Organometallics **2004,** *23,* 5389−5391

Crystal Structures of (+)-Sparteine Surrogate Adducts of Methyllithium and Phenyllithium[†]

Carsten Strohmann,[*,‡] Katja Strohfeldt,[‡] Daniel Schildbach,[‡]
Matthew J. McGrath,[§] and Peter O'Brien[§]

*Institut für Anorganische Chemie, Universität Würzburg, Am Hubland,
97074 Würzburg, Germany, and Department of Chemistry, University of York,
Heslington, York, U.K. YO10 5DD*

Received July 8, 2004

*Summary: The crystal structures of aggregates between MeLi and PhLi and a (+)-sparteine surrogate ((+)-**2**) have been determined. The MeLi adduct **4** reveals a 2:2 dimer, while the PhLi adduct **6** forms a rare example of a 4:2 ladder structure, each capped by two of the diamine ligands. The observation that (+)-**2** is equally effective as (−)-sparteine in s-BuLi-mediated asymmetric deprotonations, but leading to the opposite sense of stereoselectivity, is explained on the basis of the crystal structures and a computational study. Moreover, the crystal structure of the 2;2 dimer between MeLi and (−)-sparteine has been redetermined with advanced accuracy.*

The first-generation chiral bases formed from adducts between alkyllithium bases and (−)-sparteine have become an important tool for the generation of enantiomerically enriched alkyllithiums (with a metalated stereogenic carbon center).[1] The most frequently used combination has been *s*-BuLi[2] and (−)-sparteine, but *n*-BuLi[2a,3] or *i*-PrLi[4] and (−)-sparteine have also been successfully applied to kinetically controlled enantiotopos-differentiating deprotonation, mostly with high stereoselectivity. In addition, adducts of MeLi, *n*-BuLi, and PhLi with (−)-sparteine have been used in stereoselective nucleophilic addition reactions.[5]

Recently, the crystal structures of the *t*-BuLi,[6a] *n*-BuLi and *i*-PrLi,[6b] and MeLi and PhLi[6c,d] adducts of (−)-sparteine were determined. Nonetheless, in the case of MeLi,[6d] the metalated carbon center could not be refined anisotropically by the authors, resulting from only 1152 measured independent reflections (57% completeness). This proves the necessity for high-quality crystals allowing complete measurement of reflections at high diffraction angles.[7] Thus, the crystallographic data of [MeLi·(−)-sparteine]$_2$ are presented herein and have been redeposited with the CCDC (Figure 1).[8,9]

(+)-Sparteine is available by resolution of racemic lupanine[11a] or via multistep asymmetric synthesis.[11b] However, the (+)-sparteine surrogate (1*R*,2*S*,9*S*)-11-methyl-7,11-diazatricyclo[7.3.1.0^{2,7}]tridecane [(+)-**2**, whose synthesis was optimized recently[12]] is equally as effective as (−)-sparteine in *s*-BuLi-mediated asymmetric deprotonations, leading to the opposite sense of stereoselectivity.[12b] Thus, crystal structures of the corresponding alkyllithium−(+)-**2** adducts are of great interest in order to explain the observed stereoselectivities, and the question arose: are the comparable enantiomeric ratios based on similar molecular structures? Furthermore, such crystal structures will allow more insight into the

---

[*] To whom correspondence should be addressed. Tel: +49 (0)931 8884613. Fax: +49 (0)931 8884605. E-mail: mail@carsten-strohmann.de.

[†] Dedicated to Professor Michael Veith on the occasion of his 60th birthday.

[‡] Universität Würzburg.

[§] University of York.

(1) In general, we speak of enantiomerically enriched alkyllithiums when we focus on the stereogenic lithiated carbon center. In reality, such alkyllithiums are almost always diastereomerically enriched.

(2) (a) Hoppe, D.; Hense, T. *Angew. Chem., Int. Ed.* **1997**, *36*, 2282. (b) Basu, A.; Thayumanavan, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 716.

(3) Pippel, D. J.; Weisenburger, G.; Wilson, S. R.; Beak, P. *Angew. Chem., Int. Ed.* **1998**, *37*, 2522.

(4) Beak, P.; Kerrick, S. T.; Wu, S.; Chu, J. *J. Am. Chem. Soc.* **1994**, *116*, 3231.

(5) (a) Alexakis, A.; Vrancken, E.; Mangeney, P. *Synlett* **1998**, *11*, 1165. (b) Norsikian, S.; Marek, I.; Klein, S.; Poisson, J. F.; Normant, J. F. *Chem. Eur. J.* **1999**, *5*, 2055. (c) Denmark, S. E.; Nakajima, N.; Nicaise, O. J.-C. *J. Am. Chem. Soc.* **1994**, *116*, 8797.

(6) (a) Strohmann, C.; Seibel, T.; Strohfeldt, K. *Angew. Chem., Int. Ed.* **2003**, *42*, 4531. (b) Strohmann, C.; Strohfeldt, K.; Schildbach, D. *J. Am. Chem. Soc.* **2003**, *125*, 13672. (c) Strohfeldt, K.; Schildbach, D.; Seibel, T.; Strohmann, C. 3rd International Conference on the Chemistry of Alkali and Alkaline Earth Metals, Alkchem-3; Würzburg, Germany, 2003; Poster No. P03. (d) Vestergren, M.; Eriksson, J.; Hilmersson, G.; Håkansson, M. *J. Organomet. Chem.* **2003**, *682*, 172.

(7) A solution of 140 mg (5.97×10^{-4} mol) of (−)-sparteine in *n*-pentane (5 mL) was cooled to −78 °C, and 56.0 μL (8.96×10^{-4} mol) of MeLi (solution in diethyl ether, $c = 1.6$ mol L^{-1}) was added. The mixture was warmed to −30 °C over 12 h. Colorless block-shaped single crystals of compound **3** were obtained.

(8) Crystallographic data for **3** (colorless needles from *n*-pentane/diethyl ether, 0.40 × 0.30 × 0.30 mm^3): $C_{32}H_{58}Li_2N_4$, $M_r = 512.70$, orthorhombic, space group $P2_12_12$ (No. 18), $a = 13.432(3)$ Å, $b = 10.439(2)$ Å, $c = 11.186(2)$ Å, $U = 1568.4(5)$ Å^3, $Z = 2$, $D_c = 1.086$ Mg/m^3, type of radiation Mo Kα, $\lambda = 0.710\,73$ Å, $\mu = 0.062$ mm^{-1}. Measurements: Bruker Apex CCD, $T = -100$ °C. The structure was solved using direct and Fourier methods. A total of 14 798 reflections were measured with 2θ in the range 3.84−50.00°, with 2770 reflections being unique and 2164 having $I > 2\sigma(I)$. Refinement was by full-matrix least-squares methods (based on F_o^2, SHELXL-97), with anisotropic thermal parameters for all non-H atoms in the final cycles. The H atoms were refined on a riding model in their ideal geometric positions, except for H(1a), H(1b), and H(1c), which were refined isotropically. $R = 0.0508$ ($I > 2\sigma(I)$); $R_w(F_o^2) = 0.1221$ (all data).

(9) Due to the lack of heavy atoms, the Flack parameter (or absolute structure factor), which usually indicates the refinement of the absolute structure, is not significant for each of the crystal structures reported. Therefore, it is neither listed nor discussed (see also: Flack, H. D.; Bernardinelli, G. *J. Appl. Crystallogr.* **2000**, *33*, 1143). Nevertheless, the refinement of the absolute structure is unambiguous, on account of the fixed absolute configurations at the chiral ligands (determination of the relative configuration). For the absolute and relative stereochemistry of (−)-**1** see refs 2a and 11b; for (+)-**2** see ref 12a,b.

(10) Keller, E. *Schakal99*; University of Freiburg, Freiburg, Germany, 1999.

(11) (a) Ebner, T.; Eichelbaum, M.; Fischer, P.; Meese, C. O. *Arch. Pharm.* **1989**, *322*, 399. (b) Smith, T. B.; Wendt, J. A.; Aubé, J. *Org. Lett.* **2002**, *4*, 2577.

(12) (a) Hermet, J.-P. R.; Porter, D. W.; Dearden, M. J.; Harrison, J. R.; Koplin, T.; O'Brien, P.; Parmene, J.; Tyurin, V.; Whitwood, A. C.; Gilday, J.; Smith, N. M. *Org. Biomol. Chem.* **2003**, *1*, 3977. (b) Dearden, M. J.; Firkin, C. R.; Hermet, J.-P. R.; O'Brien, P. *J. Am. Chem. Soc.* **2002**, *124*, 11870. (c) Harrison, J. R.; O'Brien, P.; Porter, D. W.; Smith, N. M. *Chem. Commun.* **2001**, 1202.

10.1021/om0494871 CCC: $27.50
Publication on Web 10/07/2004

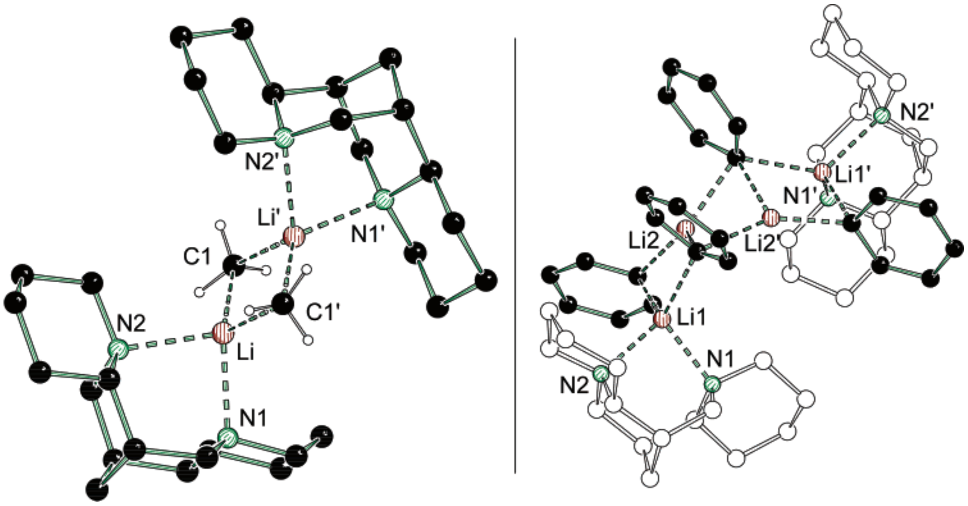


Figure 1. Crystal structures of [MeLi·(−)-sparteine]$_2$ (**3**) (left) and [(PhLi)$_4$·{(−)-sparteine}$_2$] (**5**) (right) (*Schakal* plots[10]).[6c]

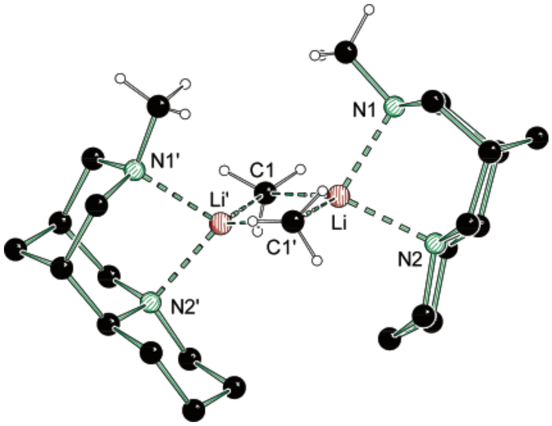
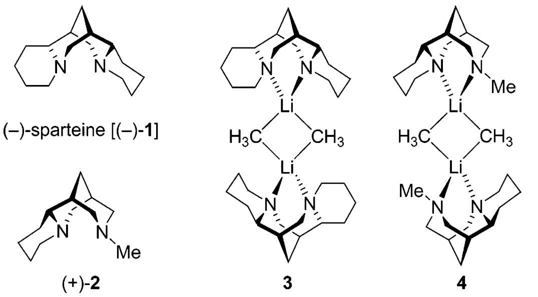


Figure 2. Molecular structure of **4** in the solid state (*Schakal* plot[10]). Selected bond lengths (Å) and angles (deg): Li−C(1) = 2.245(6), Li−C(1)′ = 2.243(6), Li−N(1) = 2.134(6), Li−N(2) = 2.174(6); Li−C(1)−Li′ = 66.6(2), C(1)−Li−C(1)′ = 113.4(2), N(1)−Li−N(2) = 84.1(2), N(1)−Li−C(1)′ = 116.1(3), N(2)−Li−C(1)′ = 106.8(2), N(1)−Li−C(1) = 107.6(2), N(2)−Li−C(1) = 126.0(3).

Chart 1



structure-determining principles of alkyllithiums to be gained (Chart 1).

Figure 2 shows the molecular structure of the dimer **4** in the solid state,[13] which crystallized from an *n*-pentane/diethyl ether mixture in the orthorhombic crystal system, space group $P2_12_12$.[9,14] The asymmetric unit contains one adduct of MeLi·(+)-**2**, the whole dimer being formed by a C_2 symmetry operation. The molecular structure is indeed similar to that observed for the (−)-sparteine adduct **3** (Figure 1). The central structural motif is a planar four-membered Li−C−Li−C ring, and as a result of the C_2 symmetry, the *N*-methyl groups are pointing to the same side of the ring plane. This sterically unexpected arrangement of the diamine ligands comes along with a C_2 symmetry axis orthogonal to the four-membered-ring plane. The coordination number of the lithium centers amounts to 4 due to two Li−C and two Li−N interactions. The two Li−C distances are equal within the margin of error, whereas the Li−N distances are slightly different. Unusual features of both MeLi adducts **3** and **4** are the elongated Li−N distances, in comparison to the distances in the PhLi adducts **5** and **6** (Figures 1 and 3), which may be explained by the steric repulsion of the two diamine ligands opposite to each other: Li−N(1) = 2.134(6) Å (2.160(4) Å for **3**) and Li−N(2) = 2.174(6) Å (2.187(4) Å for **3**). Moreover, compounds **3** and **4** are the only dimeric examples of MeLi aggregates in the solid state reported to date (Figure 2).[15]

PhLi adducts **5** and **6** are examples of the noncyclic ladder type of aggregation, which is only rarely observed.[6c,d,16] Focusing on the ladder framework of these two compounds, C_2 symmetry for the 4:2 PhLi ladder structure of (−)-sparteine adduct **5** can be found. In contrast, approximate inversion symmetry for the ladder framework of the adduct between (+)-**2** and PhLi

---

(13) A solution of 74.1 mg (3.81×10^{-4} mol) of (+)-**2** in *n*-pentane (5 mL) was cooled to −78 °C, and 36.0 μL (5.72×10^{-4} mol) of MeLi (solution in diethyl ether, $c = 1.6$ mol L^{-1}) was added. The mixture was warmed to −30 °C over 12 h. Colorless block-shaped single crystals of compound **4** were obtained.

(14) Crystallographic data for **4** (colorless needles from *n*-pentane/diethyl ether, 0.40 × 0.20 × 0.30 mm^3): $C_{26}H_{50}Li_2N_4$, $M_r = 432.58$, orthorhombic, space group $P2_12_12$ (No. 18), $a = 10.071(3)$ Å, $b = 13.909(7)$ Å, $c = 9.755(3)$ Å, $U = 1366.5(9)$ Å^3, $Z = 2$, $D_c = 1.051$ Mg/m^3, type of radiation Mo Kα, $\lambda = 0.710\ 73$ Å, $\mu = 0.060$ mm^{-1}. Measurements: Stoe IPDS, $T = -100$ °C. The structure was solved using direct and Fourier methods. A total of 12 072 reflections were measured with 2θ in the range 5.00−50.00°, with 2410 reflections being unique and 1628 having $I > 2\sigma(I)$. Refinement was by full-matrix least-squares methods (based on F_o^2, SHELXL-97), with anisotropic thermal parameters for all non-H atoms in the final cycles. The H atoms were refined on a riding model in their ideal geometric positions, except for H(1a), H(1b), and H(1c), which were refined isotropically; $R = 0.0579$ ($I > 2\sigma(I)$); $R_w(F_o^2) = 0.1469$ (all data).

(15) Stey, T.; Stalke, D. In *The Chemistry of Organolithium Compounds*; Rappoport, Z., Marek, I., Eds.; Wiley: Chichester, U.K., 2004; p 47, and literature cited therein.

(16) (a) Wijkens, P.; Jastrzebski, J. T. B. H.; Veldman, N.; Spek, A. L.; van Koten, G. *Chem. Commun.* **1997**, 2143. (b) Dinnebier, R. E.; Behrens, U.; Olbrich, F. *J. Am. Chem. Soc.* **1998**, *120*, 1430. (c) Donkervoort, J. G.; Vicario, J. L.; Rijnberg, E.; Jastrzebski, J. T. B. H.; Kooijman, H.; Spek, A. L.; van Koten, G. *J. Organomet. Chem.* **1998**, *463*, 463. (d) Strohmann, C.; Abele, B. C. *Organometallics* **2000**, *19*, 4173.

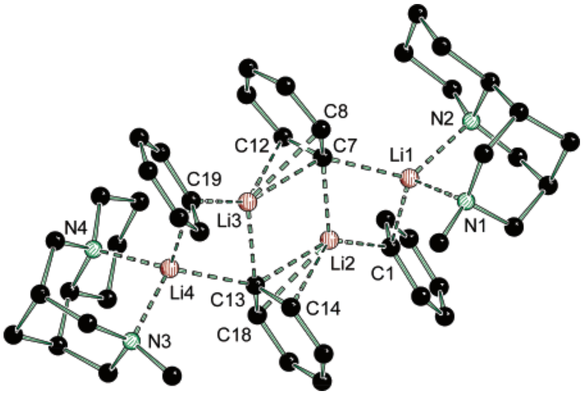
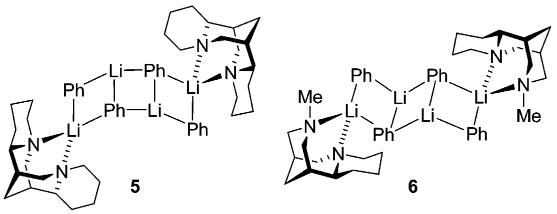


Figure 3. Molecular structure of **6** in the solid state (*Schakal* plot[10]). Selected bond lengths (Å) and angles (deg): Li(1)−C(1) = 2.293(5), Li(1)−C(7) = 2.296(5), Li(2)−C(1) = 2.104(5), Li(2)−C(7) = 2.160(5), Li(2)−C(13) = 2.322(6), Li(2)−C(18) = 2.511(6), Li(2)−C(14) = 2.720(6), Li(3)−C(7) = 2.333(6), Li(3)−C(8) = 2.495(6), Li(3)−C(12) = 2.616(6), Li(3)−C(13) = 2.169(6), Li(3)−C(19) = 2.122(5), Li(4)−C(13) = 2.283(5), Li(4)−C(19) = 2.311(5), Li(1)−N(1) = 2.074(5), Li(1)−N(2) = 2.133(5), Li(4)−N(3) = 2.086(5), Li(4)−N(4) = 2.108(5); Li(1)−C(1)−Li(2) = 67.0(2), Li(3)−C(19)−Li(4) = 67.4(2).

Chart 2



(**6**) is observed, which is only broken by the chiral diamine ligands capping both ends of the aggregate (Chart 2).

Figure 3 shows the molecular structure of compound **6** in the solid state,[17] which crystallized from *n*-pentane in the monoclinic crystal system, space group $P2_1$.[9,18] A ladder framework consisting of four PhLi units can be found as the central structural motif, which is capped by two diamine ligands (+)-**2**. The two "external" lithium centers Li(1) and Li(4) have a coordination number of 4 due to two Li−C and two Li−N interactions each. The "internal" lithium centers Li(2) and Li(3) formally have a coordination number of 5. This structural feature is even more pronounced in the solid-state structure of Lewis base free phenyllithium.[16b] Due to incomplete coordination spheres at these two metal centers, two additional Li−C$_{\text{ortho}}$ interactions along with three Li−C$_{\text{ipso}}$ interactions are observed. The result is a η^3 coordination for Li(2) and Li(3) in compound **6**, which cannot be formed in the C_2-symmetric (−)-sparteine adduct **5** for steric reasons (Figure 3).

By preliminary quantum-chemical analyses at the B3LYP/6-31+G(d) level[19] of theory, we were able to show that the model system {[MeLi·(+)-**2**]$_2$ + 2 OMe$_2$} is energetically favored over the model system {$^1/_2$ [MeLi·OMe$_2$]$_4$ + 2 (+)-**2**} by 8 kJ/mol. This underlines the trend for the formation of the dimer **4** in the experiment, in contrast to an ether-coordinated MeLi tetramer, which should exist in ethereal solution in the absence of (+)-**2**.

Together with these computational results, the crystal structures of the (+)-sparteine surrogate adducts of MeLi (**4**) and PhLi (**6**) emphasize the essential structure-determining principles of ligands with a bispidine backbone. The similar crystal structures for the MeLi adduct of (−)-sparteine and (+)-**2** are in line with the similar degrees of stereoselectivity exhibited in asymmetric deprotonation reactions using *s*-BuLi and the diamines (−)-**1** and (+)-**2**. Whether the structural difference between the PhLi adducts **5** and **6** in the solid state has an impact on the reactivity and selectivity of these compounds has to be cleared up in combination with studies on the solution behavior of compounds **4** and **6**, which are currently in progress.

Acknowledgment. We are grateful to the Institut für Anorganische Chemie Würzburg, the DFG, the Graduiertenkolleg 690, and the FCI for financial support. We thank the FCI for the award of two scholarships (D.S. and K.S.) and the EPSRC for postdoctoral support (M.J.M.).

Supporting Information Available: Experimental, computational, and crystallographic data (atomic positional parameters, bond lengths and angles, atomic displacement parameters, hydrogen atom parameters, ORTEP plots, and CIF files). This material is available free of charge via the Internet at http://pubs.acs.org.

OM0494871

---

(17) A solution of 83.0 mg (4.27 × 10^{-4} mol) of (+)-**2** in *n*-pentane (5 mL) was cooled to −78 °C, and 26.0 μL (4.69 × 10^{-4} mol) of PhLi (solution in a mixture (70:30) of cyclohexane and diethyl ether, c = 1.8 mol L^{-1}) was added. The mixture was warmed to −30 °C over 12 h. Colorless block-shaped single crystals of compound **4** were obtained.

(18) Crystallographic data for **6** (colorless needles from *n*-pentane/diethyl ether/cyclohexane, 0.20 × 0.20 × 0.10 mm^3): $C_{48}H_{64}Li_4N_4$, M_r = 724.79, monoclinic, space group $P2_1$ (No. 4), a = 12.6284(15) Å, b = 9.8217(12) Å, c = 17.538(2) Å, β = 99.331(2)°, U = 2146.5(4) Å^3, Z = 2, D_c = 1.121 Mg/m^3, type of radiation Mo Kα, λ = 0.710 73 Å, μ = 0.063 mm^{-1}. Measurements: Bruker Apex CCD, T = −100 °C. The structure was solved using direct and Fourier methods. A total of 21 527 reflections were measured with 2θ in the range 3.26−50.00°, with 7546 reflections being unique and 5566 having $I > 2\sigma(I)$. Refinement was by full-matrix least-squares methods (based on F_o^2, SHELXL-97), with anisotropic thermal parameters for all non-H atoms in the final cycles. The H atoms were refined on a riding model in their ideal geometric positions. $R = 0.0571$ ($I > 2\sigma(I)$); $R_w(F_o^2) = 0.0916$ (all data).

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