**Directing Lithiation**

# Controlling Chemoselectivity in the Lithiation of Substituted Aromatic Tertiary Amides[**]

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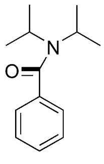
Aromatic compounds can be elaborated by directed lithiation in a number of ways[1] and both *ortho* and lateral metallation have been employed as synthetic tools generally[2] and in a host of recent total syntheses specifically.[3,4] Whereas *ortho* metallation occurs both because the directing group can inductively raise the acidity of the *ortho* hydrogen atom and also because the incoming organometallic substrate closely approaches this position, lateral metallation results from the directing function coordinating an organometallic substrate whilst conjugatively withdrawing electrons from a benzylic group. Consequently, the processes are competitive and, as such, result from the presence of similar directing agents. Recently, ring substitution and lateral-group branching[5] have been employed, in addition to the use of α-silyl lateral groups,[6] as means of controlling the regioselectivity of deprotonation. The use of deuterium as a protecting group at kinetically acidic positions has been reported both for amides[7] and N-heterocyclic systems.[8] Overall, studies to date have clearly established that, for either class of reaction, amide-type groups are among the most useful directors of reaction.[2]

Transformations of *ortho*- and laterally lithiated tertiary amides have been investigated,[9] with directing effects having been attributed to the rate-determining deprotonation of a substrate–organolithium complex.[10–12] However, it is only very recently that solid-state structural evidence has been presented in support of the nature of lithiated intermediates in either reaction pathway. For **1** and **2** *ortho* lithiation has led to the characterization of solid-state dimers, **3**, and isostructural *N,N*-diisopropyl-2-lithionaphthamide–THF complex, **4**, respectively. These are based on core C···Li interactions, support of the metals coming from (amide)O–Li bonding with concomitant modulation of the sterically induced twist angle between the amide and the plane of the aromatic ring.[13] Contrastingly, the laterally deprotonated salt of **5** reveals a tris(thf) solvate, **6**, in which the metal center is only coordinated by O atoms with no C···Li interaction, thus allowing the amide and aromatic planes to be near to perpendicular in the solid state.[14] These data suggest a link between the number of donor atoms per solvent molecule (solvent denticity) and reaction chemoselectivity and lead us to report here on the competitive deprotonation of 2-ethyl-*N,N*-diisopropyl-1-benzamide, **7**.



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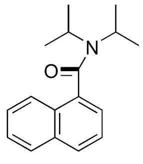

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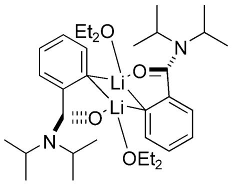

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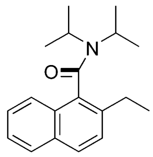

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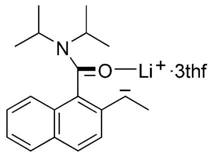

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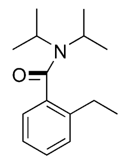

**7**

Treatment of **7** in THF/toluene at −78 °C with 1 equivalent of *t*BuLi gave a maroon solution from which, on storage at −30 °C, crystals were deposited. Surprisingly, in light of previous work,[2,12,15] these were identified as *N,N*-diisopropyl-2-ethyl-6-lithiobenzamide–THF, **8**, by X-ray crystallography.[16] In accordance with our own recent studies,[13] **8** forms a solid-state dimer based on the stabilization of each metal component in a $\{(CLi)_2\}$ core (C2–Li1 = 2.345(5) Å, C2A–Li1 = 2.187(5) Å] by an amide-O center (O1–Li1 = 1.972(5) Å) and one THF molecule (Scheme 1 and Figure 1). A comparison of these parameters with those recorded for **3** and **4**[13] reveals that the core dimensions in **8** are more closely related to those of the latter complex. Consistent with this, the amide–arene torsional angles in **4** and **8** are both significantly greater (at 65.7° and 59.9°, respectively) than that of 47.8° in **3**. The relative magnitudes of these angles, representing as they do a compromise between the maintenance of amide–metal bonding and the introduction of amide–arene interaction, are consistent with the similar steric properties of C2 (in **7**) and C8a (in **2**).

Attempts to isolate and fully characterize the lateral lithiate of **7** combine the knowledge that THF solvation results in the isolation only of dimeric **8** with the recent structural determination of the charge-centre separated tris(thf) solvate **6**.[14] Accordingly, tridentate Lewis base

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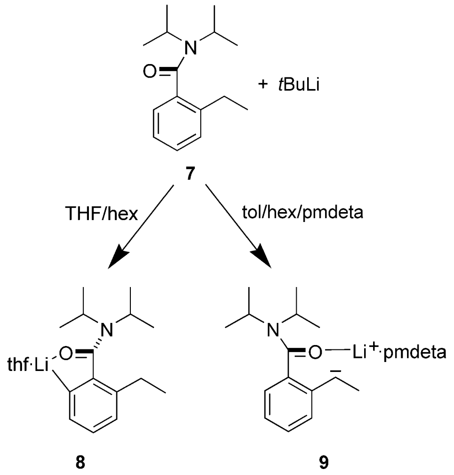


*Scheme 1.* Syntheses of **8** and **9** from **7**; hex = hexane, tol = toluene.

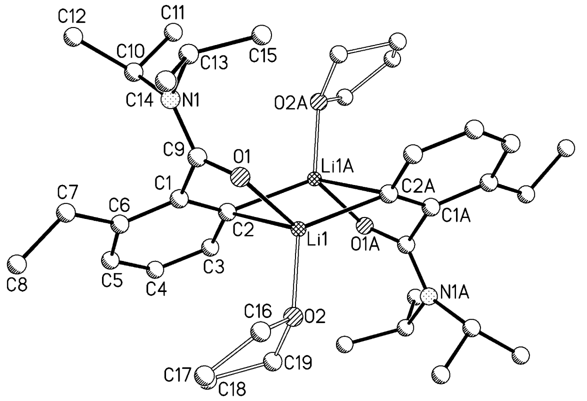


*Figure 1.* Molecular structure of $(\mathbf{8})_2$; hydrogen atoms and minor Et disorder omitted for clarity. Selected bond lengths [Å] and angles [°]: C2-Li1 2.345(5), C2-Li1A 2.187(5), O1-Li1 1.972(5), O2-Li1 1.972(5), C2-C1 1.411(4), C1-C9 1.512(4), C9-O1 1.249(3), Li1-C2-Li1A 68.7(2), C2-Li1-C2A 111.3(2), C1-C2-Li1 91.99(19), C2-C1-C9 113.9(2), C1-C9-O1 117.9(2), C9-O1-Li1 108.4(2).

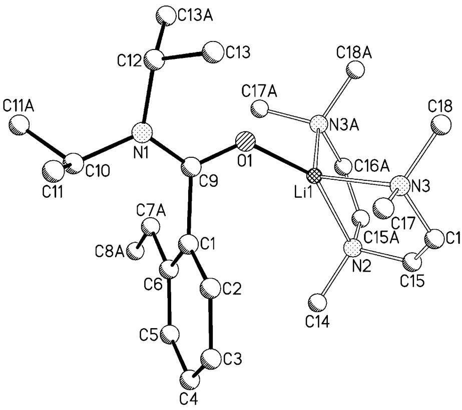
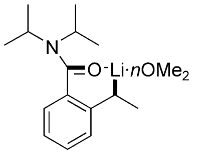


*Figure 2.* Molecular structure of **9**; hydrogen atoms and aromatic disorder omitted for clarity. Selected bond lengths [Å] and angles [°]: O1-Li1 1.873(9), N2-Li1 2.116(9), N3-Li1 2.121(6), C6-C7A 1.400, C7A-C8A 1.516(14), C1-C9 1.555(7), C9-O1 1.234(6), C9-O1-Li1 129.5(4), C1-C9-O1 117.0(5), C6-C1-C9 115.2(4), C6-C7A-C8A 122.1.

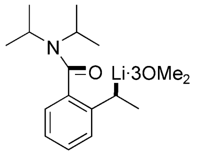
stabilization is enforced by effecting the lithiation of **7** in pmdeta/hexane (pmdeta = *N*,*N*,*N*′,*N*″,*N*″pentamethyldiethylenetriamine). The resulting crystalline deposit is revealed by X-ray diffraction to be α-lithio-2-ethyl-*N*,*N*-diisopropyl-1-benzamide–pmdeta, **9** (Scheme 1 and Figure 2).[17] While the solid-state structure reveals extensive disorder in the positioning of the aryl fragment, the essential features are clear. An observed amide–arene torsional angle of 79.2(4)° compares with that of 82.5(5)° in **6**. In both cases, the large angle between the amide and aromatic planes is allowed by solvent-induced C–Li bond cleavage, with tris(thf) solvation in **6** being closely mimicked by the imposition of pmdeta coordination in **9**.

As with **6**,[14] NMR spectroscopy reveals diastereotopic isopropyl groups at low temperature for samples of both **8** and **9** in [D$_8$]THF solution. In fact, for both of these complexes, data indicate that dissolution is accompanied by significant structural reorganization to afford three solution entities in a 2:10:1 ratio and $^1$H NMR spectra that, notwithstanding the presence of THF (see **8**) or pmdeta (see **9**), are essentially identical (see the Supporting Information). A comparison of these spectra with that of the starting material suggests that the resonances due to the first of these solution types are consistent with the reformation of **7** on dissolution (species no. 1, see Experimental Section)—a process that could not be eradicated in spite of repeated spectroscopic experiments. The last two species yield the following $^7$Li data; at −50 °C $\delta = -1.11$ (1 Li), −1.76 ppm (0.1 Li) for **8** and $\delta = 0.18$ (1 Li), −0.30 ppm (0.1 Li) for **9**. More instructively, whereas each $^1$H NMR spectrum shows four major sets of aromatic signals for the dominant metallated unit in solution (species no. 3), three of these resonances are associated with trace analogue signals (species no. 2). For **8** at −50 °C we observe $\delta = 6.35$ (d, 0.1 H), 6.22 (dd, 1 H), 6.02 (dd, 0.1 H), 6.00 (d, 1 H), 5.51 (d, 1 H), 5.03 (dd, 0.1 H), 4.84 ppm (dd, 1 H). At the same temperature **9** yields $\delta = 6.35$ (d, 0.1 H), 6.21 (dd, 1 H), 6.02 (dd, 0.1 H), 5.94 (d, 1 H), 5.50 (d, 1 H), 5.03 (dd, 0.1 H), 4.77 ppm (dd, 1 H). For both **8** and **9**, similar patterns are also observed for NCH signals, though dynamics lead to convolution of the remaining isopropyl signals such that those consistent with trace species (no. 2) are not confidently attributable (see Experimental Section). Taken together, these data show that the dominant product in solution created from either **8** or **9** contains four different aromatic hydrogen atoms and is laterally metallated, whereas the trace species is an *ortho*-lithiate. Hence, **9** has essentially retained its solid-state-structure type while **8** has rearranged to yield the dominant lateral metallate on dissolution.

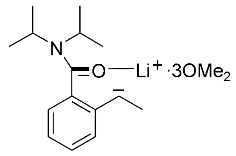
This propensity for reorganization into, or retention of, a laterally lithiated structure (for **8** and **9**, respectively) has been probed by using Gaussian 98[18] (see the Supporting Information). Exploratory geometry optimizations (HF/6-31G*)[19] were followed by a frequency calculation and suitable geometries were refined by using density functional theory (DFT) procedure (MPW1PW91[20]/6-311G**[21]). Reported geometries come from DFT calculations with energies relating to DFT results scaled by the (0.91) zero-point energy correction obtained from the HF study. Results indicate that for unsolvated, mono- and bis(Me$_2$O)-solvated monomers, amide-stabilized lateral metallates (**10a–c**) derived from **7** are preferred to analogous *ortho*-lithiates (**11a–c**) by 10.30, 10.98 and 11.12 kcal mol$^{-1}$, respectively. Meanwhile, tris($Me_2O$)-solvated, amide-stabilized laterally metallated monomer **10e** is preferred to $C_\alpha$-bonded analogue **10d** and to similarly solvated *ortho*-lithiate **11d** by 2.87 and 10.01 kcal mol$^{-1}$, respectively. Hence, if aggregation is inhibited by external solvation then thermodynamic deprotonation gives an amide-bonded lateral metallate (see **9**). It is only with the modeling of unsolvated dimer **12** that the experimental observation of **8** is explained. This species reveals both an enthalpy of dimerization of 19.16 kcal mol$^{-1}$ monomer$^{-1}$ (note the preference for **10a** over **11a**) and incorporates monomeric components that are each 8.87 kcal mol$^{-1}$ more stable than **10a**.



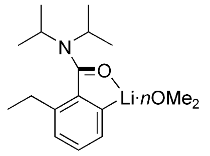
n = 0 **10a**, 1 **10b**, 2 **10c**



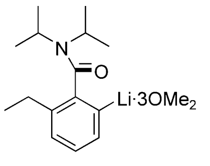
**10d**



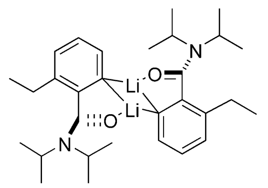
**10e**



n = 0 **11a**, 1 **11b**, 2 **11c**



**11d**



**12**

Plainly, theory is in accordance with both the crystallographic characterization of **8** and **9** and the observation that, when dissolved in excess donor (that is, when external solvation is enforced in place of aggregation), an equilibrium mixture is established in which the dominant component is laterally metallated. These data strongly suggest that competition between *ortho* and lateral metallation is solvent dependent. Polar media inhibit association and favor the formation of a thermodynamically α-deprotonated monomer, as evidenced by the solvent-induced migration of the lithium center in **8** to the α carbon atom, while the ability of the kinetic *ortho* metallate to dimerize is crucially important to the retention of its structural integrity. Ongoing investigations are presently seeking to further elucidate the ability of species such as those reported here to reorganize and/or to reprotonate in solution, the exact solution structures (C–Li bonded or charge-center separated) of lateral lithiates and the imperatives for chemoselectivity in these systems.

## Experimental Section

Synthesis of **8**: *t*BuLi (0.15 mL, 1.7 M in pentane, 0.25 mmol) was added to a solution of **7** (0.058 g, 0.25 mmol) in THF/hexane (0.4 mL:0.2 mL) under nitrogen at −78 °C. The resultant maroon solution was transferred directly to a −30 °C freezer. Dark-red crystals of **8** were obtained after 1 day at this temperature. Yield 12 mg (15 %); mp 104–106 °C; elemental analysis (%) calcd for $C_{38}H_{60}Li_2N_2O_4$: C 73.29, H 9.10, N 4.50; found: C 72.81, H 8.86, N 4.65; $^1H$ NMR (400 MHz, [D$_8$]THF, −50 °C, TMS): $\delta = 7.28$ (m, 0.4 H; $C_6H_4$ no. 1), 7.19 (m, 0.2 H; $C_6H_4$ no. 1), 7.10 (m, 0.2 H; $C_6H_4$ no. 1), 6.35 (d, 0.1 H; $C_6H_3$ no. 2), 6.22 (dd, 1 H; $C_6H_4$ no. 3), 6.02 (dd, 0.1 H; $C_6H_3$ no. 2), 6.00 (d, 1 H; $C_6H_4$ no. 3), 5.51 (d, 1 H; $C_6H_4$ no. 3), 5.03 (dd, 0.1 H; $C_6H_3$ no. 2), 4.84 (dd, 1 H; $C_6H_4$ no. 3), 4.72 (m, br, 0.1 H; NCH no. 2), 4.50 (m, br, 1 H; NCH no. 3), 3.62 (m, 5 H; THF), 3.46 (m, br, 1 H; NCH no. 3), 2.93 (q, $^3J$(H,H) = 6.7 Hz, 0.2 H; Ar$CH_2$ no. 2), 2.61 (q, $^3J$(H,H) = 7.5 Hz, 0.4 H; Ar$CH_2$ no. 1), 2.52 (q, $^3J$(H,H) = 5.7 Hz, 1 H; Ar*CH* no. 3), 1.79 (m, 5 H; THF), 1.53 (dd, 1.2 H; NCH*Me* no. 1), 1.48–1.40 (v br, 6 H; NCH*Me* no. 3), 1.42 (d, $^3J$(H,H) = 5.7 Hz, 3 H; CH*Me* no. 3), 1.21 (t, $^3J$(H,H) = 7.5 Hz, 0.6 H; $CH_2$*Me* no. 1), 1.15 (br, 6 H; NCH*Me* no. 3), 1.09 (dd, 1.2 H; NCH*Me* no. 1), 0.90 ppm (m, 0.3 H; $CH_2$*Me* no. 2). $^7Li$ NMR spectroscopy (155 MHz, [D$_8$]THF, −50 °C, PhLi): $\delta = -1.11$ (s, 1 Li), −1.76 ppm (s, 0.1 Li).

Synthesis of **9**: *t*BuLi (0.15 mL, 1.7 M in pentane, 0.25 mmol) was added to a solution of **7** (0.058 g, 1 mmol) in toluene/hexane (0.5 mL:0.1 mL) that contained pmdeta (0.052 mL, 0.25 mmol) under nitrogen at −78 °C. The resultant maroon solution was stored at −30 °C for 2 days whereupon purple crystals of **9** were deposited. Yield 65 mg (63 %); mp 132–134 °C; elemental analysis (%) calcd for $C_{24}H_{45}LiN_4O$: C 69.87, H 10.99, N 13.58; found: C 69.85, H 11.04, N 13.47 %; $^1H$ NMR (500 MHz, [D$_8$]THF, −50 °C, TMS): $\delta = 7.29$ (m, 0.4 H; $C_6H_4$ no. 1), 7.19 (m, 0.2 H; $C_6H_4$ no. 1), 7.12 (m, 0.2 H; $C_6H_4$ no. 1), 6.35 (d, 0.1 H; $C_6H_3$ no. 2), 6.21 (dd, 1 H; $C_6H_4$ no. 3), 6.02 (dd, 0.1 H; $C_6H_3$ no. 2), 5.94 (d, 1 H; $C_6H_4$ no. 3), 5.50 (d, 1 H; $C_6H_4$ no. 3), 5.03 (dd, 0.1 H; $C_6H_3$ no. 2), 4.77 (dd, 1 H; $C_6H_4$ no. 3), 4.75 (m, br, 0.1 H; NCH no. 2), 4.59 (m, br, 1 H; NCH no. 3), 3.65 (sept, 0.2 H; NCH no. 1), 3.57 (sept, 0.2 H; NCH no. 1), 3.46 (m, br, 1 H; NCH no. 3), 3.41 (m, br, 0.1 H; NCH no. 2), 3.01 (q, $^3J$(H,H) = 5.9 Hz, 0.2 H; Ar$CH_2$ no. 2), 2.80 (q, $^3J$(H,H) = 6.0 Hz, 0.4 H; Ar$CH_2$ no. 1), 2.64 (q, $^3J$(H,H) = 7.7 Hz, 1 H; Ar*CH* no. 3), 2.42 (br, 8 H; pmdeta), 2.29 (s, 3 H; pmdeta), 2.16 (s, 12 H; pmdeta), 1.55 (dd, 1.2 H; NCH*Me* no. 1), 1.58 (br, 3 H; NCH*Me* no. 3), 1.46 (d, $^3J$(H,H) = 5.7 Hz, 3 H; CH*Me* no. 3), 1.40 (br, 3 H; NCH*Me* no. 3), 1.23 (t, $^3J$(H,H) = 7.8 Hz, 0.6 H; $CH_2$*Me* no. 1), 1.16 (br, 6 H; NCH*Me* no. 3), 1.11 (dd, 1.2 H; NCH*Me* no. 1), 0.92 ppm (t, $^3J$(H,H) = 7.1 Hz, 0.3 H; $CH_2$*Me* no. 3). $^7Li$ NMR spectroscopy (194 MHz, [D$_8$]THF, −50 °C, PhLi): $\delta = 0.18$ (s, 1 Li), −0.30 ppm (s, 0.1 Li).

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[1] H. W. Gschwend, H. R. Rodriguez, *Org. React.* **1979**, *26*, 1–360; V. Snieckus, *Chem. Rev.* **1990**, *90*, 879–933; R. D. Clark, A. Jahangir, *Org. React.* **1995**, *47*, 1–314.

[2] J. Clayden, *Organolithiums: Selectivity for Synthesis*, Pergamon, Oxford, **2002**.

[3] For directed *ortho* metallation see, for example: D. L. Boger, J. Y. Dong, M. Hikota, M. Ishida, *J. Am. Chem. Soc.* **1999**, *121*, 2471–2477; G. E. Keck, S. F. McHardy, J. A. Murry, *J. Am. Chem. Soc.* **1999**, *121*, 5176–5190; M. A. Brimble, S. A. Chan, *Aust. J. Chem.* **1998**, *51*, 235–242; F. Trécourt, M. Mallet, O. Mongin, G. Quéguiner, *J. Org. Chem.* **1994**, *59*, 6173–6178.

[4] For directed lateral metallation see, for example: R. D. Clark, Jahangir, *J. Org. Chem.* **1989**, *54*, 1174 – 1178; T. R. Kelly, N. Ohashi, R. J. Armstrong-Chong, S. H. Bell, *J. Am. Chem. Soc.* **1986**, *108*, 7100 – 7101.

[5] J. J. Court, D. J. Hlasta, *Tetrahedron Lett.* **1996**, *37, 1335–1338.*

[6] R. J. Mills, N. J. Taylor, V. Snieckus, *J. Org. Chem.* **1989**, *54*, 4372 – 4385; J. Clayden, L. W. Lai, *Tetrahedron Lett.* **2001**, *42*, 3163 – 3166.

[7] J. Clayden, J. H. Pink, N. Westlund, F. X. Wilson, *Tetrahedron Lett.* **1998**, *39*, 8377 – 8380.

[8] A. I. Meyers, G. Milot, *J. Org. Chem.* **1993**, *58*, 6538 – 6540; M. E. Kopach, A. I. Meyers, *J. Org. Chem.* **1996**, *61*, 6764 – 6765.

[9] J. Clayden, J. H. Pink, *Tetrahedron Lett.*, **1997**, *38*, 2565 – 2568; S. Thayumanavan, A. Basu, P. Beak, *J. Am. Chem. Soc.* **1997**, *119*, 8209 – 8216; J. Clayden, J. H. Pink, N. Westlund, C. S. Frampton, *J. Chem. Soc. Perkin Trans. 1* **2002**, 901 – 917; J. Clayden, M. Helliwell, J. H. Pink, N. Westlund, *J. Am. Chem. Soc.* **2002**, *124*, 12449 – 12457.

[10] P. Beak, A. I. Meyers, *Acc. Chem. Res.* **1986**, *19*, 356 – 363; P. Beak, J. E. Hunter, Y. M. Jun, *J. Am. Chem. Soc.* **1983**, *105*, 6350 – 6351.

[11] E. Resek, P. Beak, *J. Am. Chem. Soc.* **1994**, *116*, 405 – 406.

[12] D. R. Anderson, N. C. Faibish, P. Beak, *J. Am. Chem. Soc.* **1999**, *121*, 7553 – 7558.

[13] J. Clayden, R. P. Davies, M. A. Hendy, A. E. H. Wheatley, *Angew. Chem.* **2001**, *113*, 1282 – 1285; *Angew. Chem. Int. Ed.* **2001**, *40*, 1238 – 1240.

[14] D. R. Armstrong, J. Clayden, R. Haigh, D. J. Linton, P. Schooler, A. E. H. Wheatley, *Chem. Commun.* **2003**, 1694 – 1695.

[15] P. Beak, D. R. Anderson, M. D. Curtis, J. M. Laumer, D. J. Pippel, G. A. Weisenburger, *Acc. Chem. Res.* **2000**, *33*, 715 – 727.

[16] Crystal data for **8**: $C_{38}H_{60}Li_2N_2O_4$, $M_r = 622.76$, triclinic, space group $P\bar{1}$, $a = 9.8195(11)$, $b = 9.8670(6)$, $c = 10.4580(11)$ Å, $\alpha = 88.128(6)$, $\beta = 70.921(4)$, $\gamma = 82.049(6)°$, $V = 948.31(16)$ Å$^3$, $Z = 1$, $\rho_{calcd} = 1.090\ g\,cm^{-3}$; $Mo_{K\alpha}$ radiation, $\lambda = 0.71069$ Å, $\mu = 0.068\ mm^{-1}$, $T = 180$ K. 6605 data (2060 unique, $R_{int} = 0.0440$, $\theta < 25.07°$) were collected on a Nonius Kappa CCD diffractometer. The structure was solved by direct methods and refined by full-matrix least-squares on $F^2$ values of all data (G. M. Sheldrick, SHELXTL manual, Bruker AXS Inc., Madison, WI, USA, 1998, version 5.1) to give $wR2 = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2} = 0.2066$, conventional $R = 0.0694$ for $F$ values of 3287 reflections with $F_o^2 > 2\sigma(F_o^2)$, $GoF = 0.975$ for 213 parameters. Ethyl groups showed positional disorder and each was refined isotropically over two sites with partial occupancies. Residual electron density extrema 0.534 and $-0.325\ e\,Å^{-3}$. CCDC-223507 (**8**) and 223508 (**9**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk).

[17] Crystal data for **9**: $C_{24}H_{45}LiN_4O$, $M_r = 412.58$, monoclinic, space group $P2(1)/m$, $a = 9.411(2)$, $b = 13.891(3)$, $c = 10.297(2)$ Å, $\beta = 103.40(3)°$, $V = 1309.5(5)$ Å$^3$, $Z = 2$, $\rho_{calcd} = 1.036\ g\,cm^{-3}$; $Mo_{K\alpha}$ radiation, $\lambda = 0.71069$ Å, $\mu = 0.063\ mm^{-1}$, $T = 180$ K. 4400 data (1118 unique, $R_{int} = 0.0521$, $\theta < 20.60°$) were collected on a Nonius Kappa CCD diffractometer. The structure was solved by direct methods and refined by full-matrix least-squares on $F^2$ values of all data (G. M. Sheldrick, SHELXTL manual, Bruker AXS Inc., Madison, WI, USA, 1998, version 5.1) to give $wR2 = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2} = 0.2057$, conventional $R = 0.0776$ for $F$ values of 1392 reflections with $F_o^2 > 2\sigma(F_o^2)$, $GoF = 1.080$ for 179 parameters. The $C_6H_4Et$ unit showed positional disorder over two positions related by a mirror plane and non-hydrogen atoms C1–C8 were refined anisotropically with half occupancy. Atoms C1A–C8A are generated by symmetry. Residual electron density extrema 0.258 and $-0.264\ e\,Å^{-3}$.

[18] Gaussian 98 (Revision A.9), M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. G. Johnson, W. Chen, M. W. Wong, J. L. Andres, M. Head-Gordon, E. S. Replogle, J. A. Pople, Gaussian, Inc., Pittsburgh, PA, **1998**.

[19] W. J. Hehre, R. Ditchfield, J. A. Pople, *J. Chem. Phys.* **1972**, *56*, 2257 – 2261; P. C. Hariharan, J. A. Pople, *Theor. Chim. Acta* **1973**, *28*, 213 – 222, J. D. Dill, J. A. Pople, *J. Chem. Phys.* **1975**, *62*, 2921 – 2923.

[20] C. Adamo, V. Barone, *J. Chem. Phys.* **1998**, *108*, 664 – 675.

[21] A. D. McLean, G. S. Chandler, *J. Chem. Phys.* **1980**, *72*, 5639 – 5648.