J. Am. Chem. Soc. 1990, 112, 1467-1471

MNDO Study of the Lithiation of 1- and 2-Naphthol

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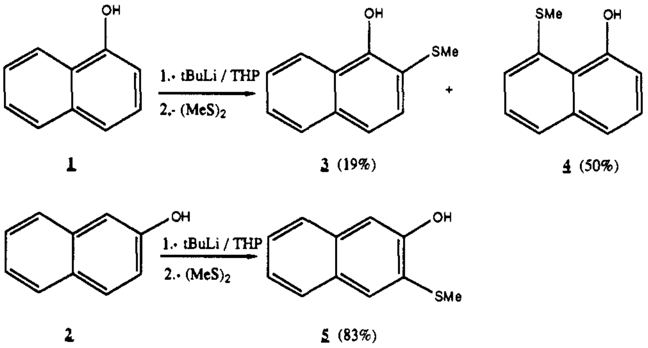
Abstract: The MNDO semiempirical treatment of the lithiation of 1- and 2-naphthol provides satisfactory explanations for the experimentally observed results. Agostic activation of the nearby hydrogens can be traced at the stage of lithium naphthoxide–methyllithium aggregates provided that a tricoordinated lithium atom exists. Thus, for the 1-naphthol case, C_8–H appears to be more strongly "recognized" than C_2–H, whereas no significant agostic activation of C_3–H and C_1–H is present at this stage of the reaction coordinate for the lithiation of 2-naphthol. In accordance with the reported regioselectivity, calculated ΔG values reveal that the direct lithiation of 2-naphthol at C_1 is the only clear-cut endergonic process. Furthermore, these values also provide evidence of the key importance of such experimental variables as the temperature of operation and concentration. Finally, MNDO calculations predict that the more stable structures of the resulting dilithio derivatives should be of the π-type.

In spite of the enormous wealth of knowledge acquired over the past few years on the structure of organolithium compounds,[1] little is known about the mechanistic details of the formation and reaction pathways available for these valuable reagents. Moreover, in spite of its vital importance in synthetic organic chemistry, aromatic ortho lithiation[2] is very poorly understood, in terms of both structure and reactivity. Nevertheless, the advent of modern NMR (^{6}Li and ^{7}Li) techniques[3] such as HOESY,[4] and powerful computational means, will likely change this state of affairs in the very near future.

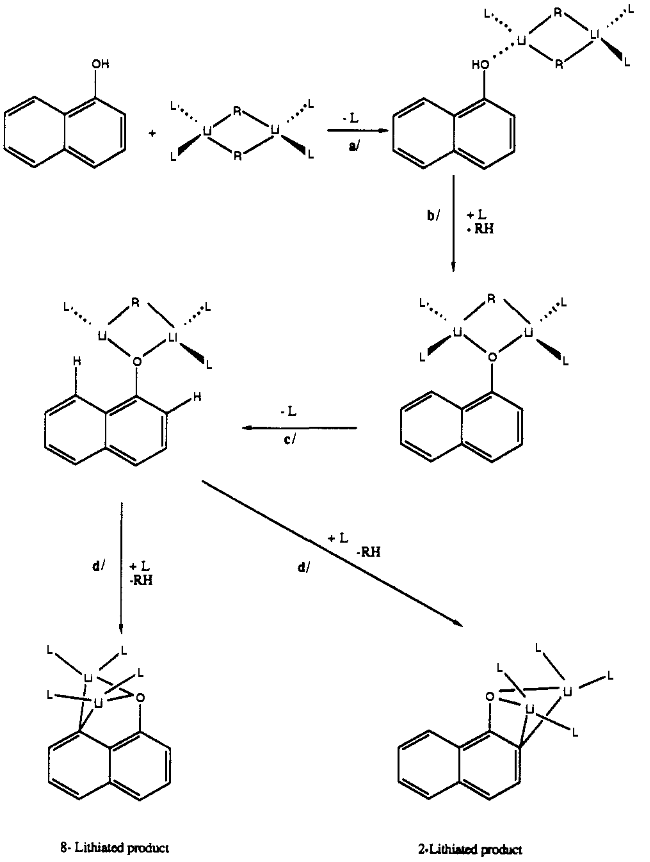
Recent work on the lithiation of hydroxyaromatics has shown that the direct lithiation of simple phenols and naphthols can be achieved by working under appropriate conditions, thus proving that the –OLi group can act as an effective directing group in ortho lithiations of aromatics.[5-7] In fact, the lithiation of hydroxyaromatics has been found useful for the introduction of a wide variety of functional groups and alkyl side chains.[5-7]

In particular, the case of naphthols[6,8] merits special comment. Regioselectivity of naphthol lithiation was found to be in contrast with that of naphthoic acid derivatives such as carboxamides,[9] naphthol ethers,[10] naphthol *O*-carbamates,[11] or [(dialkylamino)methyl]naphthalenes and the like.[12] Thus, as shown by trapping with a variety of electrophiles, the direct lithiation of 2-naphthol (**2**) regioselectively provided the corresponding 3-lithio derivative, whereas that of 1-naphthol (**1**) led to mixtures of the 2-lithio and 8-lithio derivatives (Scheme I), the latter species being apparently the more thermodynamically stable.[6]

Scheme I



Scheme II. Proposed Mechanism for the Reaction of 1-Naphthol and $(RLi)_2$ Dimer in Donor Solvents (L)



The present report shows the results of our theoretical studies of the above reactions, aimed at providing a better description of the competing pathways available for the lithiation of naphthol systems. Though thermodynamic experimental data for the

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(1) (a) Schleyer, P. v. R. *Pure Appl. Chem.* **1984**, *56*, 151. (b) Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1624.

(2) For reviews on the subject, see: (a) Gschwend, H. W.; Rodriguez, H. R. *Org. React.* **1979**, *26*, 1. (b) Wakefield, B. J. *The Chemistry of Organolithium Compounds*: Pergamon Press: New York, 1974. (c) Beak, P.; Snieckus, V. *Acc. Chem. Res.* **1982**, *15*, 306. (d) Beak, P.: Meyers, A. I. *Ibid.* **1986**, *19*, 356. (e) Narasimhan, N. S.; Mali, R. S. *Synthesis* **1983**, 957.

(3) Günther, H.: Moskau. D.: Bast, P.; Schmalz. D. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1212.

(4) Bauer, W.; Clark. T.: Schleyer, P. v. R. *J. Am. Chem. Soc.* **1987**, *109*, 970. See also ref 16 and 23.

(5) Posner, G. H.; Canella, K. A. *J. Am. Chem. Soc.* **1985**, *107*, 2571.

(6) Coll, G.: Morey. J.; Costa, A.; Saá, J. M. *J. Org. Chem.* **1988**, *53*, 5345.

(7) Saá. J. M.: Llobera. A.: García-Raso. A.; Costa, A.; Deyá, P. M. *J. Org. Chem.* **1988**. *53*, 4263.

(8) 2-Mercaptonaphthol (2-naphthalenethiol) has been recently reported to undergo selective lithiation at C_3. See: (a) Block. E.; Eswarakrishnan, V.: Gernon, M.: Ofori-Okai. G.: Saha, C.; Tang. K.: Zubieta, J. *J. Am. Chem. Soc.* **1989**, *111*, 658. For other work on the lithiation of thiophenols see: (b) Figuly. G. D.: Loop, C. K.: Martin. J. C. *J. Am. Chem. Soc.* **1989**, *111*, 654. (c) Smith, K.: Lindsay, C. M.: Pritchard, G. J. *Ibid.* **1989**. *111*, 665.

(9) (a) Beak, P.; Brown, R. A. *J. Org. Chem.* **1977**, *42*, 1823: (b) *Ibid.* **1979**. *44*, 4463.

(10) (a) Kamikawa, T.; Kubo, I. *Synthesis* **1986**, 431. See also: (b) Narasimhan, N. S.: Mali, R. S. *Tetrahedron* **1975**, *31*. 1005. (c) Shirley, D. A.: Cheng, C. F. *J. Organomet. Chem.* **1969**, *20*, 251.

(11) Snieckus, V.: Sibi. M. P. *J. Org. Chem.* **1983**, *48*, 1937.

(12) (a) Gay, R. L.: Hauser, C. R. *J. Am. Chem. Soc.* **1967**, *89*, 2297. (b) Comins. D. L.; Brown, J. D.: Mantlo, N. B. *Tetrahedron Lett.* **1982**, *23*, 3979. (c) Comins. D. L.; Brown. J. D. *J. Org. Chem.* **1984**, *49*, 1078.

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monolithio derivatives of naphthol methyl ethers have been reported,[13] to our knowledge the analogous data for the dilithiated naphthols have not been described.

Calculations for the lithiation of **1** and **2** were outlined along the mechanistic pathway illustrated in Scheme II (only **1** is shown), which, in the first step, involves complexation[14] of the lithiating species with the phenolic substrate (1-naphthol or 2-naphthol) followed by intramolecular reaction to produce RH and a mixed complex (steps a and b).[15] The resulting complex, at a late stage, should undergo the expected lithiation step that was foreseen as an intramolecular rearrangement with concomitant loss of RH.

Several assumptions had to be made in order to be able to perform our theoretical calculations in a reasonable amount of computer time. Dimeric CH_3Li solvated with two H_2O molecules (per lithium) was selected as our working model.[16] This kind of modelization, a usual practice in computational chemistry,[17] has proven to be highly useful for qualitatively describing important mechanistic features regarding lithium coordination in organolithium compounds.[16]

Computational Method

Theoretical calculations were carried out at the restricted Hartree-Fock (RHF) level with the MNDO[18] semiempirical SCF-MO method, as implemented in a modified version[19] of the MOPAC[20] program. Although the energy of the C-Li bond is overestimated by MNDO,[21] this is considered to be the method of choice for studying the structure of large organolithium species (such as lithiated aromatics), otherwise impossible to tackle by ab initio calculations.

All geometric parameters were optimized without symmetry constraints. All stationary points on the potential energy surfaces were characterized by calculating and diagonalizing the Hessian matrix and by checking the number of negative eigenvalues.[22]

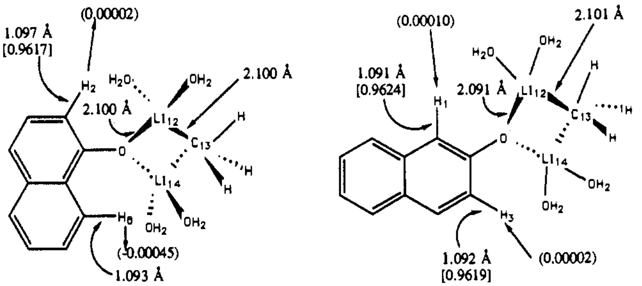
Results and Discussion

As mentioned above, calculations were performed following the general principles established by the mechanistic proposal illustrated in Scheme II.

As expected, formation of lithium naphthoxides from **1** and **2** was found to be exothermic for both naphthols ($\Delta H° = -12.2$ and -11.3 kcal/mol for 1- and 2-naphthol, respectively). Such a process involves complexation of each naphthol with the alkyllithium reagent (dimeric and solvated) followed by formation of a mixed dimer (lithium naphthoxide-methyllithium) and methane (steps a and b, Scheme II). In agreement with the results of recent ab initio calculations[17] that used monomeric unsolvated lithium hydride as a model for their studies, we have found that complexation of naphthols with dimeric solvated methyllithium (step a, Scheme II) is an endothermic process for both 1-naphthol ($\Delta H° = 6.5$ kcal/mol) and 2-naphthol ($\Delta H° = 7.9$ kcal/mol). Yet, when complexation of 1-naphthol with unsolvated dimeric methyllithium was considered, the process was found to be exothermic ($\Delta H° = -8.2$ kcal/mol).

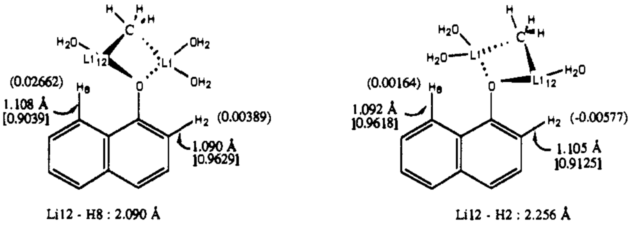
Chart I. MNDO-Optimized Geometries[a]

(a) Mixed Dimers **6** and **7**



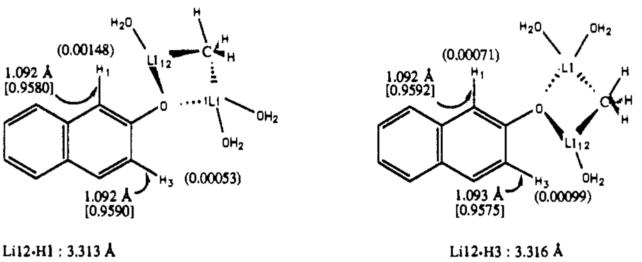
6 **7**

(b) Mixed Aggregates Solvated with Three H_2O Molecules (1-Naphthol)



A **B**

(c) Mixed Aggregates Solvated with Three H_2O Molecules (2-Naphthol)



C **D**

[a] Key: atomic distances (Å), coefficients (parentheses), and bond orders (brackets).

It is worth remarking on several relevant features of the calculated structures for the resulting mixed dimers **6** and **7** (Chart Ia). C-Li and O-Li bond distances in the mixed dimers (optimized geometries) are abnormally close (see Chart Ia). This must be attributed to the above-mentioned tendency of MNDO to overestimate C-Li bond energies, while O-Li bonds are rather accurately reproduced.[21] Most interestingly, none of the vicinal hydrogen atoms (H_2 and H_8 in **6** or H_1 and H_3 in **7**) appear to be "recognized" by the lithiating species, since the C-H distances, bond orders (C_2-H vs C_8-H in **6** and C_1-H vs C_3-H in **7**), and corresponding Li-H distances are nearly identical. Furthermore, the LUMO 1s orbital coefficients of these hydrogen atoms are quite small and almost identical, thus again suggesting that no activation occurs at this point.[23] This was to be expected since lithium in structures **6** and **7** does not have any coordination sites available.

However, loss of a water molecule from **6** or **7**, a slightly endothermic process ($\Delta H° = 2$–4 kcal/mol), renders the resulting mixed aggregates capable of recognizing the proximal hydrogens,[16] via conformers **A** and **B**, or **C** and **D** (Chart Ib,c). Accordingly, we propose that the term agostic activation be applied also to this kind of mixed organolithium species.[24]

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(13) (a) Klumpp, G. W.; Sinnige, M. J. *Tetrahedron Lett.* **1986**, *27*, 2247. For a closely related determination see: (b) Beak, P.; Siegel, B. *J. Am. Chem. Soc.* **1974**, *96*, 6803.

(14) (a) Al-Aseer, M.; Beak, P.; Hay, D.; Kempf, D. J.; Mills, S.; Smith, S. G. *J. Am. Chem. Soc.* **1983**, *105*, 2080. (b) Meyers, A. I.; Rieker, N. F.; Fuentes, L. M. *J. Am. Chem. Soc.* **1983**, *105*, 6155.

(15) Mixed complexes are known, see: (a) McGarrity, J. F.; Ogle, C. A. *J. Am. Chem. Soc.* **1984**, *107*, 1805. (b) McGarrity, J. F.; Ogle, C. A.; Brich, Z.; Loosli, H.-R. *Ibid.* **1985**, *107*, 1810. (c) Bates, T. F.; Clarke, M. T.; Thomas, R. D. *Ibid.* **1988**, *110*, 5109.

(16) Bauer, W.; Feigel, M.; Müller, G.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1988**, *110*, 6033.

(17) Monomeric unsolvated LiH has been used as model for alkyllithiums and their aggregates. See: (a) Kaufmann, E.; Sieber, S.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1989**, *111*, 121. (b) Kaufmann, E.; Schleyer, P. v. R.; Houk, K. N.; Wu, Y. D. *Ibid.* **1985**, *107*, 5560. (c) Houk, K. N.; Rondan, N. G.; Schleyer, P. v. R.; Kaufmann, E.; Clark, T. *Ibid.* **1985**, *107*, 2821.

(18) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899.

(19) Olivella, S. *QCPE Program No. 486.*

(20) VAX Version: Stewart, J. J. P. *QCPE Bull.* **1983**, *3*, 101. Lithium parametrization: Thiel, W.; Clark, T. Unpublished work. (Thiel, W. Personal communication to S. Olivella, Jan 1982).

(21) Schleyer, P. v. R. *Pure Appl. Chem.* **1983**, *55*, 355.

(22) McIver, J. W.; Komornicki, A. *J. Am. Chem. Soc.* **1972**, *94*, 2625.

(23) Bauer, W.; Müller, G.; Pi, R.; Schleyer, P. v. R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1103, and references therein.

(24) Brookhart, M.; Green, M. L. H. *J. Organomet. Chem.* **1983**, *250*, 395. An extension of the original term introduced by Green et al. for transition organometallics was first applied to organolithium compounds by Schleyer et al. See: Reference 16. Kaufmann, E.; Raghavachari, K.; Reed, A. E.; Schleyer, P. v. R. *Organometallics* **1988**, *7*, 1597.

Table I. Relevant C–Li Distances (Å) for π-Coordinated Dilithionaphthols (Only Distances to π-Coordinated Lithium Shown)

structure	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}
8c					2.336	2.332	2.294	2.353	2.385	2.410
9	2.509	2.335	2.253	2.252					2.449	2.366
10	2.236	2.458	2.379	2.318					2.353	2.403
11	2.324	2.470	2.366	2.331					2.300	2.328

For the 1-naphthol case, Chart Ib shows the following: (1) Both C_8–H (in **A**) and C_2–H (in **B**) have slightly elongated bonds, the former (1.108 Å) being somewhat larger than the latter (1.105 Å). (2) Bond orders for C_8–H (in **A**) and C_2–H (in **B**) are significantly small (0.9039 and 0.9125, respectively). (3) The LUMO 1s orbital coefficients of hydrogen atoms at C-8 (−0.026 62, in **A**) and C-2 (−0.003 89, in **B**) are large, the former being much larger. (4) Short distances were found for both Li_{12}–H_8 (2.090 Å, in **A**) and for Li_{12}–H_2 (2.256 Å, in **B**). These facts clearly confirm the existence of an agostic activation at this stage, C_8–H apparently being more noticeably activated.

In accordance with these results, the transition states (TS) for peri and ortho lithiation of 1-naphthol were expected to closely resemble starting materials, thus suggesting that the lithiation step should be exothermic (Hammond postulate).[25]

The corresponding results for the 2-naphthol case (Chart Ic, conformers **C** and **D**) clearly indicate a much lower activation of hydrogens C_1–H and C_3–H. Moreover, since C–H distances (1.092 Å in **C** vs 1.093 Å in **D**), C–H bond orders (0.9580 for C_1–H in **C** vs 0.9575 for C_3–H in **D**), LUMO coefficients of the hydrogen atoms involved in lithiation (0.001 48 in **C** vs −0.000 99 in **D**), and Li–H distances (3.313 Å in **C** vs 3.316 Å in **D**) are very close in value, it is difficult to assess whether or not hydrogen activation occurs in this case. The difference in all the above indicators, however small, points to C_3–H as the most activated hydrogen at this stage. However, no prediction can be advanced as to the exo- or endothermic nature of the lithiation at either C_3 or C_1.

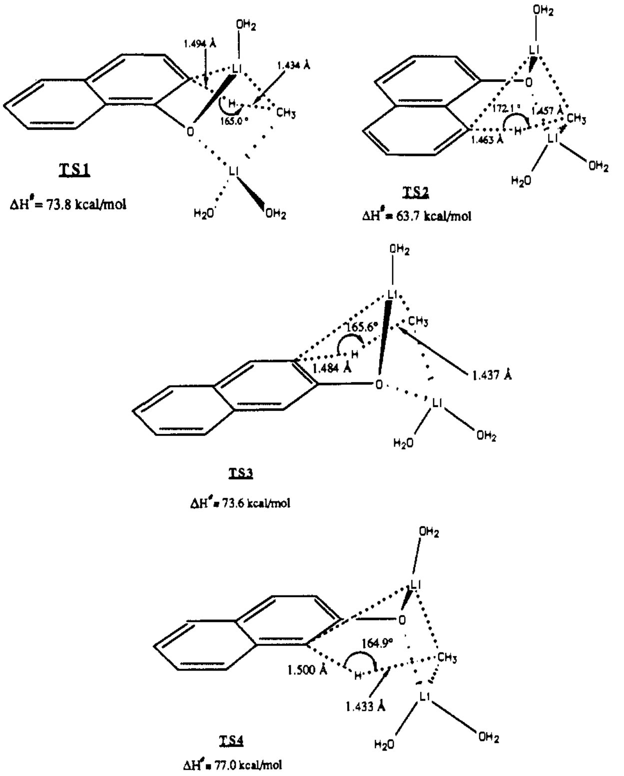
The actual lithiation step was studied by the normal reaction coordinate method, starting from the above mixed aggregates **A**–**D**. It is worth mentioning that only with a lineal combination of two interatomic distances as the reaction coordinate could the transition structures be located. These **TS1**–**TS4** structures show one negative eigenvalue of the Hessian matrix.[22] Their main features are illustrated in Chart II.

The activation energy for ortho lithiation of 1-naphthol (**TS1**, Chart II) was found to be 73.8 kcal/mol, relative to the mixed dimer **6**, whereas that for peri lithiation (**TS2**, Chart II) was 63.7 kcal/mol (10.1 kcal/mol lower than **TS1**). Interestingly, the C–H–C angle for proton transfer in peri lithiation (seven-membered ring) was calculated to be 172.1° whereas the corresponding angle in ortho lithiation (six-membered ring) was found to deviate from linearity (165.0°) considerably more.[26] This observation supports the hypothesis that such deviations of the key proton-transfer process (anion–proton–base) give rise to a considerable energy cost.

It is worth remarking that the very high values obtained for $\Delta H^{\ddagger}$ correspond to the "gas-phase" conditions of our calculations. In the context of the present investigation, only $\Delta(\Delta H^{\ddagger})$ is really meaningful, and this clearly shows that hydrogen abstraction in 1-naphthol is much easier at C_8 than at C_2.

For 2-naphthol, the transition structures leading to the alternative C_1- or C_3-dilithiated compounds involve very close C–H–C angles of proton transfer, as both occur via six-membered ring processes: 165.6° for **TS3** (lithiation at C_3) and 164.9° for **TS4** (lithiation at C_1). Most significantly, the energy barrier found for lithiation at C_3 (73.6 kcal/mol) was 3.4 kcal/mol lower than that for the corresponding lithiation at C_1 (77.0 kcal/mol), thus suggesting that deprotonation at the former carbon is kinetically favored.

Chart II. MNDO-Calculated Energies (kcal/mol) and Optimized Geometries (Distances in Angstroms. Angles in Degrees) for the Transition States of 1- and 2-Naphthol Dilithiation



TS1

ΔH‡ = 73.8 kcal/mol

TS2

ΔH‡ = 63.7 kcal/mol

TS3

ΔH‡ = 73.6 kcal/mol

TS4

ΔH‡ = 77.0 kcal/mol

As expected for reactions of organolithium compounds, typically dominated by solvation energies, the calculated $\Delta S^{\ddagger}$ values are in both cases large and negative (−30 eu).[27]

To complete the reaction energy diagram, the potential surface of the dilithiated naphthols was explored. Three geometries for each final product, corresponding to stationary points in that surface, were located and characterized as minima. Chart III illustrates the calculated structures of the C_8 dilithio derivative of 1-naphthol, namely the doubly bridged structure **8a**[28] and π-complexed organolithium derivatives **8b** and **8c**. Also shown

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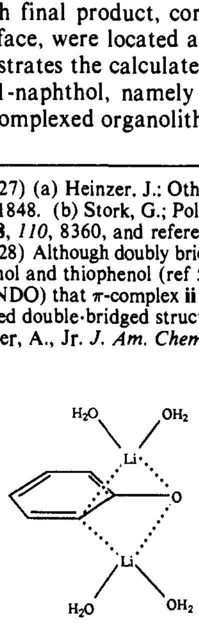
[25] Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334.

[26] Liotta, D.; Saindane, M.; Waykole, L.; Stephens, J.; Grossman, J. *J. Am. Chem. Soc.* **1988**, *110*, 2667, and ref 6.

[27] (a) Heinzer, J.; Oth, J. F. M.; Seebach, D. *Helv. Chim. Acta.* **1985**, *68*, 1848. (b) Stork, G.; Polt, R. L.; Li, Y.; Houk, K. N. *J. Am. Chem. Soc.* **1988**, *110*, 8360, and references therein.

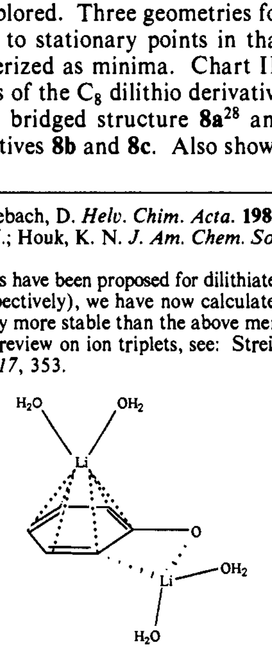
[28] Although doubly bridged structures have been proposed for dilithiated phenol and thiophenol (ref 5 and 8b, respectively), we have now calculated (MNDO) that π-complex **ii** is significantly more stable than the above mentioned double-bridged structure **i**. For a review on ion triplets, see: Streitwieser, A., Jr. *J. Am. Chem. Soc.* **1984**, *17*, 353.



i

ΔH°_f = -333.6 kcal/mol

μ = 8.3 D

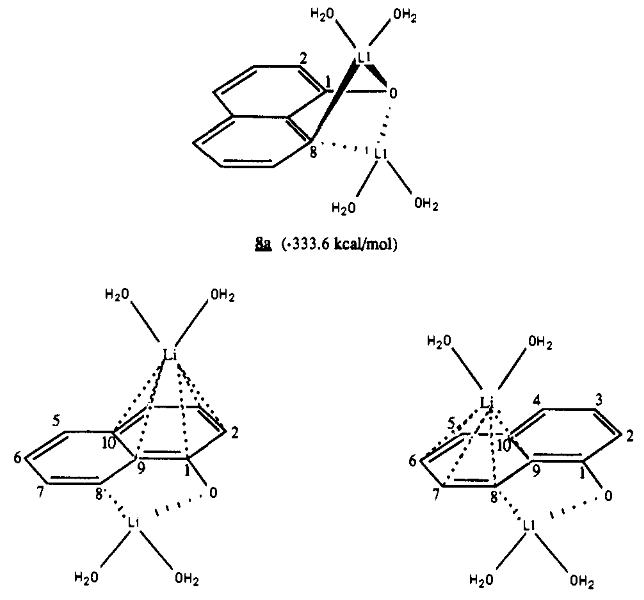


ii

ΔH°_f = -344.6 kcal/mol

μ = 6.9 D

Chart III

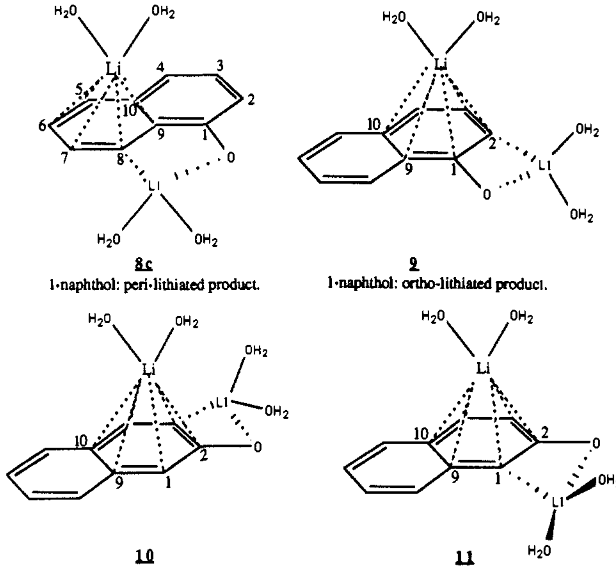


8a (-333.6 kcal/mol)

8b (-338.5 kcal/mol)

8c (-339.7 kcal/mol)

Chart IV. MNDO-Optimized Geometries of Dilithiated Naphthols



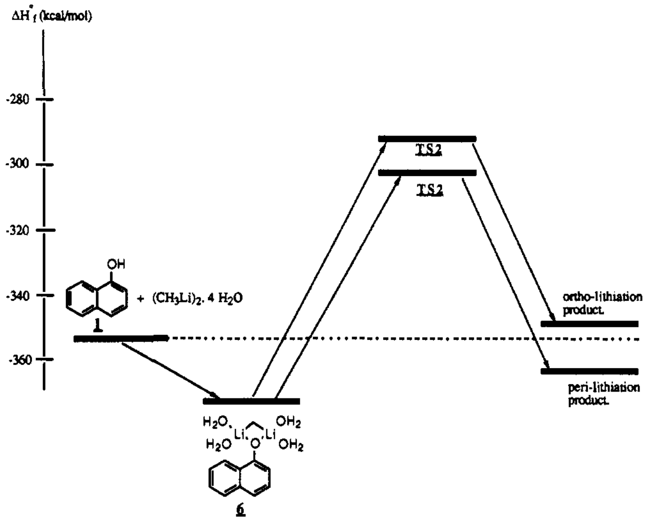
8c
1-naphthol: peri-lithiated product.

9
1-naphthol: ortho-lithiated product.

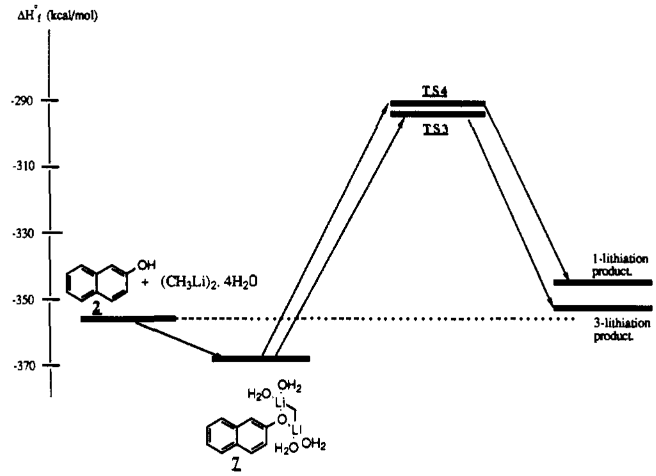
10
2-naphthol: 3-lithiated product.

11
2-naphthol: 1-lithiated product.

Scheme III. Schematic Representation of the Minimum Energy Path for the Reaction of 1-Naphthol and Solvated $(MeLi)_2$ Dimer



Scheme IV. Schematic Representation of the Minimum Energy Path for the Reaction of 2-Naphthol and Solvated $(MeLi)_2$ Dimer



is the corresponding computed heat of formation. Remarkably, the most stable structure found is that in which a lithium atom is located above the plane of the molecule, almost equidistant from all ring carbon atoms.

Calculated geometries for dilithiated naphthols are shown in Chart IV and the relevant interatomic C–Li distances in Table I. These organolithium η^6 complexes can be interpreted in terms of multicentered covalent interactions between the unoccupied p orbitals of lithium and the appropriate occupied MO of the lithium naphthoxide system.[29] Obviously, experimental work has to be done to substantiate these structures.

According to the calculated enthalpies, the diagrams for lithiation of **1** and **2** (Schemes III and IV) show that peri lithiation is the only thermodynamically allowed process. Nevertheless, when the entropy changes undergone in moving from starting materials **1** and **2** to products are taken into consideration, the above results do make sense. Thus, by entering the ΔS values (calculated at the reaction temperature of 50 °C) for peri (8 eu) and ortho lithiation (12 eu) of 1-naphthol (**1**), the following ΔG values arise: −12.5 kcal/mol for peri lithiation and 0.7 kcal/mol for ortho lithiation. On the other hand, the ΔG values for lithiation of 2-naphthol (**2**) at C_3 (ΔS = 14 eu) and C_1 (ΔS = 15 eu) were found to be −0.8 and 6.4 kcal/mol, respectively.

Therefore, the high regioselectivity experimentally found[6] for the lithiation of 2-naphthol appears to reflect the fact that only one of the competing processes is exothermic, namely that leading to deprotonation at C_3. Calculations also demonstrate that peri lithiation of 1-naphthol is both kinetically and thermodynamically favored. By assuming that the activation barrier for liquid-phase lithiation can be surmounted at the temperature of operation, one would expect that the product of peri lithiation would predominate, as experimentally observed.[6]

Finally, another remarkable fact noticed both by Posner[5] and ourselves[6] is reproduced by the above calculations. This is the strong dependence of the reaction on such experimental variables[30] as temperature of operation, concentration of the metalating agent, and volume of solvent employed. Thus, only by working at room temperature and rapidly adding a solution of *t*-BuLi (2 M) to a concentrated solution of **1** or **2** (exothermic reaction) did the reaction go to a reasonably high conversion. These experimental observations are in complete agreement with the key influence played by the entropy term on ΔG.

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(29) Setzer, W. N.; Schleyer, P. v. R. *Adv. Organomet. Chem.* **1985**, *24*, 353.

(30) It has been suggested (ref 5 and 6) that the solvent used (THF), or rather the alkoxide resulting from its (at least partial) cleavage by *t*-BuLi, might play a significant role in phenol lithiations by complexing the lithium reagent. No attempt at studying this seemingly important effect has been made in this work. See ref 15 for recent publications on the subject.

Conclusions

The semiempirical treatment (MNDO) applied to the lithiation of 1- and 2-naphthol reveals that mixed dimers of lithium naphthoxide–methyllithium having tetracoordinated lithium atoms do not "recognize" the proximal hydrogens. However, several degrees of agostic activation of the nearby hydrogens were evident when a ligand was withdrawn from the above fully coordinated mixed dimers. In particular, for the case of 1-naphthol, both hydrogens at C_8 and C_2 were clearly activated at this stage, as evidenced by all four indicators: C–H interatomic distances, C–H bond orders, LUMO 1s orbital coefficient of the hydrogen atoms, and H–Li distances. In contrast, the analogous mixed dimer resulting from 2-naphthol did not show significant (if any) agostic activation of the hydrogens at C_1 and C_3.

The subsequent lithiation was found to be exothermic only for 1-naphthol at C_8 (**1**→**8c**) but endothermic at C_2 (**1**→**9**). For 2-naphthol, lithiation is endothermic at both C_3 (**2**→**10**) and C_1 (**2**→**11**). The calculated enthalpies for these processes suggest that experimental factors, such as concentration and temperature, play a major role in the lithiation of naphthols. In fact, the calculated ΔG values obtained from ΔH and ΔS explain the apparent anomaly. Only lithiation of 2-naphthol at C_1 is now shown to be a clear-cut endergonic process (T = 328 K, ΔG = 6.4 kcal/mol), thus providing a simple explanation for the observed regioselectivity in the lithiation of 2-naphthol.[31]

Remarkably, MNDO calculations predict that the π-type structures of the dilithio derivatives of naphthols having two ligands per lithium atom are significantly more stable than the conventional ones.[28] Unfortunately no experimental proof (or disproof) for this is available yet.

Acknowledgment. Time allocation for calculations, performed with VAX 11/750 and VAX 8350 computers, was generously provided by the Centre de Càlcul de la Universitat de les Illes Balears. Financial support by the DGICYT (Grant PB87-0019) is gratefully acknowledged. We are indebted to Prof. S. Olivella (University de Barcelona, Spain) for helpful discussions and also for making his modified version of MOPAC available to us.

Registry No. 1, 90-15-3; **2**, 135-19-3.

Supplementary Material Available: Tables of Cartesian coordinates of the optimized molecular structures (14 pages). Ordering information is given on any current masthead page.

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[31] Note added in proof: Attention is called to a paper on the mechanism of other lithiations. Bauer, W.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1989**, *111*, 7191.

Theoretical Structure–Spectrum Relationships in the Circular Dichroism of Chiral Crown Ethers: Application to Chiral Pyridine-Substituted Crowns

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Received May 22, 1989

Abstract: A general sector function methodology is shown to be derivable from the GSR/ISP (generalized selection rule/independent systems perturbation) approach to the circular dichroism (CD) of achiral probe chromophore/chiral host systems and applied specifically to C_{2v} achiral probes. Coupled with an interpretative model encompassing physical assumptions regarding the electronic properties of the probe transitions and host system, the method is applied to a series of chiral pyridine-substituted crowns. The theoretical results are in good agreement with experimental behavior and suggest that the n → π^* pyridine transition is a sensitive probe of any species occupying the crown "holes" and thus of its association characteristics, whereas the L_a pyridine transition probes the crown backbone structure.

The structures of crown complexes in solution are a sensitive function of solution conditions. For crowns with chiral centers, circular dichroism (CD) constitutes a sensitive probe of solution conformation. Several experimental studies have been reported.[1,2] In particular, the attachment of an achiral aromatic substituent chromophore (A) to the chiral crown macrocycle (C_M) leads to an induced CD of the A transitions, which are in principle amenable to both a detailed experimental and theoretical analysis. The latter is fundamental to a proper definition of the relationship of the empirical CD behavior to the combined A/C_M structural relationships and hence to the internal structure of the macrocycle C_M. It is with such a detailed theoretical analysis of the CD of pyridine-substituted crowns that this paper is principally concerned.

The recent development of a fully symmetry-adapted formulation[3] of the well-known independent systems/perturbation (ISP) approach[4] to CD theory makes such a detailed theoretical analysis possible, thereby avoiding entirely the ambiguity implicit in postulation of qualitative or empirical "sector rules" and leading to analytic expressions for the CD that are always, in principle, capable of yielding both absolute sign and magnitude of the CD. The symmetry-adaptation procedure has its origin in the generalized selection rule (GSR) scheme for spectroscopic processes,[5,6] which provides a method of *analytically* symmetry-adapting perturbation expressions to the relevant symmetries of the interacting systems. The method has been implemented for both the cases of magnetic dipole allowed (mda)[3] and electric dipole allowed (eda)[7] transitions of A.

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† Work completed while on Study Leave from the University of Sydney.

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(1) Speelman, J. C.; Talma, A. G.; Kellogg, R. M.; Meetsma, A.; de Boer, J. L.; Beurskens, P. T.; Bosman, W. P. *J. Org. Chem.* **1989**, *54*, 1055.

(2) Dyer, R. B.; Palmer, R. A.; Ghirardelli, R. G.; Bradshaw, J. S.; Jones, B. A. *J. Am. Chem. Soc.* **1987**, *109*, 4780.

(3) Schipper, P. E.; Rodger, A. *Chem. Phys.* **1986**, *109*, 173.

(4) Richardson, F. S. *Chem. Rev.* **1979**, *79*, 17.

(5) Schipper, P. E. *J. Am. Chem. Soc.* **1978**, *100*, 3658.

(6) Schipper, P. E.; Rodger, A. *Chem. Phys.* **1986**, *98*, 29.

0002-7863/90/1512-1471$02.50/0