstr.* **1985**, *102*, 33733.

(15) Taskinen, E. *Struct. Chem.* **2000**, *11*, 293–301; *Chem. Abstr.* **2000**, *134*, 41897.

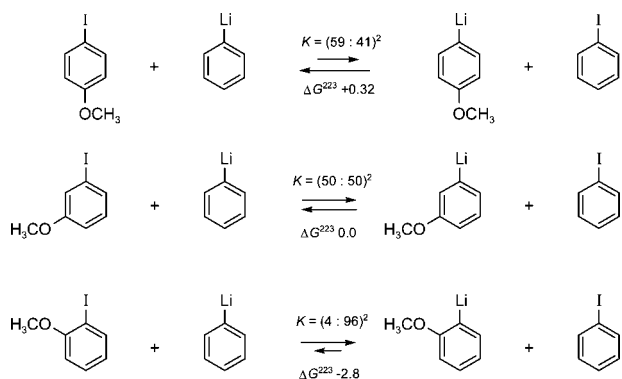
(16) Gilman, H.; Jones, R. G. *J. Am. Chem. Soc.* **1941**, *63*, 1441–1443.

(17) Winkler, H. J. S.; Winkler, H. J. *Am. Chem. Soc.* **1966**, *88*, 964–969.

The concentrations of the bromo- or iodoarenes were quantified by gas chromatography using a calibrated internal standard. In the same way the amounts of products derived from the aryllithium intermediates by electrophilic trapping (using molecular iodine if the exchange partners were bromoarenes and 1,2-dibromotetrafluoroethane if they were iodoarenes; see Experimental Section) were determined. The two sets of data have to be complementary to be meaningful. In concrete terms, if two aryllithiums were found to coexist in a 90:10 ratio, the corresponding bromoarene or iodoarene permutation partners (introduced in equimolar quantities) have to be present in a 10:90 ratio, and consequently the equilibrium constant K amounts to 81. Such an ideal component balance ordinarily prevailed. Noticeable deviations were encountered when 2-chlorophenyllithium was involved. This intermediate tends to slowly undergo lithium chloride elimination accompanied by aryne formation even at $-100\text{ }^{\circ}\text{C}$.

We started our work by juxtaposing phenyllithium to each of the three isomeric anisyllithiums (Scheme 3). The intercon-

SCHEME 3. Halogen/Metal Permutational Equilibration of 2-, 3-, and 4-Anisyllithium with Phenyllithium

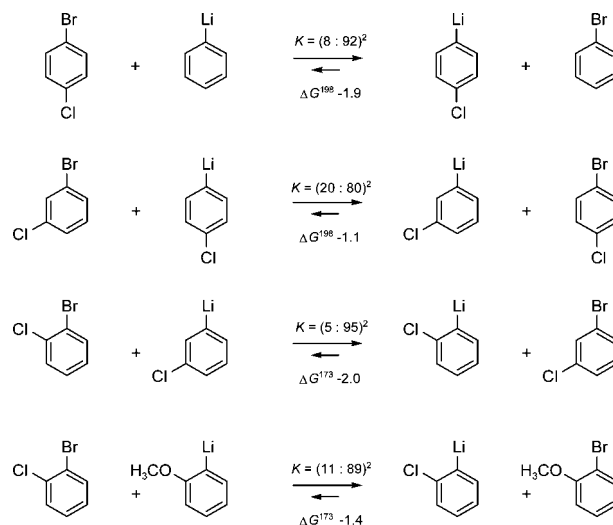


version with the corresponding iodoarenes proceeded in tetrahydrofuran even at $-50\text{ }^{\circ}\text{C}$ fairly slowly, equilibrium being attained after 2–30 h. The basicities of the organometallic species involved being not too different, it was possible to determine all equilibrium constants K (see preceding paragraph) and, as a corollary, the relative protodelithiation free energies $\Delta\Delta G$ (in kcal/mol) with sufficient accuracy. The introduction of a methoxy group into a *meta* position of phenyllithium was found to have virtually no effect on the basicity. In contrast it destabilizes the aryllithium when attached to the *para* position and stabilizes it considerably when located at an *ortho* position.

Next we turned to the chlorophenyllithiums. Whereas the equilibrium position of the 4-isomer relative to phenyllithium could be readily probed, the 2- and 3-isomers proved to be too much stabilized to coexist with phenyllithium any more. Therefore, 3-chlorophenyllithium was compared with 4-chlorophenyllithium, and 2-chlorophenyllithium was examined in competition with both 3-chlorophenyllithium and 2-anisyllithium (Scheme 4).

As mentioned above, the chloroarene data are less reliable than all others because of β -elimination of lithium chloride occurring to a minor extent even at $-100\text{ }^{\circ}\text{C}$. The two last equilibria (in Scheme 4) enable us to check on the accuracy of our approach. If the basicity of 2-chlorophenyllithium relative to phenyllithium is evaluated using 3- and 4-chlorophenyllithium as relay species, one counts a difference of $2.0 + 1.1 + 1.9 = 5.0$ kcal/mol. This number shrinks to $4.2 (= 2.8 + 1.4)$ kcal/

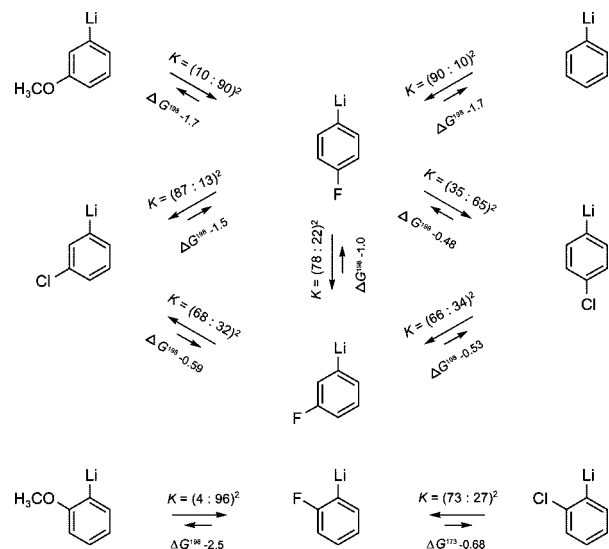
SCHEME 4. Halogen/Metal Permutational Equilibration of 4-, 3-, and 2-Chlorophenyllithium with Phenyllithium, Other Chlorophenyllithiums, or 2-Anisyllithium



mol if the gap between 2-chlorophenyllithium and phenyllithium is bridged by 2-anisyllithium. Assuming the latter number to be more reliable, we assign 4.4 kcal/mol as a nonarithmetic average value. Such bona fide adjustments were made in all following cases where a direct equilibration with phenyllithium was not possible. For clarity, the bromoarenes and iodoarenes exchange partners are omitted from the equilibration schemes shown below.

The interconversion of 4-fluorophenyllithium with phenyllithium, 3-anisyllithium, and 3- and 4-chlorophenyllithium gave coinciding relative basicities of -1.5 to -1.7 , i.e., on average 1.6 kcal/mol (Scheme 5). Upon equilibration with 3-fluorophe-

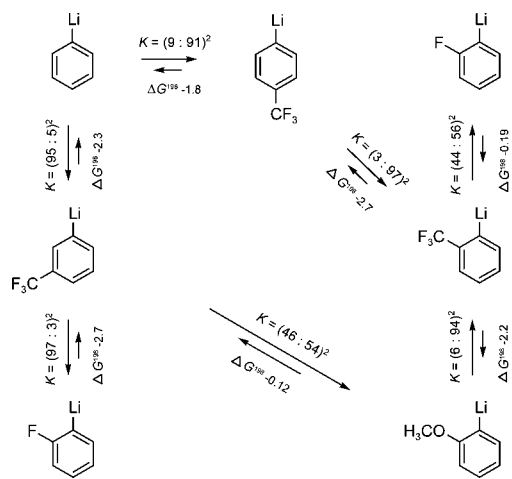
SCHEME 5. Relative Basicities of 4-, 3-, and 2-Fluorophenyllithium As Revealed by Halogen/Metal Permutational Equilibrations



nyllithium, the latter was found to be 1.0 kcal/mol more stable. Together with the permutation data involving 3- and 4-chlorophenyllithium, the averaged relative basicity of -2.5 kcal/mol was deduced (Scheme 5). Finally, when 2-fluorophenyllithium was assessed relative to 3-methoxyphenyllithium and 3-chlorophenyllithium, the same value of -5.3 kcal/mol resulted (Scheme 5).

The assessment of the relative basicities of the (trifluoromethyl)phenyllithium isomers also allowed for experimental redundancy as a control and check on the accuracy of the equilibration method. The comparison of 3-(trifluoromethyl)phenyllithium with phenyllithium, 2-anisyllithium, 2-fluorophenyllithium, and 4-(trifluoromethyl)phenyllithium (at -1.8 kcal/mol) gave a median value of -2.4 kcal/mol (Scheme 6).

SCHEME 6. Relative Basicities of 4-, 3-, and 2-(Trifluoromethyl)phenyllithium As Revealed by Halogen/Metal Permutational Equilibrations



According to the data collected with 2-anisyllithium, 2-fluorophenyllithium, and 4-(trifluoromethyl)phenyllithium, 2-(trifluoromethyl)phenyllithium was placed at -5.0 kcal/mol on the basicity scale (Scheme 6).

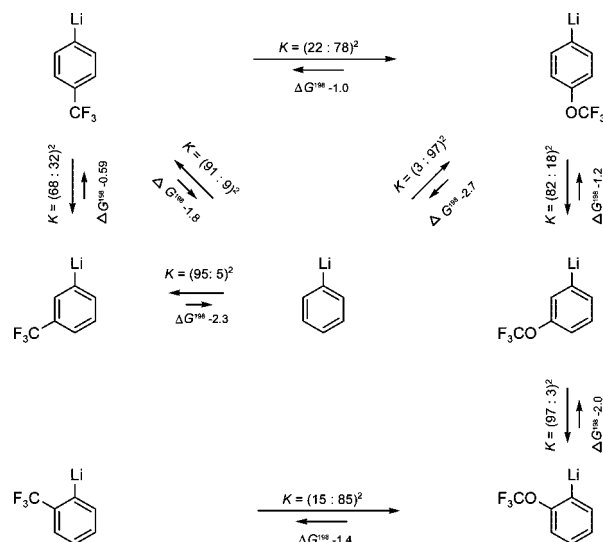
The “exotic” trifluoromethoxy substituent attracts more and more curiosity.¹⁸ Quantum chemical calculations⁷ have ranked it, as far as its acidifying effect is concerned, on the top of all substituents having no double bonds. For this reason we deemed it indispensable to include it into the present investigation. 2-, 3-, and 4-(Trifluoromethoxy)phenyllithium were found to be indeed less basic than any of the other *ortho*-, *meta*-, and *para*-substituted species investigated by us so far (Scheme 7). Thus, 4-(trifluoromethoxy)phenyllithium exhibited a relative basicity of -2.8 kcal/mol. In the same way, 3- and 2-(trifluoromethoxy)phenyllithium proved to be clearly less basic than 3- and 2-(trifluoromethyl)phenyllithium, relative basicity increments of -4.0 and -6.0 kcal/mol being assigned.

We have drawn attention to the exceptional acidity of 2,2-difluoro-1,3-benzodioxole already on previous occasions and have demonstrated how this property can be advantageously exploited for synthetic purposes.^{10,19–22} This heterocyclic unit sets indeed a new record mark ($\Delta\Delta G = -8.7$ kcal/mol) as the lithiated species is still 2.5 kcal/mol less basic than 2-(trifluoromethoxy)phenyllithium (Scheme 8).

Discussion

The differences in the basicities of the substituted aryllithiums relative to phenyllithium are listed together with the gas-phase

SCHEME 7. Relative Basicities of 4-, 3-, and 2-(Trifluoromethoxy)phenyllithium As Revealed by Halogen/Metal Permutational Equilibrations



SCHEME 8. Basicity of 4-(2,2-Difluoro-1,3-benzodioxolyl)lithium Relative to 2-(Trifluoromethoxy)phenyllithium

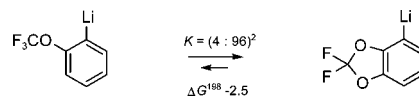


TABLE 2. Increments $\Delta\Delta G$ Quantifying the Proton Affinity of *para*-, *meta*-, and *ortho*-Substituted Aryllithiums^a

substituent	at the <i>para</i> position	at the <i>meta</i> position	at the <i>ortho</i> position
H ₃ CO	+0.3 (+0.2)	0.0 (−1.6)	−2.7 (−9.4)
F	−1.6 (−4.3)	−2.6 (−6.5)	−5.1 (−12.7)
Cl	−1.9 (−7.6)	−3.0 (−9.8)	−4.4 (−14.5)
F ₃ C	−1.8 (−11.3)	−2.4 (−11.0)	−4.6 (−13.9)
F ₃ CO	−2.8 (−9.8)	−4.0 (−11.1)	−6.0 (−17.1)

^a Present work. In tetrahydrofuran solution, relative to that of phenyllithium and, in parentheses, differential protonation enthalpies $\Delta\Delta H_g$ of the corresponding aryl anions,^{7,23} in the gas phase, relative to the parent benzenide (phenyl) ion. All numbers are given in kcal/mol.

protonation enthalpies of the corresponding aryl anions (Table 2). In the case of aryl anions, we quote computational (ab initio⁷ and density functional²³) rather than experimental protonation data as the latter are not always available, at least not with the required reliability.

A comparison of enthalpies with free energies is acceptable in the given case. The ΔH values of deprotonation in the gas phase exceed the corresponding ΔG values by an almost constant factor of 8 kcal/mol (representing the entropy change due to proton detachment and the change in rotational symmetry).⁶ The equilibrium entropy in solution is assumed to be small as substituent effects on the aggregation and solvation of the examined aryllithium should be minute.

The aryllithium basicity increments $\Delta\Delta G$ were plotted separately for the *para*-, *meta*-, and *ortho*-substituted species against the protonation enthalpies ΔH_g of the corresponding naked aryl anions in the gas phase. In all three regioisomeric

(18) Leroux, F.; Jeschke, P.; Schlosser, M. *Chem. Rev.* **2005**, *105*, 827–856.

(19) Castagnetti, E.; Schlosser, M. *Eur. J. Org. Chem.* **2001**, 691–695.

(20) Schlosser, M.; Gorecka, J.; Castagnetti, E. *Eur. J. Org. Chem.* **2003**, 452–462.

(21) Gorecka, J.; Leroux, F.; Schlosser, M. *Eur. J. Org. Chem.* **2004**, 64–68.

(22) Leroux, F.; Gorecka, J.; Schlosser, M. *Synthesis* **2004**, 326–328.

(23) Hyla-Kryspin, I.; Grimme, S.; Büker, H. H.; Nibbering, N. M. M.; Cottel, F.; Schlosser, M. *Chem. Eur. J.* **2005**, *11*, 1251–1256.

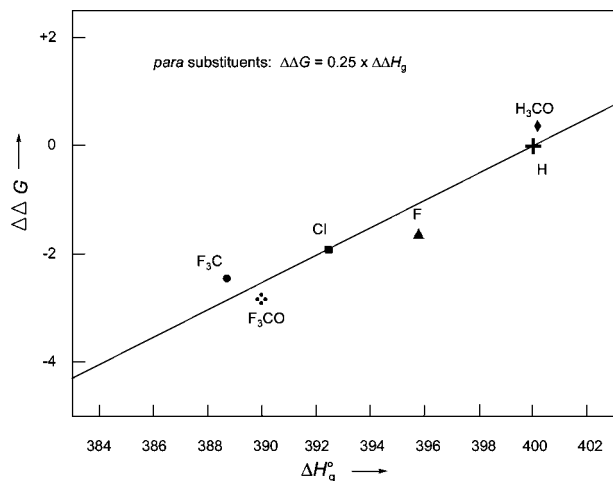


FIGURE 1. *para*-Substituted aryllithiums: their exchange-monitored basicities relative to phenyllithium plotted against the protonation enthalpies ΔH_g^o of the corresponding aryl anions in the gas phase (all numbers being given in kcal/mol).

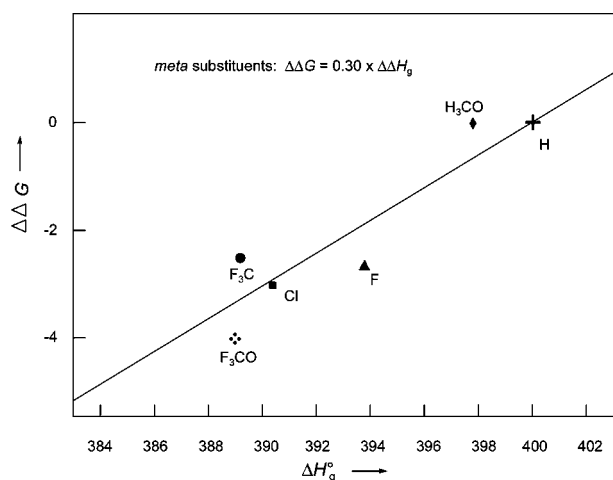


FIGURE 2. *meta*-Substituted aryllithiums: their exchange-monitored basicities relative to phenyllithium plotted against the protonation enthalpies ΔH_g^o of the corresponding aryl anions in the gas phase (all numbers being given in kcal/mol).

series, the points were reasonably well accommodated by straight lines having slopes of 0.25, 0.30, and 0.36 with correlation coefficients R of 0.93, 0.90, and 0.86, respectively (Figures 1–3). The quasi-coincidence of our increments for *p*-, *m*-, and *o*-fluorine (−1.6, −2.6, −5.1) and *p*-, *m*-, and *o*-chlorine (−1.9, −3.0, −4.4) substitution with those derived by Streitwieser et al.²⁴ from polyhalophenylcesium equilibrium basicities (F −1.4, −3.0, −5.2; Cl −2.1, −2.7, −4.2) is noteworthy.

The linear correlation established between gas phase anion and solution organolithium basicities are unprecedented and unpredicted. The relatively moderate deviations from linearity, in particular regarding fluoro and methoxy substituents in the *meta* and *ortho* series, may, but must not, be meaningful. Possibly they merely reflect numerical errors made in the kinetic determination of the $\Delta\Delta G$ increments (estimated as ± 0.2 kcal/mol) or the computation of gas-phase protonation enthalpies ΔH_g^o (probably exceeding 1.0 kcal/mol).

The linear relationship found between aryl anions and *ortho*-substituted aryllithiums rules out any intramolecular coordina-

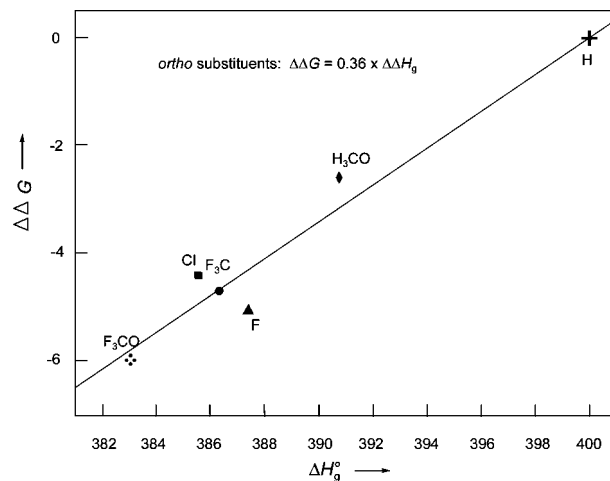
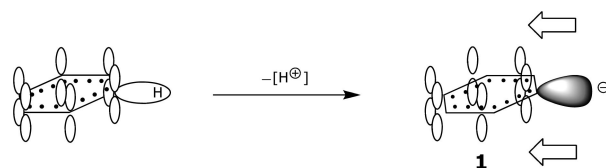


FIGURE 3. *ortho*-Substituted aryllithiums: their exchange-monitored basicities relative to phenyllithium plotted against the protonation enthalpies ΔH_g^o of the corresponding aryl anions in the gas phase (all numbers being given in kcal/mol).

tion of the metal with the heteroelements oxygen, fluorine, or chlorine in solution. This conclusion does not hold for gas-phase structures or transition states (unless independent evidence²⁵ becomes available). Even in solution a different ground-state behavior may be encountered when flexible electron-donor substituents such as dimethylaminomethyl^{26,27} are examined.

The substituent effects are substantially attenuated when one moves from the naked anions to aryllithiums in solution, and more intriguingly, the degree of this attenuation is position-dependent. The differences in the slopes of 0.25, 0.30, and 0.36 (Figures 1–3) cannot be attributed alone to a field effect as purely electrostatic interactions would level off with a higher exponential power of the distance. To rationalize the findings we proceed stepwise. We start with a working hypothesis that will be tested and refined in future investigations. How is the electron density distribution in a benzene molecule perturbed upon proton abstraction? Having lost its second binding partner, the lone pair will come closer to the sole remaining one, the *ipso*-carbon atom of the benzenide ion (**1**), and expand spherically. To minimize electron–electron repulsion, the neighboring σ -bonds become polarized by accumulating electron density at the vicinal carbon atoms (C-2 and C-6) and by depleting the negatively charged center (C-1). At the same time σ – π coupling^{3,10,28} causes the π -electron cloud to drift away from C-1 and move toward C-4.

SCHEME 9. Electronic Reorganization upon Deprotonation of Benzene



An electron-withdrawing substituent X placed at the *ortho* position will accentuate the *through-bond* σ -polarization (of the C-1/C-2 and C-2/C- X bonds) and also attract the electron excess

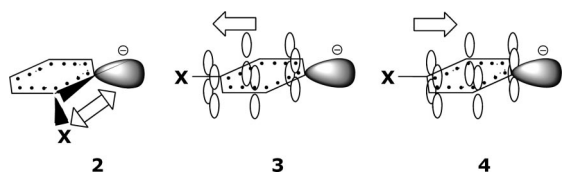
(25) Chadwick, S. T.; Rennels, R. A.; Rutherford, J. L.; Collum, D. B. *J. Am. Chem. Soc.* **2000**, *122*, 8640–8647.

(26) Jones, F. N.; Vaulx, R. L.; Hauser, C. R. *J. Org. Chem.* **1963**, *28*, 3461–3465.

(24) Stratakis, M.; Wang, P. G.; Streitwieser, A. *J. Org. Chem.* **1996**, *61*, 3145–3150.

at C-1 through space by its effective nuclear charge. Thus, the substituent exerts simultaneously σ -inductive and field effects, both of them stabilizing the carbanion (2). Analogously the same happens between the negatively charged center and an electron-donating substituent, although this time both effects are destabilizing. Such electrostatic effects level off with distance and should vanish for substituents accommodated at the *para* position. However, the location of the π -cloud, little affected by an *ortho* substituent, must respond very sensitively to *para* substituents irrespective of whether they act as electron acceptors (3) or donors (4). Finally, *meta* substituents should exhibit a blend of σ -inductive, field, and π -polarizing effect if all of them are in weakened form (Scheme 10).

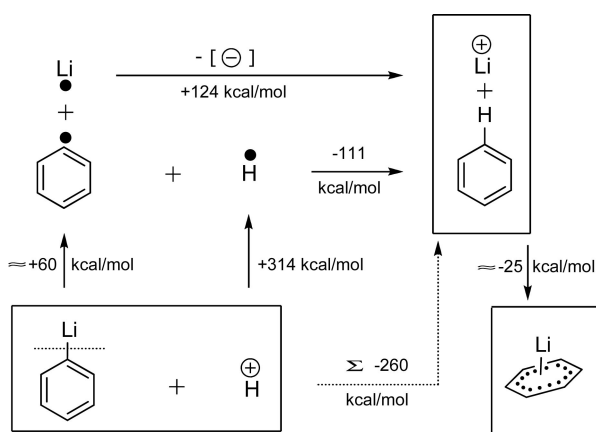
SCHEME 10. σ -Polarization by *ortho* Substituents X and π -Polarization by *para* Substituents X



Combining benzenide (the phenyl anion) with a lithium cation will attenuate the electron excess of the original carbanion to a considerable extent. This must weaken the σ -coupled π -drift significantly. As a consequence, the stabilizing or destabilizing effect of *para* substituents shrinks to 25% of the value established for the metal-free (naked) anions. Qualitatively the same is encountered with *meta* and *ortho* substituents. Their stabilizing effects on the aryllithiums decrease to, respectively, 30% and 36% of the carbanion numbers.

In this context one may feel tempted to ask how closely phenyllithium resembles the phenyl anion as far as their basicity is concerned. A crude guess can be based on a thermochemical cycle that leads to an estimate of the protodelithiation enthalpy of phenyllithium in the gas phase (Scheme 11). Making the plausible^{29–33} assumption that the C–Li bond strength (ho-

SCHEME 11. “Carbanion-Like” Nature of Phenyllithium



molytic dissociation energy) approximates 60 kcal/mol, the protolysis of phenyllithium should be exothermic by some 240

- (27) Klein, K. P.; Hauser, C. R. *J. Org. Chem.* **1967**, *32*, 1479–1483.
 (28) Schlosser, M.; Ginanneschi, A.; Leroux, F. *Eur. J. Org. Chem.* **2006**, 2956–2969.
 (29) Fowell, P. A.; Mortimer, C. T. *J. Chem. Soc.* **1961**, 3793–3796.
 (30) Holm, T. *J. Organomet. Chem.* **1974**, *77*, 27–30.
 (31) Klumpp, G. W. *Recl. Trav. Chim. Pays-Bas* **1986**, *105*, 1–21.
 (32) Arnett, E. M.; Moe, K. D. *J. Am. Chem. Soc.* **1991**, *113*, 7068–7069.

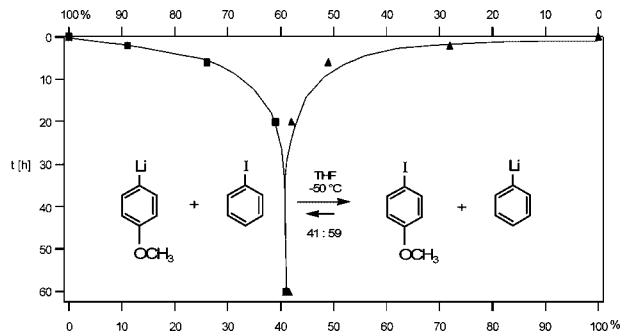


FIGURE 4. Equilibration between *p*-anisyllithium and phenyllithium by halogen/metal permutation with the corresponding iodoarenes.

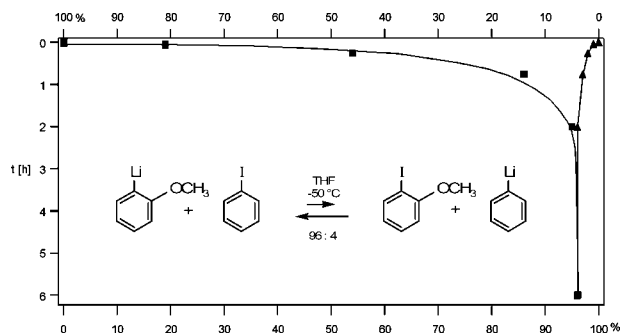


FIGURE 5. Equilibration between *o*-anisyllithium and phenyllithium by halogen/metal permutation with the corresponding iodoarenes.

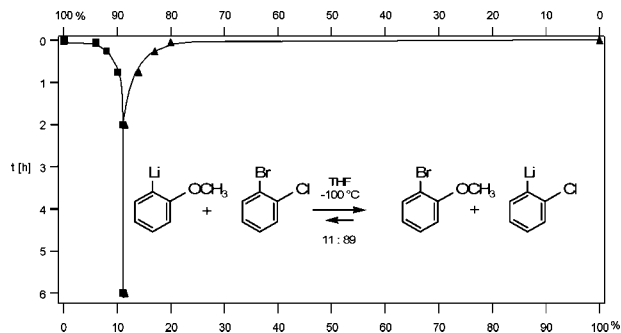


FIGURE 6. Equilibration between *o*-anisyllithium and *o*-chlorophenyllithium by halogen/metal permutation with the corresponding bromoarenes.

or even 260 kcal/mol, if the lithium cation set free combines with the benzene formed to afford a π -arene complex.^{34–36} These numbers correspond to 60% or 65% of the protonation enthalpy of the naked phenyl anion.

The basicity of phenyllithium will be further lowered in the condensed phase where aggregation and solvation provide extra stability. Our rule-of-thumb according to which organolithiums retain roughly 40% of carbanion character thus seems to match reality fairly well.³⁷

(33) van Eikema Hommes, N. J. R.; Schleyer, P. V. R. *Angew. Chem.* **1992**, *104*, 768–771; *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 755–758.

(34) Woodin, R. L.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1978**, *100*, 501–508.

(35) Kaufmann, L.; Vitze, H.; Bolte, M.; Lerner, H.-W.; Wagner, M. *Organometallics* **2007**, *26*, 1771–1776.

(36) Rodgers, M. T.; Armentrout, P. B. *Int. J. Mass Spectrom.* **2007**, *267*, 167–182.

(37) Schlosser, M. In *Organometallics in Synthesis: A Manual*, 2nd ed.; Schlosser, M., Ed.; Wiley: Chichester, 2002; pp 1–352; spec. 47–49.

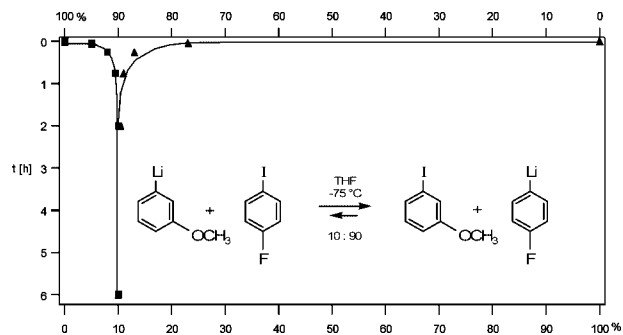


FIGURE 7. Equilibration between *m*-anisyllithium and *p*-fluorophenyllithium by halogen/metal permutation with the corresponding iodoarenes.

Experimental Section

Generalities. Solutions of *tert*-butyllithium in pentanes (1.7 M) were supplied by Chemetall (D-60487 Frankfurt, Germany). Air- and moisture-sensitive materials were stored in Schlenk tubes or Schlenk burettes. They were protected by and handled under an atmosphere of 99.995% pure nitrogen, using appropriate glassware (Glasergerätebau Pfeifer, D-98711 Frauenwald, Germany). Diethyl ether and tetrahydrofuran were dried by distillation from sodium wire after the characteristic blue color of in situ generated sodium biphenyl ketyl (benzophenone-sodium “radical-anion”) had been found to persist. The temperature of dry ice/methanol baths is consistently indicated as $-75\text{ }^{\circ}\text{C}$. Further details concerning experimental routine can be found in previous reports from this laboratory.^{2,3,8–40}

Starting Materials and Products. All isomers of methoxy-, chloro-, fluoro-, trifluoromethyl-, or trifluoromethoxy-substituted bromobenzenes and iodobenzenes are commercial (Acros Organics, B-2440 Geel, Aldrich-Fluka, CH-9479 Buchs, and Apollo Scientific, Stockport UK-SK6 2QR). The same holds for 4-bromo-2,2-difluoro-1,3-benzodioxole, whereas the 4-iodo analog had to be prepared according to a literature procedure.^{20,21}

Equilibration Experiments. At -50 , -75 , or $-100\text{ }^{\circ}\text{C}$, *tert*-butyllithium in pentanes (5.9 mL, 1.7 M, 10 mmol) was added to a solution of a brominated substrate (5.0 mmol) in tetrahydrofuran (10 mL). After 45 min, a solution of the second brominated substrate (5.0 mmol) and biphenyl (approximately 0.3 g, 2 mmol), as an “internal standard” for gas chromatographic quantification, in tetrahydrofuran (4.0 mL) was added to the reaction mixture. Aliquots (of approximately 2.0 mL) were withdrawn regularly after 3, 15, 45, 180, 360 min and, if needed, 20 and 60 h and added to a solution of iodine (0.51 g, 2.0 mmol) in diethyl ether (4.0 mL). The organic phase was washed with a saturated aqueous solution (1.0 mL) of sodium thiosulfate before being subjected to gas chromatographic analysis (2 m, 5%, SE-30, $100\text{ }^{\circ}\text{C}$ [10 min] \rightarrow $200\text{ }^{\circ}\text{C}$, heating rate $25\text{ }^{\circ}\text{C}/\text{min}$; 2 m, 5%, C-20 M, $100\text{ }^{\circ}\text{C}$ [10 min] \rightarrow $200\text{ }^{\circ}\text{C}$, heating rate $25\text{ }^{\circ}\text{C}/\text{min}$; 30 m, DB-Wax, $75\text{ }^{\circ}\text{C}$ [10 min] \rightarrow $200\text{ }^{\circ}\text{C}$, heating rate $25\text{ }^{\circ}\text{C}/\text{min}$; 30 m, DB-23, $75\text{ }^{\circ}\text{C}$ [10 min] \rightarrow $200\text{ }^{\circ}\text{C}$, heating rate $25\text{ }^{\circ}\text{C}/\text{min}$). The amounts of iodo and bromo compounds were calculated from the products/standard ratios and corrected using separately determined calibration factors. Some reactions started from iodinated rather than bromo-substituted substrates. In such cases the samples withdrawn were trapped with a solution of 1,2-dibromo-1,1,2,2-tetrafluoroethane (0.24 mL, 0.52 g, 2.0 mmol) in diethyl ether (4.0 mL).

(38) Masson, E.; Schlosser, M. *Eur. J. Org. Chem.* **2005**, 4401–4405.

(39) Leroux, F.; Lefebvre, O.; Schlosser, M. *Eur. J. Org. Chem.* **2006**, 3147–3151.

(40) Heiss, C.; Marzi, E.; Mongin, F.; Schlosser, M. *Eur. J. Org. Chem.* **2007**, 669–675.

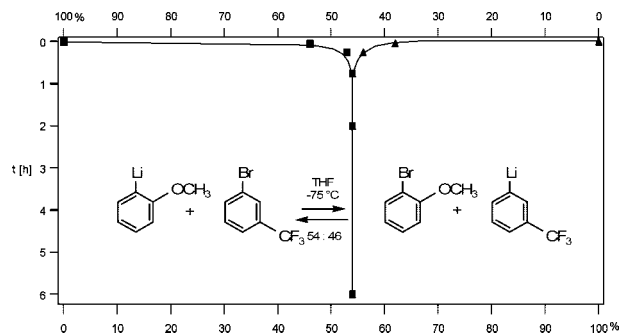


FIGURE 8. Equilibration between *o*-anisyllithium and *m*-(trifluoromethyl)phenyllithium by halogen/metal permutation with the corresponding bromoarenes.

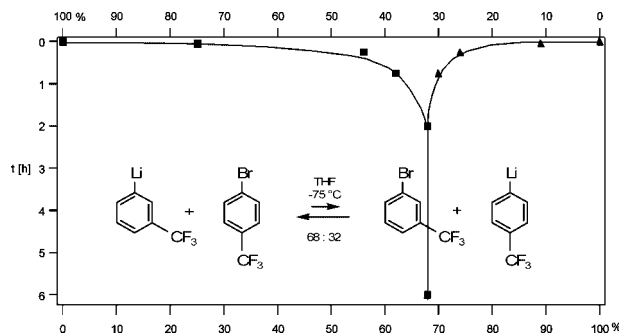


FIGURE 9. Equilibration between *m*-(trifluoromethyl)phenyllithium and *p*-(trifluoromethyl)phenyllithium by halogen/metal permutation with the corresponding bromoarenes.

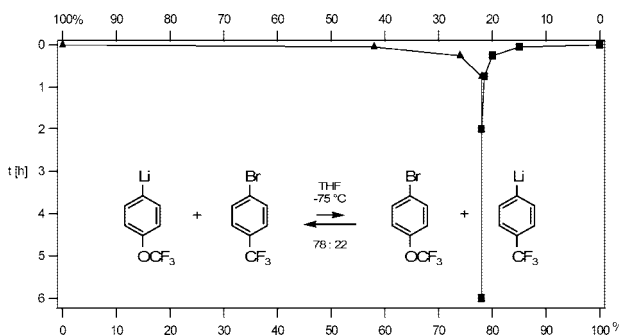


FIGURE 10. Equilibration between *p*-(trifluoromethoxy)phenyllithium and *p*-(trifluoromethyl)phenyllithium by halogen/metal permutation with the corresponding bromoarenes.

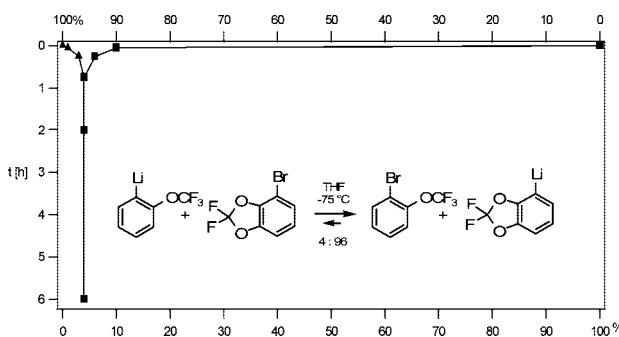


FIGURE 11. Equilibration between *o*-anisyllithium and 4-(2,2-difluoro-1,3-benzodioxyl)lithium by halogen/metal permutation with the corresponding bromoarenes.

A few representative equilibration diagrams are shown below (Figures 4). They feature various couples of aryllithiums. Some of those have almost identical basicities, whereas others have very divergent ones (e.g., 54:46 vs 96:4, Figures 8 and 5, respectively).

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