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A DFT Theoretical Analysis of Aldehyde Condensation Pathways onto Methyllithium, Lithium Dimethylamide, and Their Aggregates

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A DFT analysis of the condensation of monomeric methyllithium and lithium dimethylamide (LMA), as well as their homo and hetero dimers, on formaldehyde and acetaldehyde is reported. A stable complex, exhibiting a directional interaction between a lone pair of the oxygen on the aldehyde and a lithium, is first found. At this stage, the aldehyde carbonyl and the Li−X (X = C or N) bonds lie in the same plane. To proceed, the condensation reaction has to go through a transition state that mainly consists of a rotation of the aldehyde plane, placing it perpendicular to the C−C or C−N forming bond. The reaction then leads, in a strongly exothermic final step, to the addition product that is a lithium alcoholate or α-amino alcoholate, associating into an hetero-aggregate with the remaining moiety of the initial dimer. From the relative heights of the activation barriers, it appears that, for the heterodimer MeLi−LMA, the formation of the C−N bond should be kinetically favored over the C−C one, while the lithium ethylate resulting from the C−C binding is the thermodynamic product. A decomposition of the activation energy barriers has been carried out in order to determine the physicochemical forces responsible for the variation of the condensation activation barriers with the structure of the final species formed. The results obtained are discussed in relation with corresponding experimental data.

Introduction

Organolithium compounds are among the handiest nucleophilic reagents in organic synthesis, mainly because of their availability and their high affinity for most electrophiles. However, this latter advantage turns into a handicap when it comes to asymmetric synthesis since it requires particularly well suited chiral inductors to obtain chiral complexes more reactive than the nonasymmetric species present in the reaction medium. One solution to force an alkyllithium reagent to interact with a chiral partner prior to the reaction with the electrophile is to take advantage of the strong tendency, established both experimentally and theoretically, of these organometallics to form clusters organized around polycoordinated lithium atoms.[1] Chiral lithium amide, of which efficiency in asymmetric synthesis is not to be demonstrated anymore (especially as chiral bases),[2] have been rarely employed as mixed aggregates with alkyllithiums yet.[3] Consequently, these complexes have been the object of a restricted number of spectroscopical[4] and theoretical[5] investigations.

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(1) See, inter alia: (a) Brown, T. L. *Pure Appl. Chem*. **1970**, *23*, 447−462. (b) Novak, D. T.; Brown, T. L. *J. Am. Chem. Soc.* **1972**, *94*, 3793−3798. (c) Fraenkel, G.; Henrichs, M.; Hewitt, J. M.; Su, B. M.; Geckle, M. J. *J. Am. Chem. Soc.* **1980**, *102*, 3345−3350. (d) Schleyer, P. v. R. *Pure Appl. Chem*. **1984**, *56*, 151−162. (e) Bauer, W.; Winchester, W. R.; Schleyer, P. v. R. *Organometallics* **1987**, *6*, 2371−2379. (f) Sannigrahi, A. B.; Kar, T.; Guha Niyogi, B.; Hobza, P.; Schleyer, P. v. R. *Chem. Rev*. **1990**, *90*, 1061−1076. (g) Mulvey, R. E. *Chem. Soc. Rev.* **1991**, *20*, 167−209. (h) Collum, D. *Acc. Chem. Res.* **1993**, *26*, 227−234. (i) Bickelhaupt, F. M.; Eikema Hommes, N. J. R. v.; Fonseca Guerra, C.; Baerends, E. J. *Organometallics* **1996**, *15*, 2923−2931. (j) Abbotto, A.; Streitwieser, A.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1997**, *119*, 11255−11268. (k) Thompson, A.; Corley, E. G.; Huntington, M. F.; Grabowski, E. J. J.; Remenar, J. F.; Collum, D. B. *J. Am. Chem. Soc.* **1998**, *120*, 2028−2038. (l) Reich, H. J.; Sikorski, W. H.; Gudmundsson, B. O.; Dykstra, R. R. *J. Am. Chem. Soc.* **1998**, *120*, 4035−4036. (m) Reich, H. J.; Green, D. P.; Medina, M. A.; Goldenberg, W. S.; Gudmundsson, B. O.; Dykstra, R. R.; Phillips, N. H. *J. Am. Chem. Soc.* **1998**, *120*, 7201−7210. (n) Facchetti, A.; Streitwieser, A. *J. Org. Chem*. **1999**, *64*, 2281−2286.

(2) Reviews: a) Cox, P. J.; Simpkins, N. S. *Tetrahedron*: *Asymmetry* **1991**, *2*, 1−26. (b) O'Brien, P. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1439−1457. Recent important applications: (c) Amadji, M.; Vadecard, J.; Plaquevent, J. C.; Duhamel, L.; Duhamel, P. *J. Am. Chem. Soc.* **1996**, *118*, 12483−12484. (d) Evans, D. E.; Nelson, S. G. *J. Am. Chem. Soc*. **1997**, *119*, 6452−6453. (e) Manabe, S. *J. Chem. Soc., Chem. Commun*. **1997**, 737−738. (f) Shirai, R.; Sato, D.; Aoki, K.; Tanaka, M.; Kawasaki, H.; Koga, K. *Tetrahedron* **1997**, *53*, 5963−5972. (g) Aggarwal, V. K.; Humphries, P. S.; Fenwick, A. *Angew. Chem., Int. Ed. Engl*. **1999**, *38*, 1985−1986.

(3) (a) Eleveld M. B.; Hogeveen, H. *Tetrahedron Lett.* **1984**, *25*, 5187−5190. (b) Corruble, A.; Valnot, J. Y.; Maddaluno, J.; Duhamel, P. *Tetrahedron*: *Asymmetry* **1997**, *8*, 1519−1523. (c) Corruble, A.; Valnot, J. Y.; Maddaluno, J.; Duhamel, P. *J. Org. Chem*. **1998**, *63*, 8266−8275. (d) Arvidsson, P. I.; Hilmersson, G.; Davidsson, O. *Chem. Eur. J.* **1999**, *5*, 2348−2355. (e) Arvidsson, P. I.; Davidsson, O.; Hilmersson, G. *Tetrahedron*: *Asymmetry* **1999**, *10*, 527−534.

(4) (a) Hilmersson, G.; Davidsson, O. *J. Organomet. Chem.* **1995**, *489*, 175−179. (b) Corruble, A.; Valnot, J. Y.; Maddaluno, J.; Prigent, Y.; Davoust, D.; Duhamel, P. *J. Am. Chem. Soc.* **1997**, *119*, 10042−10048. (c) Williard, P. G.; Sun, C. *J. Am. Chem. Soc.* **1997**, *119*, 11693−11694. (d) Arvidsson, P. I.; Ahlberg, P.; Hilmersson, G. *Chem. Eur. J.* **1999**, *5*, 1348−1354. E)

(5) (a) Pratt, L.; Khan, I. M. *J. Comput. Chem*. **1995**, *16*, 1067−1080. (b) Fressigné, C.; Corruble, A.; Valnot, J. Y.; Maddaluno, J.; Giessner-Prettre, C. *J. Organomet. Chem.* **1997**, *549*, 81−88. (c) Balamraju, Y.; Sharp, C. D.; Gammill, W.; Manuel, N.; Pratt, L. M. *Tetrahedron* **1998**, *54*, 7357−7366. (d) Fressigné, C.; Maddaluno, J.; Giessner-Prettre, C. *J. Chem. Soc., Perkin Trans. 2* **1999**, 2197−2201.

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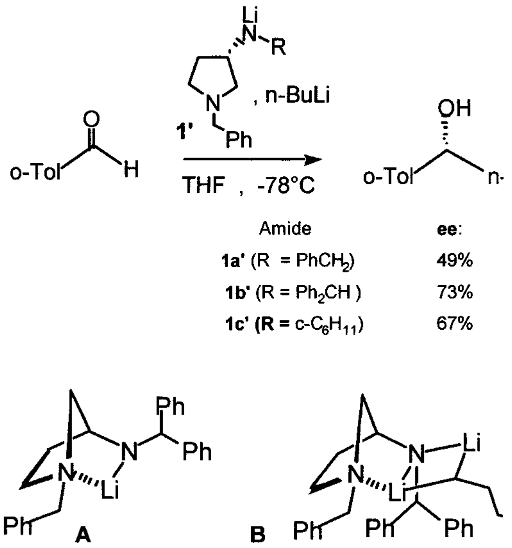
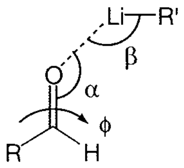
Scheme 1



Scheme 2



We have recently focused on complexes between alkyllithium compounds and chiral 3-aminopyrrolidine (3-AP) lithium amides. This system reacts with aldehydes, yielding the corresponding condensation alcohols in good yields and ee up to 73% (Scheme 1).[3b,c] A multinuclear NMR analysis together with an ab initio study have led us to propose the formation of a 1:1 complex between the 3-AP and the alkyllithium in solution at low temperature in THF.[4b,5b] The peculiar substitution pattern of the 3-AP folds the pyrrolidine skeleton following a norbornyl-like topology around the lithium atom upon deprotonation (Scheme 1A). Both experimental NMR and DFT calculations indicate that this folding is preserved upon complexation of the alkyllithium and leads to species in which the two lithium atoms belong to a quadrilateral N−Li−C−Li core (Scheme 1B).[4b,5b] In absence of any clue about a link between the existence of such a chiral aggregate and the observed asymmetric induction after the aldehyde condensation step, and considering that getting clear spectroscopic evidences during the final microsteps would constitute a technical challenge,[6,7] we thought that a theoretical analysis of the evolution of the corresponding species after their preliminary complexation could offer a more appropriate way of tackling this problem.

If the trajectory of the nucleophile during addition on the C=O double bond has been the object of detailed investigations,[8] the theoretical studies dedicated to the aldehyde/alkyllithium condensation problem are relatively scarce[9] while no description of the addition pathway of lithium amides onto carbonyl compounds has been reported to our knowledge.[10] A first highly accurate examination of the reaction pathway between monomeric/dimeric methyllithium and formaldehyde has been undertaken by Houk, Schleyer and colleagues at the SCF ab initio level, using the 3-21G basis set, as early as 1985.[9a] These authors have found that the docking of dimeric methyllithium by formaldehyde leads to a stable complex **A** in which the C=O and Li atoms are almost collinear ($\alpha = 176°$, Scheme 2), the aldehyde plane and the methyllithium dimer core plane being perpendicular to each other (Figure 1, left). This step is associated to an interaction energy of −23.9 kcal/mol. The following rotation of the aldehyde is characterized by an activation barrier of +9.4 kcal/mol and a six-center transition state **B**. The carbon−carbon connection finally provides the lithium ethylate/methyllithium mixed dimer **C** and corresponds to a −74.7 kcal/mol step.

Another set of results, published in 1993/94 by Morokuma et al.,[9b,c] investigates the interaction between the same methyllithium dimer, formaldehyde and acetaldehyde (Figure 1, right). These computations, undertaken at the Hartree−Fock level with the larger 6-31+G* basis set, lead to a preliminary complex **A′** that features a directional O−Li binding along one oxygen lone pair (C−O−Li ≈ 120°), the methyllithium dimer and the aldehyde sharing the same plane this time. From this starting point, the authors describe the rotation of the aldehyde plane yielding an open dimer **A″** that finally converts, with an extremely low activation barrier, into a transition state almost identical to that found by Houk and Schleyer (**B**). The importance of one water molecule (the solvent model) on Li^1 is clearly put into evidence in this second study, since the A′ → A″ step becomes significantly endothermic in the absence of solvation (+8.8 kcal/mol), while the presence of a second molecule of water on Li^2 tends to close back the open A″ into A′.

We have based our own study on these well-established grounds; however, at least three new problems arise when dealing with mixed dimers: (1) the relative stability of these heterogeneous aggregates with respect to their homogeneous counterparts needs to be evaluated; (2) the possibility of getting a C−C or C−N bond formation requires both pathways to be investigated and the factors governing the preferences for one or the other route to be delineated; and (3) the relative stability of the final products (alkoxide vs α-aminoalkoxide) has to be examined.

To get as a complete and meaningful picture as possible, we thought necessary to investigate, at a same theoretical level, the interactions of (1) monomeric methyllithium (MeLi) and lithium dimethylamide (Me_2NLi);

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(6) A rapid-injection NMR study, such as the classical work described by McGarrity et al. (McGarrity, J. F.; Ogle, C. A.; Brich, Z.; Loosli, H. R. *J. Am. Chem. Soc.* **1985**, *107*, 1810−1815), could provide additional information, albeit it is likely to be severely limited by the rapidity of the reaction considered.

(7) For a recent application of this technique to intermediates caracterization, see: Ogle, C. A.; Wang, X. L.; Carlin, C. M.; Strickler, F. H.; Gordon, B., III. *J. Polym. Sci.* **1999**, *37*, 1157−1168.

(8) For important contributions in this field, see: (a) Bürgi, H. B.; Dunitz, J. D.; Lehn, J. M.; Wipff, G. *Tetrahedron* **1974**, *30*, 1563−1572. (b) Eisenstein, O.; Schlegel, H. B.; Kayser, M. M. *J. Org. Chem.* **1982**, *47*, 2886−2891. (c) Menger, F. M. *Tetrahedron* **1983**, *39*, 1013−1040. (d) Liotta, C. L.; Burgess, E. M.; Eberhardt, W. H. *J. Am. Chem. Soc.* **1984**, *106*, 4849−4852.

(9) (a) Kaufmann, E.; Schleyer, P. v. R.; Houk, K. N.; Wu, Y. D. *J. Am. Chem. Soc.* **1985**, *107*, 5560−5562. (b) Nakamura, M.; Nakamura, E.; Koga, N.; Morokuma, K. *J. Am. Chem. Soc.* **1993**, *115*, 11016−11017. (c) Nakamura, M.; Nakamura, E.; Koga, N.; Morokuma, K. *J. Chem. Soc., Faraday Trans.* **1994**, *90*, 1789−1798. (d) Mori, S.; Kim, B. H.; Nakamura, M.; Nakamura, E. *Chem. Lett.* **1997**, 1079−1080.

(10) This reaction has proved to be syntheticaly useful: (a) Comins, D. L.; Brown, J. D.; Mantlo, N. B. *Tetrahedron Lett.* **1982**, *23*, 3979−3982. (b) Comins, D. L. *Synlett* **1992**, 615−625. For a recent structural study on lithium α-aminoalkoxides, see: (c) Armstrong, D. R.; Davies, R. P.; Raithby, P. R.; Snaith, R.; Wheatley, A. E. H. *New J. Chem.* **1999**, *23*, 499−507.

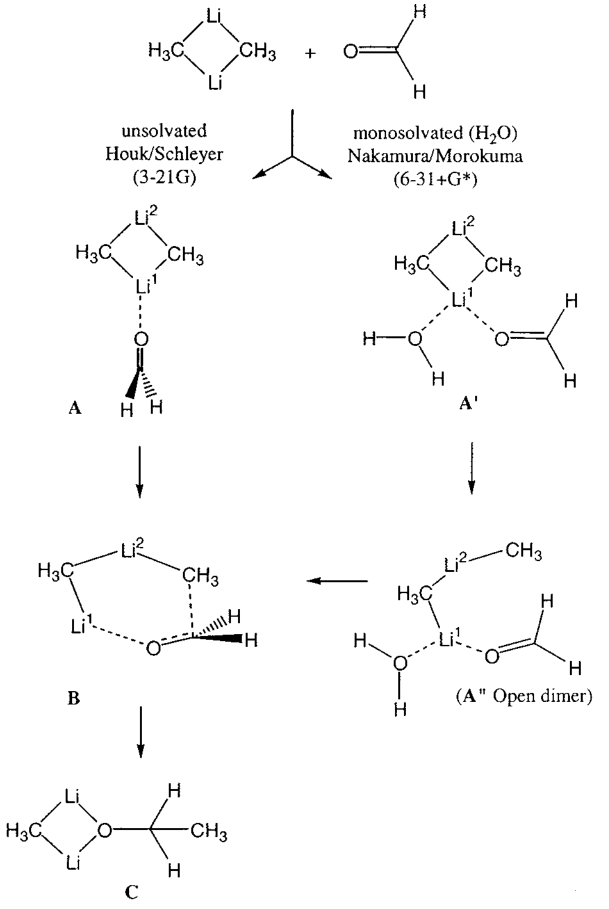

Figure 1. Condensation pathways for the formaldehyde/methyllithium dimer system according to literature (ref 9).

(2) the $(MeLi)_2$ and $(Me_2NLi)_2$ homodimers; and (3) the $MeLi-Me_2NLi$ heterodimer with two model aldehydes (formaldehyde and acetaldehyde). No higher order aggregates have been considered since dimers have been shown to hold the key role, in THF, during the condensation between butyllithium and aldehydes.[6] Furthermore, the experimental system involving 3-AP lithium amide and alkyllithium compounds at the origin of this study is considered dimeric.[4b] We want to underline that the sole addition pathways onto the aldehydes have been taken into account (while the enolization is likely to be favored with acetaldehyde)[5c] since the experimental results have been performed on nonenolizable aldehydes.[3c] It is finally important to note that we have resorted, all along this study, to DFT (B3P86) computations. The reasons underlying the choice of this technique are 2-fold: (1) the correlation is homogeneously taken into account for all steps of the reaction path; (2) our ultimate goal is the investigation of complexes between 3-AP lithium amides and alkyllithiums that are large systems difficult to account for through classical post Hartree–Fock ab initio approaches within realistic CPU times. To obtain indications on the forces responsible for the chemioselectivity of the condensation, we undertook, in the case of formaldehyde, a constrained space orbital variation (CSOV) analysis[11] of the two activation energy barriers corresponding to the formation of the C–C or C–N bonds.

Computational Details

Apart for a few exceptions mentioned below, the computations have been carried out using the 6-31G** basis set.[12] For consistency with our previous work on the systems considered in the present study, the optimizations have been done using the B3P86 hybrid functional.[13] Since DFT has been shown to underestimate this type of quantity,[14] we have repeated, for the methyllithium/formaldehyde and lithium dimethylamide/formaldehyde systems, the calculation of the activation barriers with the 6-311++G** basis, using B3P86 DFT on one hand and MP2 on the other. The results of these computations show that the relative height of the activation barriers is not depending on the method nor on the basis set.[15] This stability warrants the relevance of this study since our computations deal with simple model for which only relative values remain meaningful. It is worth mentioning that these low activation energies prompted us to perform a relaxed potential energy surface scan prior to the optimization of the transition states, the C–C/C–N distance corresponding to the bond formed being taken as the reaction coordinate. The transition states were characterized by frequency calculations and checked from intrinsic reaction coordinates (IRC) runs for the same two condensations. Finally, let us underline that neither the basis set superposition errors (BSSE) nor the zero-point energy corrections have been included in our results. These factors are indeed of relatively minor importance[16] with respect to the neglected solvation effect on the systems considered in this work (see discussion below) since they do not modify the relative order of the complex stabilities nor that of the activation barriers. These series of computations have been carried out using GAUSSIAN98.[17]

The interaction energy decompositions, which give access to the electrostatic E_{elec}, exchange/steric E_{exc}, polarization of entity A by the electric field generated by entity B E_{pol} and charge-transfer E_{ct} contributions, have been done using the constrained space orbital variation (CSOV)[11] method as implemented in a modified[18] version of HONDO95.3.[19] These computations were carried out using the B3LYP functional.[20] We had to make this shift because the B3P86 functional is not implemented in HONDO, the B3LYP being the only hybrid functional, as B3P86 is, available from this software.

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[11] Bagus, P. S.; Hermann, K.; Bauschlicher, C. W., Jr. *J. Chem. Phys.* **1984**, *80*, 4378–4386.

[12] Frisch, J. M.; Pople, J. A.; Binkley, J. S. *J. Chem. Phys.* 1984, **80**, 3265–3269.

[13] (a) Perdew, J. P. *Phys. Rev.* **1986**, *B33*, 8822–8824. (b) Becke, A. D. *J. Chem. Phys.* **1989**, *90*, 5622–5629.

[14] See, for instance: (a) Fan, L.; Ziegler, T. *J. Am. Chem. Soc.* **1992**, *114*, 10890–10897. (b) Stanton, R. V.; Merz, K. M., Jr. *J. Chem. Phys.* **1994**, *100*, 434–443.

[15] Activation energies (kcal/mol): MeLi/HCHO, B3P86/6-31G**, 0.9; B3P86/6-311++G**, 0.9; MP2/6-311++G**, 3.7. $Me_2NLi/HCHO$, B3P86/6-31G**, 0.5; B3P86/6-311++G**, 0.2; MP2/6-311++G**: 3.3.

[16] For the condensations of acetaldehyde on the mixed MeLi–$LiNMe_2$ aggregate, the complexation and activation energies, taking into account the BSSE and Zero-Point corrections, are 11.6 and 9.7 kcal/mol (instead of 16.9 and 8.9 kcal/mol) for the condensation on the carbon, and 12.0 and 2.7 kcal/mol (instead of 17.3 and 2.6 kcal/mol) for the condensation on the nitrogen (see Tables 3 and 4).

[17] GAUSSIAN 98 (Revision A5): Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewfki, V. G.; Montgomery, J. A.; 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, F.; 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 Inc., Pittsburgh, PA, 1998.

[18] CSOV implementation by A. Marquez (unpublished work).

[19] Dupuis, M.; Marquez, A.; Davidson, E. R. "HONDO 95.3" Quantum Chemistry Program Exchange (QCPE) Indiana University, Bloomington, IN 47405.

[20] Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648–5652. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev.* **1988**, *B37*, 785–789. (c) Miehlich, B.; Savin, A.; Stoll, H.; Preuss, H. *Chem. Phys. Lett.* **1989**, *157*, 200–206.

Table 1. Variation of the Energy (au) of the Optimized Linear and Bent Complexes between Formaldehyde and Methyllithium or Lithium Dimethylamide with the Computational Level and the Basis Set

entry	complex	basis set computational level	linear	bent	ΔE (kcal/mol)
1	$MeLi-H_2CO$	RHF/3-21G	−160.0186	−160.0188	−0.1
2		MP2/6-31G**	−161.4001	−161.4021	−1.3
3		B3P86/6-31G**	−162.4249	−162.4270	−1.3
4		B3P86/6-311++G (3df,3pd)	−162.4809	−162.4832	−1.4
5	Me_2NLi-H_2CO	RHF/3-21G	−253.5765	−253.5783	−1.1
6		MP2/6-31G**	−255.7975	−255.8016	−2.6
7		B3P86/6-31G**	−257.4050	−257.4057	−0.4

Results and Discussion

The directionality of the oxygen−lithium interaction constitutes an important preliminary point in this study. We therefore compared, at different computational levels and basis sets, the stability of the complexes between formaldehyde (H_2CO) and both monomeric MeLi and LMA following a linear and an angular C−O−Li arrangement (angle α, Scheme 2). The optimizations lead to two local minima that are found for the two types of complexes. The corresponding energy data, gathered in Table 1 and Table 1* (Supporting Information), show that the RHF/3-21G calculations (entry 1) give two isoenergetic arrangements for $MeLi-H_2CO$. Entries 2−4 of Table 1 and those of Table 1* also indicate that the extension of the basis set to 6-31+G*, adopted by Morokuma and colleagues[9b,c] stabilizes, at all the computational levels considered, the bent complex with respect to the linear one. For the Me_2NLi-H_2CO complex (entries 5−7), the results are qualitatively the same than those for the $MeLi-H_2CO$ system. The arrangement in which one of the oxygen lone-pair coordinates the metal cation seems therefore always preferred. Further extending the basis set improves, as expected, the overall energy of the complex but does not alter significantly the relative stabilizations, even for such extended bases as 6-311++G-(3df,3pd)[12,21,22] or D95++G(3df,3pd)[12,22,23] as can be seen from Table 1 and Table 1*. Therefore, only the bent complexes will be considered in the rest of this work.

Regarding the orientation of the nucleophile itself with respect to the aldehyde (angle β, Scheme 2), the full optimization of all the systems considered in this work leads also to a “bent” arrangement. The origins of this orientation have not been thoroughly examined but the dispersion effects seem to be involved to some extent since in the case of the $MeLi-H_2CO$ system, β varies from 132° to 122° when going from HF- to DFT-optimized complexes. Finally, the values we find for α and β are in excellent overall agreement with those reported by Ammal and colleagues[24] for the $H_2CO-LiF$ system. In all cases the dihedral angle ϕ is equal to 180°.

The absolute energies calculated at the B3P86/6-31G** level for all the monomeric and dimeric species considered in this study are given in Table 2, together with the dimerization energies. These data show that, as reported before,[5b] the mixed aggregate $MeLi-Me_2NLi$ is only slightly favored over the homogeneous complexes $(MeLi)_2$ and $(Me_2NLi)_2$ by 0.2 kcal/mol. In Table 3 are gathered the interaction energies between the two model aldehydes and their various organolithium partners to provide the corresponding complexes. This preliminary step is always exothermic and leads to a local minimum of which topology will be discussed for each case in the forthcoming paragraphs.

Table 2. Energies (au) after Complete Optimization for the Species Considered in This Work (B3P86/6-31G)[a]**

species	energy
H_2CO	−114.7837
CH_3CHO	−154.2631
MeLi	−47.6140
Me_2NLi	−142.5893
$(MeLi)_2$	−95.2992 (−44.6)
$(Me_2NLi)_2$	−285.2738 (−59.8)
$(MeLi-Me_2NLi)$	−190.2861 (−52.4)

[a] The interaction energy of the dimers is given in parantheses (kcal/mol).

Table 3. Interaction Energy (kcal/mol) in the Optimized Complexes between Aldehydes and Organolithium Compounds (B3P86/6-31G)**

organolithium	formaldehyde	acetaldehyde
MeLi	−18.3	−21.2
$(MeLi)_2$	−15.4	−17.0
$(\mathit{Me}Li-Me_2NLi)^a$	−15.3	−16.9
Me_2NLi	−20.4	−22.1
$(Me_2NLi)_2$	−14.7	−16.3
$(MeLi-Me_2\mathit{N}Li)^a$	−16.8	−17.3

[a] Bending of the carbonyl toward the underlined member of the complex.

Formaldehyde−Monomeric Species Reactivity. The $MeLi-H_2CO$ and Me_2NLi-H_2CO condensation pathways have been studied first. Starting from the bent $MeLi-H_2CO$ complex above, the system yields the final product (lithium ethylate) through a transition state located along the 90° rotation of the aldehyde plane out of the original C−Li−O plane ($\phi = 139°$, Figure 2A and Table 4). The condensation is calculated to be exothermic by 42.2 kcal/mol with respect to the initial complex and 60.6 kcal/mol with respect to the separated reagents. The low activation barrier (0.9 kcal/mol) found in this case is worth underlining and indicates that monomeric methyllithium, would it exist in solution, would act as a highly reactive species toward aldehydes. This barrier is much lower than that computed by Houk and Schleyer[9a] when starting from the linear $MeLi-H_2CO$ complex; this difference makes sense considering the better proximity between the bent complex and the TS.

The condensation of LMA with formaldehyde starts also from the bent complex and goes through a transition state lying along the aldehyde rotation process ($\phi = 148°$, Figure 2B and Table 4), as in the methyllithium case. The final product is a lithium α-amino alcoholate (lithium dimethylaminomethylate) that lies 32.3 kcal/mol lower than the starting complex, that is 52.8 kcal/mol with respect to the isolated species. The activation barrier is

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(21) (a) McLean, A. D.; Chandler, G. S. *J. Chem. Phys.* **1980**, *72*, 5639−5648. (b) Krishnan, R.; Binkley, R.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650−654.

(22) Clark, T.; Chandrasekhar, J.; Spitznagel, G. W.; Schleyer, P. v. R. *J. Comput. Chem.* **1983**, *4*, 294−301.

(23) Dunning, T. H., Jr.; Hay, P. J. In *Modern Theoretical Chemistry*; Schaeffer, H. F., III, Ed.; Plenum: New York, 1976; Vol. 3, p 1.

(24) Ammal, S. S. C.; Venuvanalingam, P.; Pal, S. *J. Chem. Phys.* **1997**, *107*, 4329−4336.

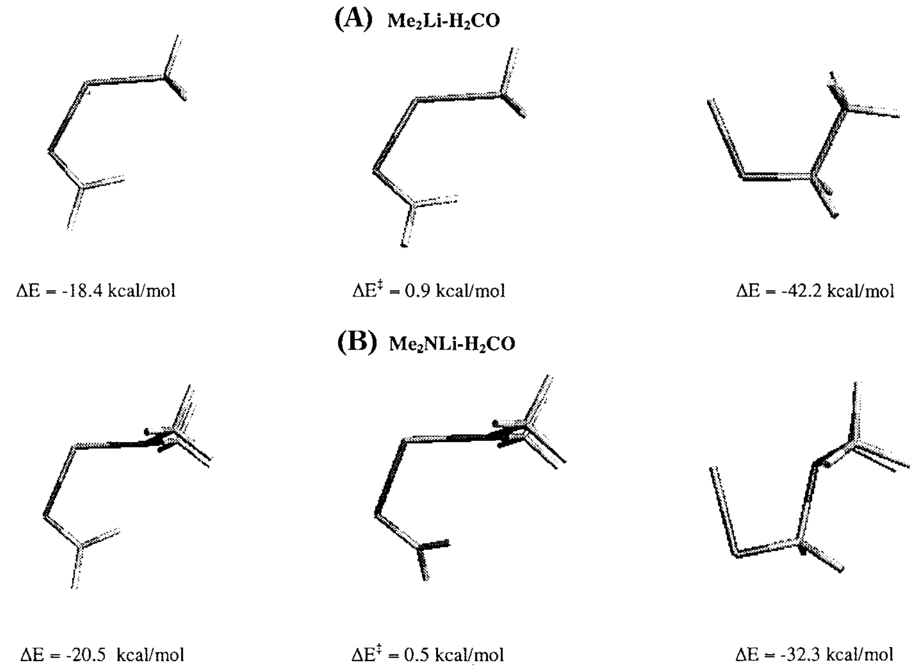


Figure 2. Optimized structures of the preliminary complex (left), transition state (center), and condensation product (right) during the reaction between formaldehyde and monomeric methyllithium (2A) and lithium dimethylamide (2B).

Table 4. Activation Barrier (kcal/mol) and Torsion Angle ϕ (Scheme 2) for the Transition State of the Condensation between Aldehydes and Organolithium Compounds (B3P86/6-31G)**

	formaldehyde		acetaldehyde	
organolithium	$\Delta E^{\ddagger}$	ϕ	$\Delta E^{\ddagger}$	ϕ
MeLi	+0.9	139	+2.5	132
$(MeLi)_2$	+5.1	97	+9.7	112
(*Me*Li-Me$_2$NLi)^a	+4.6	122	+8.9	113
Me_2NLi	+0.5	148	+1.1	143
$(Me_2NLi)_2$	+2.4	131	+2.8	124
(MeLi-Me$_2$*N*Li)^a	+1.9	158	+2.6	122

[a] Bending of the carbonyl toward the underlined member of the complex.

lower than the corresponding value for methyllithium (0.5 kcal/mol) and has not been evaluated before to our knowledge. This trend is found all along the results we have obtained in this work (vide infra) and suggests also that lithium amides tend to add extremely easily onto carbonyl. Experimentally, this reaction is well-known to give access to α-aminoalkoxides.[3b,10a,b] It is finally worth underlining that the methyllithium condensation onto the carbonyl is significantly more exothermic (by 9.9 kcal/mol).

Formaldehyde–Homodimer $(MeLi)_2$ and $(LiNMe_2)_2$ Reactivity. The interaction between the dimeric organolithium compounds and the aldehyde is probably a more realistic model of the situation in solution, according to McGarrity's experimental results on *n*-butyllithium in THF,[6] as in the case of interest to us. Let us first consider the case of dimeric methyllithium. We have previously reported the dimerization energy of MeLi (−44.7 kcal/mol) at the same computational level.[5b,d] The most stable "bent" $(MeLi)_2{-}H_2CO$ complex represented on Figure 3A is associated to a −15.4 kcal/mol complexation energy, i.e., somewhat smaller than the −18.4 kcal/mol occurring between the same aldehyde and the monomeric MeLi. From this starting point the system goes through a transition state very comparable to that described above, in which the tilting of the aldehyde plane (ϕ = 97°), originally merged with the C−Li−C−Li quadrilateral plane, is taking place to favor the formation of the new C−C bond. A 5.1 kcal/mol barrier is associated to this rotation which ends up with the formation of a mixed dimer between the newly formed lithium ethylate and the remaining MeLi unit. It is worth mentioning that no open dimer intermediate was found along the relaxed potential energy surface going from the initial complex to the final product. This is in full agreement with Nakamura−Morokuma's analysis, that had pointed out the importance, in their model, of the monosolvation of one lithium ion to reach an open dimer, described as an inflection point on the potential surface.[9c] The activation barrier associated to our TS (5.1 kcal/mol) is in the range found in the more recent previous study (3.3−9.2 kcal/mol), in which computations have been performed at two different basis set/computational levels. The topologies of the two TS are also very similar. The condensation leads to the formation of the expected mixed dimer in which the newly formed lithium ethylate shares its lithium with the remaining MeLi unit. The association between the alcoholate and the alkyllithium during the course of the reaction has also been evidenced experimentally by McGarrity for the *n*-butyllithium/benzaldehyde system.[6] Our computations place this final complex 56.9 kcal/mol lower than the starting complex, a value that compares nicely to the 62.1/66.5 kcal/mol found by Morokuma for the same system.

Let us now consider the case of $(Me_2NLi)_2$; a −59.7 kcal/mol dimerization energy is calculated for this system.[5d] The docking of formaldehyde on the lithium of this dimer leads to an angular binding represented in Figure 3B. Again, this complexation is less favored energywise (−14.7 kcal/mol) than that characterizing the monomer/aldehyde interaction (−20.5 kcal/mol). The corresponding transition state is once more associated to the rotation of the aldehyde plane (ϕ = 131°, Table 4 and Figure 3B). A 2.4 kcal/mol activation barrier is associated to this TS. When the condensation process is achieved, a mixed

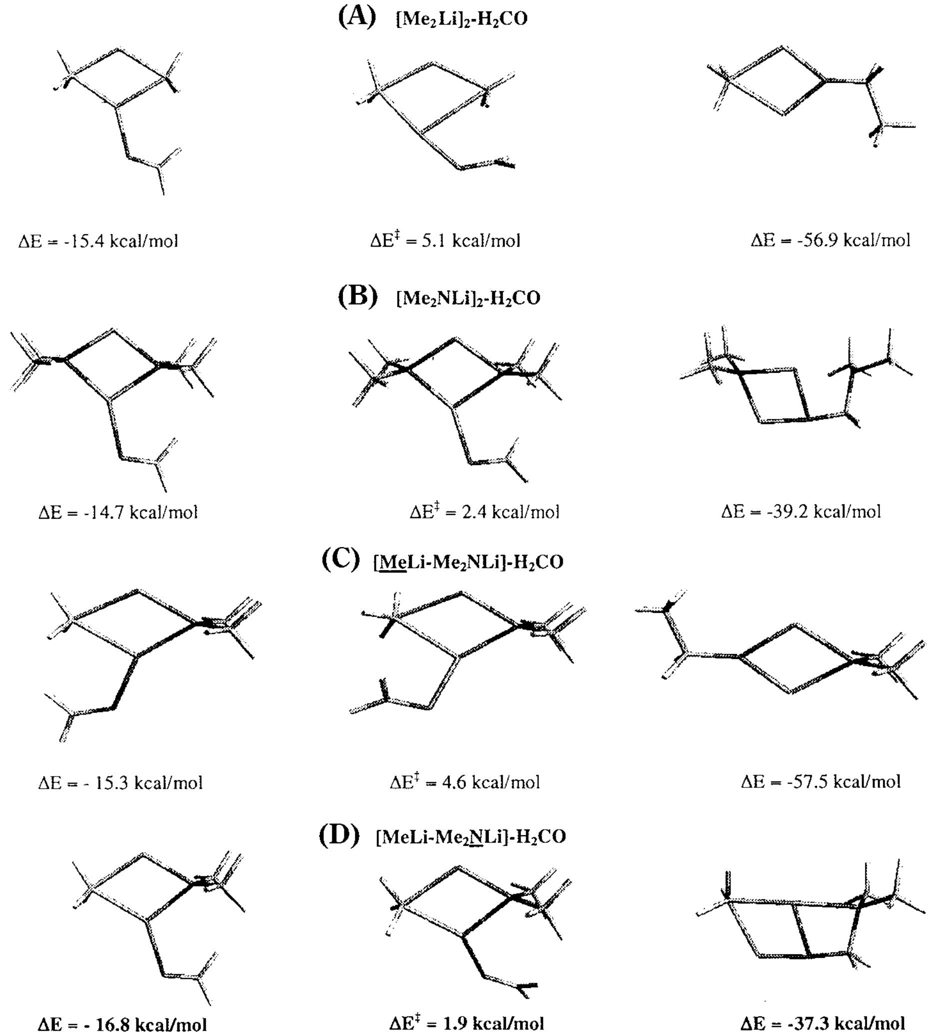


Figure 3. Optimized structures of the preliminary complex (left), transition state (center), and condensation product (right) during the reaction between formaldehyde and dimeric methyllithium (A), lithium dimethylamide (B), and the mixed aggregate between methyllithium and lithium dimethylamide, with the carbonyl bending on the carbon side (C) or on the nitrogen side (D).

dimer between the newly formed lithium dimethylaminomethylate and the remaining LMA unit is promoted. This corresponds to a stabilization energy of −39.2 kcal/mol (with respect to the starting complex). Therefore, the comparison between the alkyllithium and lithium amide leads to identical conclusions for the monomeric and dimeric situations: the condensation of the amide on the carbonyl group occurs with a lower overall activation barrier while the corresponding adducts are associated to significantly smaller exothermicities.

Formaldehyde−Heterodimer MeLi−Me$_2$NLi Reactivity. The interaction between MeLi and LMA is associated to a −49.3 kcal/mol stabilization. For this disymmetric complex, two binding orientations have to be considered. The CH_2 moiety of the formaldehyde can indeed be directed either toward the methyl group or the dimethylamino appendage. Actually, this initial arrangement is likely to exert a determining influence on the pathway further followed by the reaction. Let us first consider the case of the complexation on the methyl side (Figure 3C). A −15.3 kcal/mol stabilization energy characterizes this interaction. The complex then evolves into a TS relatively similar to those obtained for the homogeneous dimers above, viz. corresponding to a partial rotation ($\phi = 122°$, Table 4) of the aldehyde plane off the C−Li−N−Li planar core. A comparable 4.6 kcal/mol barrier is computed for this step. As expected, the system ends up yielding the mixed lithium alcoholate-lithium amide dimer which lies 57.5 kcal/mol lower than the starting complex, a value almost identical to that found for the $(MeLi)_2-H_2CO$ condensation product. This new heterodimer is stabilized by a −48.9 kcal/mol binding energy between lithium ethylate and lithium dimethylamide.

When formaldehyde is oriented toward the amino part of the complex (Figure 3D), the complexation is associated to a −16.8 kcal/mol binding energy, that is a 1.5 kcal/mol increased affinity when compared to the opposite orientation. The condensation transition state is reached after the usual rotation of the carbonyl plane ($\phi = 158°$, Table 4) and resembles greatly to that obtained above for the homogeneous $(Me_2NLi)_2$. The twist seems particularly easy in this case since a low 1.9 kcal/mol barrier is calculated. The condensation final phase provides the methyllithium/α-amino alcoholate mixed dimer through a −37.3 kcal/mol exothermic step. Finally, this new heterodimer stabilization is secured by a −48.3 kcal/mol complexation energy between its constituents.

The two initial complexes of Figure 3, parts C and D, can also interconvert one into the other by a simple

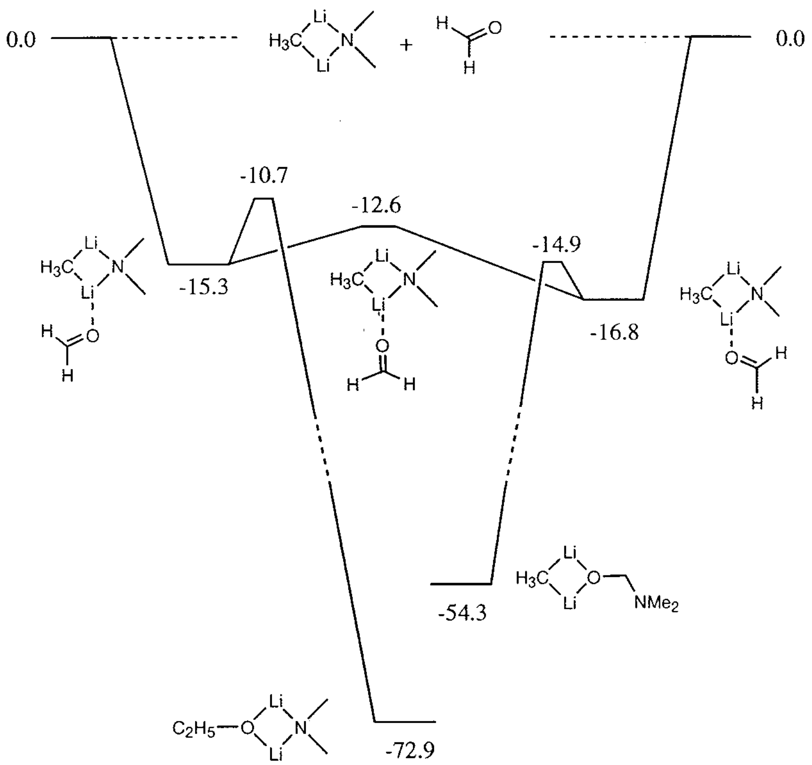


Figure 4. Energetics of the various possible pathways during the condensation of formaldehyde on the mixed MeLi−Me_2NLi aggregate.

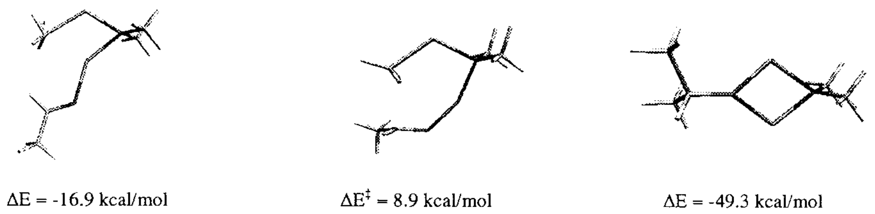
rotation of the formaldehyde group. It was thus necessary to characterize the activation barrier associated to this rearrangement. This new TS puts the aldehyde somewhat halfway between the methyl and the amide (with an almost linear C−O−Li arrangement, Figure 4) and is computed to lie 2.8 kcal/mol above initial complex 3C. This value is worth considering with respect to the 4.6 kcal/mol barrier on the MeLi−H_2CO condensation route. It indeed indicates that the less stable complex 3C, a likely prelude to the C−C bond formation, will rather rearrange into complex 3D, precursor of the C−N bond, than provide the condensation lithium ethylate (Figure 4). Therefore, kinetics favor by all means the C−N bond formation at the expenses of the C−C one, while the thermodynamics product is definitely lithium ethylate.

This result is of chemical relevance in the context of the recent applications of mixed aggregates between alkyllithium and chiral lithium amides in asymmetric synthesis.[3] The amide will indeed behave as a proper chiral inductor only if: (1) it tends to aggregate with the alkyllithium to form heterodimers, sufficiently stabilized with respect to the homodimers; (2) it is sterically crowded to make the C−N bond formation more difficult than the C−C one; and (3) its structural characteristics channels the docking of the aldehyde on the aggregate. These three requirements dictate the structural alterations to be brought to the amide to increase the chemio- and enantioselectivities of such systems in favor of the alkylation product. Also of interest is the difference between the activation energies for the C−C bond formation resulting from the $(MeLi)_2$ or from the (MeLi−Me_2NLi) interaction with formaldehyde: the 5.1 kcal/mol barrier in the first case decreases to 4.6 kcal/mol in the second situation. This difference tends to indicate that the mixed aggregate should be slightly more reactive than the alkyllithium homodimer; therefore, the chiral induction should be more or less independent of the alkyllithium to lithium amide ratio, as long as this ratio does not become too large of course. This has been verified experimentally in at least two cases[3c,e] and opens the door to the conception of efficient catalytic systems.

Reactivity with Acetaldehyde. Most points considered above for the formaldehyde-organolithium monomers/dimers interactions remain the same when switching to acetaldehyde and will therefore not be discussed in details. The preliminary complexes have basically the same geometrical characteristics, the bent complex being always favored. The methyl group of the aldehyde can be oriented in an “endo” or “exo” fashion with respect to the lithium core of the organometallic (Figure 5 and Figure S1, Supporting Information). These two situations lead to quasi-isoenergetic complexes, but only the “endo” arrangement is shown here since the “exo” situation leads to a proton transfer corresponding to an aldolisation reaction.[5c] The data in Table 3 show that this preliminary docking phase is always more exothermic with acetaldehyde than with formaldehyde, in general by 1.5−1.7 kcal/mol, except with monomeric MeLi where a large 2.9 kcal/mol gap is computed and with the mixed MeLi-Me_2NLi complex where a small 0.5 kcal/mol difference is found when the aldehyde binds to the amide side.

The passage to the transition states corresponds, in a fashion very similar to the case of formaldehyde, to a rotation of the carbonyl out of its original plane (Table 4) simultaneously to the C−C or C−N distance shortening. The activation barriers are however increased by a 2-fold factor, in the case of the C−C bond formation, and a lesser one in the case of the C−N linkage, with respect to those obtained for the smaller model aldehyde (Table 4). In the case of the mixed MeLi−Me_2NLi complex (Figure 5), the relative heights of the barriers indicate that the C−N binding is always kinetically favored (8.9

(A) [MeLi-Me$_2$NLi]-MeCHO



(B) [MeLi-Me$_2$NLi]-MeCHO

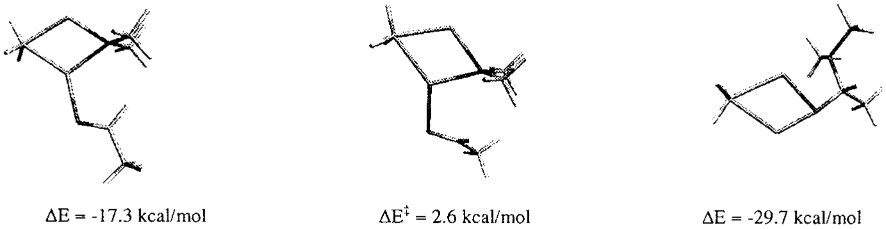


Figure 5. Optimized structures of the preliminary complex (left), transition state (center), and condensation product (right) during the reaction between acetaldehyde and the MeLi-Me$_2$NLi mixed aggregate, with the carbonyl bending on the carbon side (A) or on the nitrogen side (B).

Table 5. Values of the Different Contributions to the Activation Energy $\Delta E^\ddagger$ (Values in kcal/mol) for the Formaldehyde Condensation on Methyllithium Dimer and Methyllithium−Lithium Dimethylamide Complex (B3LYP/6-31G)**

	$(MeLi)_2-H_2CO$			*Me*Li−Me$_2$NLi−H$_2$CO			MeLi−Me$_2$*N*Li−H$_2$CO		
energy term	complex	TS	$\Delta E^\ddagger$	complex	TS	$\Delta E^\ddagger$	complex	TS	$\Delta E^\ddagger$
$E_{agg}{}^{a,b}$	−94.8797	−94.8511	17.9	−189.5753	−189.5739	0.9	−189.5720	−189.5745	−1.5
$E_{H_2CO}{}^{a}$	114.5005	−114.4970	2.2	−114.5005	−114.5006	−0.1	−114.4998	−114.5005	−0.4
$E_{dist}{}^{c,d}$			20.1			0.8			−1.9
$E_{elec}{}^{c}$	−15.9	−35.9	−20.0	−15.6	−14.6	2.0	−21.4	−16.5	4.9
$E_{exc}{}^{c}$	7.4	43.5	38.1	+7.7	12.2	4.5	24.6	10.2	−14.4
$E_1{}^{c}$	−8.5	7.6	16.1	−7.9	−2.4	5.5	3.2	−6.3	−9.5
$E_{pol(H_2CO)}{}^{c}$	−2.6	−8.3	−5.7	−2.4	−2.8	−0.4	−2.9	−2.4	0.5
$E_{ct(H_2CO\rightarrow agg)}{}^{c}$	−5.3	−7.0	−1.7	−5.3	−5.4	−0.1	−5.8	−5.3	0.5
$E_{pol(agg)}{}^{c}$	−0.5	−2.6	−2.1	−0.6	−0.7	−0.1	−2.1	−0.9	1.2
$E_{ct(agg\rightarrow H_2CO)}{}^{c}$	−1.0	−16.8	−15.8	−1.0	−1.8	−0.8	−11.0	−2.1	8.9
$E_{SCF}{}^{c}$	0.0	−4.1	−4.1	0.0	−0.1	−0.1	−1.2	−0.1	1.1
$E_2{}^{c}$	−9.5	−38.9	−29.4	−9.3	−10.8	−1.5	−23.0	−10.8	12.2
$E_1 + E_2{}^{c}$	−17.9	−31.3	−13.4	−17.2	−13.2	4.0	−19.8	−17.1	2.7
$E_{tot}{}^{a}$	−209.4088	−209.3977	7.0	−304.1033	−304.0955	4.9	−304.1036	−304.1023	0.8

[a] Values in au except for $\Delta E^\ddagger$. [b] E_{agg} is the total energy of the organolithium dimer. [c] Values in kcal/mol. [d] E_{dist} is the distortion energy undergone by the reactants in the transition state.

kcal/mol activation for the C−C binding, 2.6 for the C−N). Finally, the condensation products (viz. lithium isopropylate or 1-dimethylamino lithium ethylate) are obtained after a strongly exothermic step, the lithium ethylate deriving from the C−C bond formation being always more stable than the lithium α-aminomethylate obtained after the C−N bond formation (by about 10 kcal/mol for monomeric lithiated species and about 20 kcal/mol for the dimers, with respect to the original complexes). In the case of the dimeric reagents, the most stable final system corresponds once again to the mixed dimer between the lithium alkoxide and the unreacted lithiated moiety of the initial dimer. The factors orienting the kinetic/thermodynamic course of the reaction seem therefore to be the same for the two aldehydes considered here. Let us notice that in this case also the activation barrier for the condensation decreases when going from the homodimers to the mixed aggregate.

CSOV Analysis of the Transition State Activation Energies. The recent implementations of both the CSOV energy decomposition method and the density functional treatments (DFT) in HONDO 95.3[19] prompted us to undertake a set of calculations in an attempt to determine which physicochemical factor(s) is (are) responsible for the variation of the calculated activation energies with the exact structure of the organolithium aggregate and the nature of the bond formed (C−C vs C−N). This part of the work has been restricted to the $(MeLi)_2-H_2CO$ and [Meli−Me$_2$NLi]−H$_2$CO systems. The total activation energy is made of two distinct parts. One corresponds to the energy variation undergone by the reactants when going from the complex to the transition state. The second is due to the variation, between the complex and the transition state, of the reactants intermolecular interaction energy, the different contributions of which are given by the CSOV analysis.

The intermolecular interaction energy decomposition scheme was first applied to the three different complexes formed between the two aggregates and formaldehyde (vide supra). The same computations were repeated for the three transition states. The corresponding results are reported in Table 5 altogether with total energies of the reactants since the variation of their energy when going from the complex to the transition state contributes to the activation energy. Before discussing the results we have to underline that the activation barrier values obtained from these calculations are numerically different from those given in Table 4 for the same reaction since the functional used in these computations is B3LYP and no longer B3P86 as in optimization runs.

The tabulated values show clearly that the three activation energies studied have different origins. In the case of methyllithium dimer, it is mainly due to the deformation energy of the reactants and to E_1 the sum of the first-order contributions E_{elec} and E_{exc}, while E_2, the sum of the second-order terms (E_{pol} and E_{ct}) stabilize the transition state. The magnitude of the deformation energy of the methyllithium dimer is due to the lengthening, which takes place in the transition state, of one of the Li−C bond as can be seen from Figure 3A. Figure S1 (Supporting Information) shows that the same phenomenon takes place in the case of the addition, on this complex, of acetaldehyde. This geometry variation is to be connected to the “open dimer” obtained by Morokuma and colleagues.[9b,c] In the case of the formation of the C−C bond between formaldehyde and methyllithium−lithium dimethylamide complex the activation barrier is clearly due to E_1. There is also a small contribution from the distortion energies. In this case, E_2 provides a much smaller stabilization than in the previous case, mainly because the aggregate to aldehyde charge-transfer plummets. Altogether these results tend to show that the decrease of the activation energy of the C−C bond formation, which takes place when going from $(MeLi)_2$−H_2CO to $(MeLi\text{-}Me_2NLi)\text{-}H_2CO$ is mainly due to the lowering of the deformation and exchange contributions which are large enough to compensate the now positive value of the electrostatic contribution. The results concerning the formation of the C−N bond between formaldehyde and the mixed dimer are very different from those concerning that of the C−C bond. Surprisingly, it appears that the reactants are intrinsically more stable in the transition state than in the initial complex and that the exchange (steric) contribution decreases upon their activation. In this case, the energy barrier is entirely due to the second order terms, mainly the decrease of the charge transfer from the organolithium complex to the aldehyde.

Conclusion

This analysis has been first focused of the condensation pathway between aldehydes and monomeric and dimeric MeLi. It indicates that the DFT approach provides preliminary complexes and transition states with characteristics comparable to those obtained before with other theoretical methods. Computations on the previously unknown case of Me_2NLi and $(Me_2NLi)_2$ has led to an overall comparable reaction scheme, the height of the activation barriers being however significantly decreased (by an about 2-fold factor). The most interesting case of the MeLi-Me_2NLi mixed complex has finally been examined. Interacting aldehydes with this disymmetric structure leads to two possible complexes in which the oxygen of the carbonyl adopts an angular docking on one of the lithium atoms. Depending on the original orientation, either a C−C or C−N bond can form. The evaluation of the various activation barrier heights indicate that the C−N binding should be kinetically favored in the case of formaldehyde as well as acetaldehyde. This important feature should be taken into account for the design of chiral lithium amides to be used as mixed aggregates with alkyllithium in asymmetric synthesis.

The examination of the transition states geometry of the different systems considered here shows that we are dealing with early TS since they differ from the pre-TS complexes mainly by a rotation of the aldehyde plane (ϕ) with only minor variations of the distance between the atoms to be bound.

The analysis of the different contributions to the activation energies of the condensation reaction on methyllithium carbon shows that the decrease obtained when going from the homodimer to the mixed complex is due to that of the deformation energy of the reactants and to the first order terms which depend only on their unperturbed wave function.

Finally, it is certainly worth underlining that the relatively small energy differences we find between the competing reaction pathways involving dimers are likely to endow solvent effects with a determining role. Their importance has been well established both experimentally[25] and theoretically,[26] and has been emphasized again by very recent NMR studies by Collum[27a] and Davidsson.[27b] Our own preliminary calculations show that taking into account three dimethyl ether molecules as model for the etheral solvents tends to reverse the relative stabilities of the optimized “C-side” and “N-side” of the complexes between mixed aggregate MeLi−Me_2-NLi and acetaldehyde.[28] Moreover, such calculations on the tetrasolvated complex show the exothermicity of the docking of acetaldehyde. The solvent influence on the reaction activation barrier is currently under study.

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Supporting Information Available: Table 1* featuring the complexation energies between formaldehyde and methyllithium at various computational levels and Figures S1 A−D representing the optimized complexes, TS, and condensation products for the MeLi−MeCHO, Me_2NLi−MeCHO, $[MeLi]_2$−MeCHO, and $[Me_2NLi]_2$−MeCHO systems. This material is available free of charge via the Internet at http://pubs.acs.org.

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(25) . Inter alia: (a) Kminek, I.; Kaspar, M.; Trekoval, J. *Collect. Czech. Chem. Commun.* **1981**, *46*, 1124−1131. (b) Romesberg, F. E.; Collum, D. B. *J. Am. Chem. Soc.* **1994**, *116*, 9198−9202. (b) Hilmersson, G.; Davidsson, Ö. *J. Org. Chem.* **1995**, *60*, 7660−7669. (c) Reich, H. J.; Kulicke, K. J. *J. Am. Chem. Soc.* **1996**, *118*, 273−274. (d) Lucht, B. L.; Collum, D. B. *J. Am. Chem. Soc.* **1996**, *118*, 3529−3530. (e) Hilmersson, G.; Ahlberg, P.; Davidsson, Ö. *J. Am. Chem. Soc.* **1996**, *118*, 3539−3540. (f) Hoffmann, D.; Collum, D. B. *J. Am. Chem. Soc.* **1998**, *120*, 5810−5811. (g) Vliet, G. L. J. v.; Kanter, F. J. J. d.; Schakel, M.; Klumpp, G. W.; Spek, A. L.; Lutz, M. *Chem. Eur. J.* **1999**, *5*, 1091−1094. (h) Lucht, B. L.; Collum, D. B. *Acc. Chem. Res.* **1999**, *32*, 1035−1042.

(26) Inter alia: (a) Gareyev, R.; Streitwieser, A. *J. Org. Chem.* **1996**, *61*, 1742−1747. (b) Weiss, H.; Yakimansky, A. V.; Müller, A. H. E. *J. Am. Chem. Soc.* **1996**, *118*, 8897−8903.

(27) (a) Sun, X.; Collum, D. *J. Am. Chem. Soc.* **2000**, *122*, 2452−2458. (b) *ibid*, 2459−2463. (c) Arvidsson, P. I.; Davidsson, Ö. *Angew. Chem., Int. Ed. Eng.* **2000**, *39*, 1467−1470.

(28) Fressigné, C.; Maddaluno, J.; Giessner-Prettre, C. To be published.