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Fixation of Heterocumulenes. 1. A Theoretical Study on the Irreversible Reaction of CO_2 with a 2-Lithio-1,3-dithiane[†]

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The mechanism of electrophilic addition of CO_2 to 2-lithio-2-phenyl-1,3-dithiane−tetrahydrofuran−tetramethylethylendiamine, a Corey−Seebach "umpolungs" reagent for nucleophilic acylation, was investigated at the B3YLP/6-311+G*//HF/6-31+G* level of theory with specific solvation effects being included in the study. The overall reaction is exothermic by 18.8 kcal/mol and proceeds via precomplexation of the CO_2 (necessary for activation). The reaction barrier is calculated to be 11.9 kcal/mol (relative to the precomplex **2a**) and represents a lower boundary for the activation energy. The reaction barrier is shown to originate from specific solvent effects. A detailed survey of the electronic effects governing the reaction is given. The ab initio results were then compared with semiempirical PM3 calculations, which were extended to include the heterocumulenes COS and CS_2. As expected, the reduced electrophilicity of these molecules leads to a higher activation barrier by retention of the same reaction mechanism.

Introduction

The transformation of CO_2 into useful organic compounds, usually with the help of an organometallic reagent,[1] has received quite a lot of attention. The fixation of CO_2 can occur either reversibly or irreversibly. The reversible case is often found in nature for zinc enzymes[2] with one of the classical examples being carbonic anhydrase.[3] Reactions of CO_2 with organolithium compounds, an essential synthetic tool in modern organic chemistry,[4] are, on the other hand, irreversible stoichiometric reactions. The fixation of CO_2 on a Li−C moiety is one of the most valuable, generally applicable methods for the synthesis of carboxylates.[5] Another useful reaction is the insertion of CO_2 into a Li−N bond, which leads to a carbamate having a wide range of applications such as directed ortho metalation (DOM).[6]

To increase the number of feasible synthetic pathways in modern organic synthesis, it is desirable to develop reagents of differing polarities for the introduction of any given fragment or functional group. Carbonyl groups, for example, provide the experimentalist with either an acyl cation or an enolate anion. By employing a suitable "umpolungs" reagent,[7] it is possible to reverse the polarity of the acyl carbon thus allowing nucleophilic acylation,[8,9] to take place. The most thoroughly investigated method for nucleophilic acylation is based on dithiane compounds because of their high thermal and chemical stability.[9] Reactions can be carried out in THF at temperatures between −20 and −70 °C. The carbonyl group is converted into a cyclic thioacetal that, due to the carbanion stabilizing effect of the sulfur,[10] can be easily deprotonated. These reagents can be employed in the synthesis of aldehydes,[9] silyl and germanyl ketones,[11] optically active aldehydes and ketones,[12] cyclic carbonyl compounds,[13] carbohydrates,[9] and α-keto acids.[9]

Especially important to us is the ability of these reagents to react with CO_2 to yield α-keto carboxylic acids

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[†] Dedicated to Professor Rolf W. Saalfrank, University of Erlangen, Germany, on the occasion of his 60th birthday.

(1) Behr, A. *Carbon Dioxide Activation by Metal Complexes*; VCH: Weinheim 1988.

(2) For reviews on zinc enzymes, see: Vallee, B. L.; Auld, D. S.; *Biochemistry* **1990**, *29*, 5647. Vallee, B. L.; Auld, D. S. *Acc. Chem. Res.* **1993**, *26*, 543. Bertini, L., Luchinat, C., Maret, W., Zeppezauer, M., Eds. *Progress in Inorganic Biochemistry and Biophysics*; Birkhauser: Boston, 1986; Vol. 1. Lipscomb, W. N.; Sträter, N. *Chem. Rev.* **1996**, *96*, 2375. Aresta, M., Schloss, J. V., Eds. In *Enzymatic and Model Carboxylation and Reduction Reactions for CO_2 Utilization*; Kluwer Academic Publishers: Boston, 1990. Auld, D. S. *Struct. Bond.* **1997**, *98*, 29.

(3) Garmer, D. R. *J. Phys. Chem. B* **1997**, *101*, 2945. Lu, D.; Voth, G. A. *J. Am. Chem. Soc.* **1998**, *120*, 4006. Hartmann, M.; Clark, T.; van Eldik, R. *J. Mol. Model.* **1996**, *2*, 358. Zheng, Y.-J.; Merz, K. M., Jr. *J. Am. Chem. Soc.* **1992**, *114*, 10498. Solá, M.; Lledós, A.; Duran, M.; Bertrán, J. *J. Am. Chem. Soc.* **1992**, *114*, 869. Krauss, M.; Garmer, D. R. *J. Am. Chem. Soc.* **1991**, *113*, 6426. Jacob, O.; Cardenas, R.; Tapia, O. *J. Am. Chem. Soc.* **1990**, *112*, 8692. Bertini, I.; Luchinat, C.; Rosi, M.; Sgamelotti, A.; Tarantelli, F. *Inorg. Chem.* **1990**, *29*, 1460.

(4) Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds. *Comprehensive Organometallic Chemistry*; Vol. 1, 7, 8 Pergamon Press: New York, 1982. Setzer, W.; Schleyer, P. v. R. *Adv. Organomet. Chem.* **1985**, *24*, 353.

(5) Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon Press: Oxford, U.K., 1974.

(6) Snieckus, V. *Chem. Rev.* **1990**, *90*, 879 and references therein. Mills, R. J.; Taylor, N. J.; Snieckus, V. *J. Org. Chem.* **1989**, *54*, 4372. Narashima, N. S.; Mali, R. S. *Top. Curr. Chem.* **1987**, *138*, 63. Opitz, A.; Koch, A.; Katritzky, A. R.; Fan, W. Q.; Anders, E. *J. Org. Chem.* **1995**, *60*, 3745.

(7) For a review of the concept of umpolung, see: Seebach, D.; *Angew. Chem.* **1979**, *91*, 259; *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 239.

(8) Seebach, D. *Angew. Chem.* **1969**, *81*, 690; *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 639.

(9) Saraswathy, V. G.; Sankararaman, S. *J. Org. Chem.* **1994**, *59*, 4665. Gröbel, B. J.; Seebach, D. *Synthesis* **1977**, 357. Seebach, D.; Corey, E. J. *J. Org. Chem.* **1975**, *40*, 231. Seebach, D.; Kolb, M. *Chem. Ind. (London)* **1974**, *17*, 687. Seebach, D. *Synthesis* **1969**, 17. Corey, E. J.; Seebach, D. *Angew. Chem.* **1965**, *24*, 1134; *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 1075 and literature cited therein.

(10) Wiberg, K. B.; Castejon, H. *J. Am. Chem. Soc.* **1994**, *116*, 10489. Boche, G. *Angew. Chem.* **1989**, *101*, 286; *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 277. Bernardi, F.; Bottoni, A.; Venturini, A.; Mangini, A. *J. Am. Chem. Soc.* **1986**, *108*, 8171. Bors, D. A.; Streitwieser, A., Jr. *J. Am. Chem. Soc.* **1986**, *108*, 1397. Epiotis, N. D.; Yates, R. L.; Bernardi, F.; Wolfe, S. *J. Am. Chem. Soc.* **1976**, *98*, 5435 and literature cited therein.

(11) Corey, E. J.; Seebach, D.; Freedman, R. *J. Am. Chem. Soc.* **1966**, *89*, 434.

(12) Seebach, D.; Steinmüller, D. *Angew. Chem.* **1968**, *80*, 617; *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 619.

(13) Seebach, D.; Jones, R. J.; Corey, E. J. *J. Org. Chem.* **1967**, *33*, 300.

10.1021/jo991934c CCC: $19.00

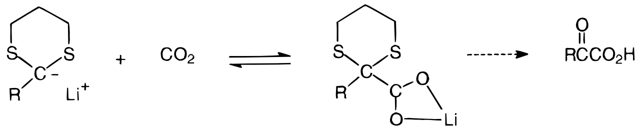

Figure 1. Reaction of a lithiated dithiane with CO_2 to yield an α-keto carboxylic acid.

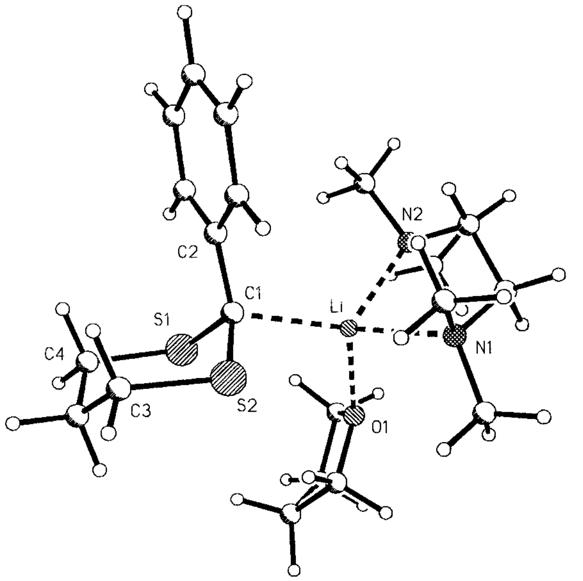

Figure 2. Solid-state structure (X-ray analysis) of the Corey–Seebach "umpolungs" reagent **1**. Reproduced from ref 15.

(Figure 1). Ab initio model calculations at the MP2 level of theory for the reaction of the model systems LiH and $LiCH_3$ with CO_2 show that the reaction proceeds with a very low activation energy (+1.5 kcal/mol for LiH and +0.9 kcal/mol for $LiCH_3$) and is quite exothermic (−56 and −62 kcal/mol, respectively).[14] An X-ray analysis of an interesting lithiated dithiane compound, 2-lithio-2-phenyl-1,3-dithiane−tetrahydrofuran−tetramethylethylendiamine[15] **1** (Figure 2) shows, however, that the lithium is coordinated not only by the dithiane but also by a cosolvent molecule of tetramethylethylendiamine (the addition of TMEDA is necessary in order to increase the activity of the metalating species) and a molecule of tetrahydrofuran (THF). A more accurate model for the reaction of organolithium compounds with CO_2 must therefore consider the initial replacement of one of the solvent molecules with CO_2. Indeed, it is to be expected that the calculation of structure−activity patterns for this class of compounds can only be achieved by explicitly considering aggregated and solvated molecules. Since compound **1** fulfills all conditions for such a model as it allows theoretical predictions on a sound experimental fundament, we undertook an ab initio study of the reaction of **1** (Figure 2) with CO_2 under explicit consideration of specific solvent coordination. This compound is a typical representative of a Corey−Seebach "umpolungs" reagent,[7] and its existence as an monomer has been shown by X-ray analysis.[15] Complicating aggregational effects thus do not have to be considered. Furthermore, we contribute to the still ongoing discussion about the origin of the carbanion-stabilizing effect observed for sulfur[10] as well as the nature of the C−Li bond.[16]

The quantum mechanical treatment of even larger molecules still exceeds the computer capacity of most research groups. The application of semiempirical MO methods, i.e., MNDO,[17] AM1,[18] and PM3,[19] is therefore clearly desirable because of their ability to calculate large molecules. A parameter set for lithium has been developed in our research group[20] for the method PM3, which has proved to be superior to MNDO and has been successfully applied to a variety of problems.[21] It has been shown that PM3 adequately reproduces the structural parameters of organolithium compounds as compared both with experiment and with higher level ab initio and DFT methods. However, the PM3 energies obtained are usually not too accurate.[22] We employed the PM3 method and varied the heterocumulene (CO_2, COS, and CS_2) in order to investigate which qualitative effect the heteroatom has upon the reaction mechanism as well as once again to assess the quality of the lithium parameter set.

Computational Details

All ab initio calculations were performed using either the Gaussian94[23] or Gaussian98[24] suite of programs. Due to the considerable size of the molecules under investigation (a typical calculation had ca. 572 basis functions or 1020 primitive Gaussians), we restricted our geometry optimizations to the HF/6-31+G* level of theory. Full geometry optimizations and harmonic frequency calculations for all intermediates were carried out at this level. All zero-point energies (ZPE) were scaled by a factor of 0.91.[25] Single-point calculations at the B3LYP/6-311+G* level of theory were carried out using the optimal HF/6-31+G* geometries in order to introduce electron correlation into the energy estimation. Atomic charges and hyperconjugative interaction energies were obtained using the natural bond orbital (NBO) analysis of Reed et al.[26] as

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[14] Kaufmann, E.; Sieber, S.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1989**, *111*, 4005.

[15] Amstutz, R.; Dunitz, J. D.; Seebach, D. *Angew. Chem.* **1981**, *93*, 487; *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 465.

[16] Sygula, A.; Rabideau, P. W. *J. Am. Chem. Soc.* **1992**, *114*, 821 and literature cited therein.

[17] Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899.

[18] Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.

[19] Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 209; 221.

[20] Anders, E.; Koch, R.; Freunscht, P. *J. Comput. Chem.* **1993**, *11*, 1301.

[21] Koch, R.; Anders, E. *J. Org. Chem.* **1994**, *59*, 4529.

[22] Arvidsson, P. I.; Hilmersson, G.; Ahlberg, P. *J. Am. Chem. Soc.* **1999**, *121*, 1883. Abbotto, A.; Streitwieser, A.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1997**, *119*, 11255. Weiss, H.; Yakimansky, A. V.; Müller, A. H. E. *J. Am. Chem. Soc.* **1996**, *118*, 8897.

[23] GAUSSIAN94, Revision D.3: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez C.; Pople, J. A. Gaussian, Inc., Pittsburgh, PA, 1995.

[24] GAUSSIAN98, Revision A.5: 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.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. Gaussian, Inc., Pittsburgh, PA, 1998.

[25] Grev, R. S.; Jansen, C. L.; Schaefer, H. F., III. *J. Chem. Phys.* **1991**, *95*, 5128 and references therein.

[26] Reed, A. E.; Weinstock, R. B.; Weinhold, F. J. *J. Chem. Phys.* **1985**, *83*, 735.

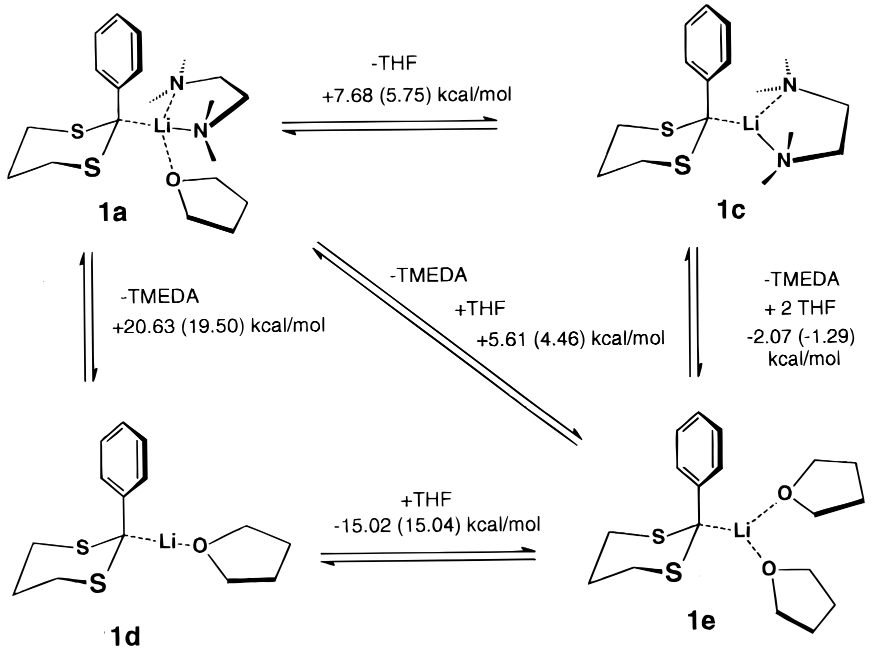

Figure 3. Solvation equilibria for compound **1** calculated at the B3LYP/6-311+G*//HF/6-31+G* level of theory; the HF/6-31+G* values are given in parentheses.

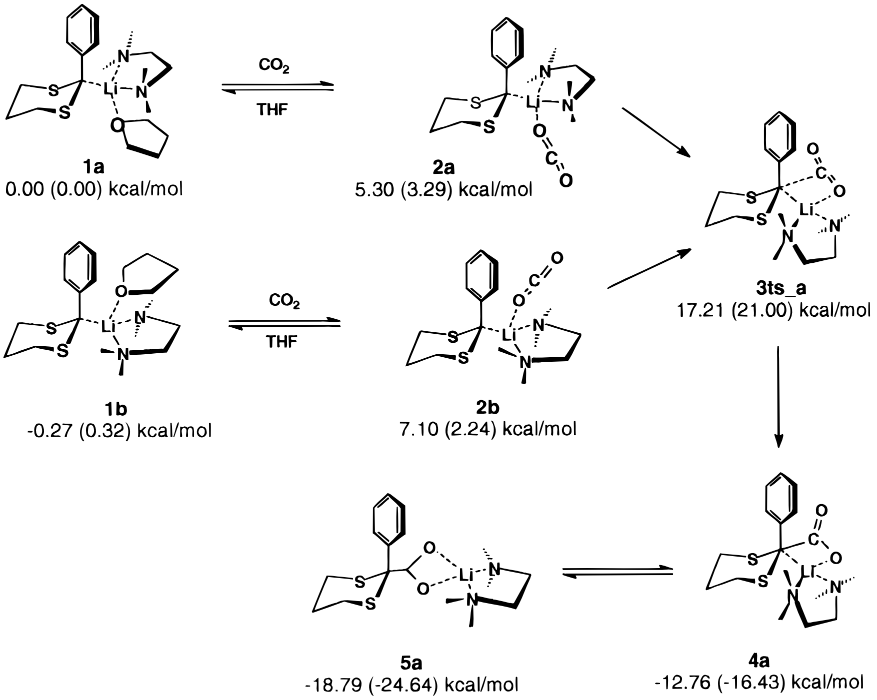

Figure 4. Mechanism of the addition of CO_2 to the Cory−Seebach "umpolungs" reagent **1**. Calculated at the B3LYP/6-311+G*//HF/6-31+G* level of theory, HF/6-31+G* values are given in parentheses.

implemented in Gaussian98. The PM3 calculations were carried out using MOPAC93.[27] Default convergence criteria were used for all calculations.

The six-membered dithiane ring was always calculated in the chair conformation in the results presented here. For the intermediates **2**, **4**, and **5** (Figure 4), we verified that the chair conformation is indeed the most stable conformation at the HF/6-31+G* level of theory. In all three cases, the chair form was found to be more stable than the boat form with energy differences lying between 3.9 and 6.5 kcal/mol.

All calculations were performed with the lithium in the equatorial and the phenyl substituent in the axial ring position. This structure corresponds to that found in the X-ray analysis of the lithiated dithiane **1**[15] and can be easily rationalized due to the steric bulk of the solvated lithium cation. In addition, an NBO analysis indicates the presence of a favorable negative hyperconjugation interaction between the lone pair on the metalated carbon atom and the antibonding orbital of the sulfur carbon bond ($n_C \rightarrow \sigma^*_{S-C}$) when the lithium assumes an equatorial position (see Table 2). Our calculations suggest that electronic and not steric effects prevail since the lithium favors an equatorial position even in the absence of solvent molecules.

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Table 1. Absolute Energies and Zero-Point Energies for the Species Involved in the Reaction of Compound 1 with CO_2 (All Values Were Calculated at the B3LYP/6-311+G*//HF/6-31+G* Level of Theory and Are Given in Hartrees)

	E	ZPE[a]		*E*	ZPE[a]
1a	−1772.129 187	0.568 893	**3ts_a**[b]	−1728.238 595	0.454 596
1b	−1772.129 462	0.568 728	**3ts_b**[b]	−1380.396 952	0.212 493
1c	−1539.607 145	0.440 678[c]	**4a**	−1728.289 337	0.457 872
1d	−1424.271 156	0.325 812	**4b**	−1380.420 112	0.215 764
1e	−1656.804 308	0.453 403	**5a**	−1728.299 187	0.458 133
1f	−1191.738 853	0.198 911	**5b**	−1380.424 143	0.215 866
2a	−1728.261 984	0.459 428	CO_2	−188.645 624	0.012 828
2b	−1728.259 102	0.454 837	THF	−232.507 462	0.125 674
2c	−1380.397 016	0.454 837	TMEDA[d]	−347.821 555	0.238 891

[a] Zero-point energy values were taken from the HF/6-31+G* calculations. [b] First-order transition structure. [c] An imaginary frequency of $-7\ \mathrm{cm}^{-1}$ corresponding to a methyl rotation was calculated for this complex. [d] Anti conformer.

The anti form of TMEDA was calculated to be 3.02 kcal/mol more stable than the corresponding syn form (necessary for bidentate coordination to lithium). All solvent equilibria in which a noncoordinated TMEDA is present were therefore calculated using the most stable (anti) form of TMEDA.

Results and Discussion

Solvation Equilibria. To determine which solvated species is most likely to be present in solution under experimental conditions, we explicitly calculated various solvated complexes of the lithiated dithiane **1** (see Figure 3 and Table 1). It takes only 7.7 kcal/mol to detach a THF molecule from **1a** to form **1c**. In contrast to this, removing the TMEDA to generate **1d** is energetically considerably more demanding and requires 20.6 kcal/mol. Interestingly enough, the solvate complex which incorporates one TMEDA and one THF (**1a**) is 5.6 kcal/mol more stable than the complex containing two molecules of THF (**1e**). This result is in agreement with the X-ray structural analysis of **1**, which also shows a mixed coordination (Figure 2). A comparison between complexes **1c** and **1d** shows that a complex containing two THF molecules is only slightly more stable (2.1 kcal/mol) than one solvated solely by TMEDA (a bidentate ligand). Entropy effects will, however, clearly favor the TMEDA complex. An incoming electrophile (CO_2) will thus preferentially displace a THF molecule. At no point in the reaction is it to be expected that TMEDA will be replaced by THF.

Although the X-ray structural analysis of **1** gives the position of the solvent molecules relative to the carbon skeleton (TMEDA assumes a cis position to the phenyl ring with respect to the C−Li bond), there is no reason to assume that this (**1a**) is the only stable solvated complex of **1** in solution. We therefore performed a conformational analysis on **1** for rotation about the C−Li bond using the semiempirical method PM3. A second stable conformer (**1b**) was located which was then reoptimized at the HF/6-31+G* level of theory (see Figure 4). **1b** is only very slightly (0.3 kcal/mol) more stable than **1a** at the B3LYP/6-311+G*//HF/6-31+G* level, thus indicating that both species are likely to be found in solution.

An NBO analysis (Table 2) shows that the electronic structures of **1a** and **1b** are almost equivalent to each other. Specific solvation is expected to lower the ionic character of the Li−C bond. In agreement with this, the charge on lithium in the complexes **1a**/**1b** (+0.87) is indeed slightly lower than that calculated for the unsolvated species **1f** (+0.90 at the HF/6-31+G* level). As an additional comparison, the charge on lithium in $Li-CH_3$ has been reported to be +0.92.[14] Due to the low polarizability of lithium, the reduction in the ionic character upon solvation is quite small so that one can still consider the metal carbon interaction in **1a**/**1b** to be essentially ionic, in agreement with the current understanding of C−Li interactions.[16] One must also take into account the fact that two opposing electronic effects are present in this molecule. The solvent molecules are donating charge to the lithium and therefore to the C−Li bond. At the same time, the negative hyperconjugation with the dithiane unit withdraws electron density from the C−Li bond.

The NBO analysis of **1a**/**1b** contributes furthermore to the growing evidence[10] that the carbanion stabilizing effect of sulfur is mainly due to a $n_C \rightarrow \sigma^*_{S-C}$ hyperconjugative interaction. d-Orbital stabilization is small in comparison.

Reaction Mechanism. The overall reaction mechanism is depicted in Figure 4. The most important structural data for the stationary points are summarized in Table 3. Due to computational limitations (single optimizations and, more especially, transition structure searches on molecules of this size take ca. 4 weeks of computational time), we were not able to explicitly investigate the complexation/displacement mechanism of an incoming CO_2 molecule. Such reactions are, however, known to be very facile. Assuming that CO_2 will displace one THF, we searched for and found two energetically stable complexes containing CO_2 coordinated in a head-on manner with the lithium cation (**2a** and **2b**). It is possible that the lithium first expands its coordination sphere to complex with the CO_2 before the THF is pushed out. Computational limitations prevented us, however, from investigating this possibility. The replacement of THF by carbon dioxide costs 5.3 (**2a**) and 7.1 kcal/mol (**2b**). This contrasts with calculations reported for the addition of CO_2 to (unsolvated) methyllithium. The unsolvated encounter complex is 8.6 kcal/mol **more stable** than the separated reactants at the MP2/6-31G*//HF/6-31G* level of theory.[14] This prompted us to investigate the reaction of the unsolvated species (**1f**) with CO_2 to form the initial encounter complex **2c** (see Table 1). In the gas phase, the formation of the initial encounter complex is **exothermic** by 7.5 kcal/mol. Introduction of specific solvation causes the reaction to become decisively **endothermic**, thus depicting clearly the necessity of including the solvent molecules in the calculation in order to draw a realistic picture of the reaction in solution.

Formation of the precomplex activates the CO_2 as can be seen from the charge polarization calculated for **2a**/**2b** (Table 3). The negative charge on the coordinated oxygen atom is larger than in free CO_2. This in turn withdraws electron density from the central carbon thus making it much more susceptible to an intramolecular nucleophilic attack from the neighboring lithiated carbon atom.

The carboxylation reaction proceeds through a single transition structure **3ts_a** (Figure 4), regardless of whether complex **2a** or **2b** is considered. Analysis of the transition vector showed that this is due to a coupled vibrational/rotational process. In the course of reaction, a rotation about the C_1-Li bond in either **2a** or **2b** takes place. As the complexed CO_2 becomes approximately perpendicular to the phenyl group, the oop vibration of

Table 2. Selected Atomic Charges (e) and Hyperconjugative Interaction Energies (kcal/mol) for the Species Involved in the Reaction of Compound 1 with CO_2 (Calculated at the HF/6-31+G* Level of Theory)

	1a	1b	1f	2a	2b	2c	3ts_a	3ts_b	4a	5a
q_{Li}	+0.871	+0.872	+0.900	+0.872	+0.867	+0.875	+0.854	+0.880	+0.889	+0.986
q_{C}	−0.904	−0.906	−0.901	−0.917	−0.920	−0.896	−0.809	−0.810	−0.456	−0.438
$q_{O(THF)}$	−0.749	−0.750								
q_{N1}	−0.681	−0.681		−0.693	−0.691		−0.698		−0.690	−0.697
q_{N2}	−0.680	−0.680		−0.692	−0.692		−0.694		−0.689	−0.671
$q_{C(CO2)}$				+1.270[a]	+1.283[a]	+1.277	+1.287	+1.244	+0.993	+0.951
$q_{O(CO2)}$[b]				−0.671	−0.687	−0.698	−0.733	−0.802	−0.998	−0.883
$q_{O(CO2)}$				−0.584	−0.586	−0.559	−0.581	−0.595	−0.766	−0.917
$n_C \rightarrow \sigma^*_{S1-C}$	10.1	10.4	11.3	9.5	10.0	11.2	1.9	8.9		
$n_C \rightarrow \sigma^*_{S2-C}$	10.1	10.1	11.3	12.2	10.0	11.2	1.9	8.9		
$n_C \rightarrow d_{S1}$	3.3	3.3	4.7	3.4	3.4	4.7	3.3	3.4		
$n_C \rightarrow d_{S2}$	3.4	3.3	4.7	3.6	3.3	4.7	3.3	3.4		

[a] The partial charge on C in free CO_2 is +1.23. On oxygen: −0.61. [b] Bound to lithium.

Table 3. Structural Parameters Calculated at the HF/6-31+G* Level of Theory for the Intermediates Involved in the Reaction of Compound 1 with CO_2 (Bond Lengths Are Given in Å and Angles in Deg)

	1a	1b	2a	2b	3ts_a	4a	5a
Li−O1	2.092	2.062					
Li−N1	2.257	2.278	2.132	2.139	2.149	2.101	2.118
Li−N2	2.264	2.253	2.165	2.145	2.243	2.112	2.111
Li−C1	2.259	2.249	2.157	2.163	2.728	3.347	3.735
Li−O2			2.279	2.229	2.063	1.761	1.926
Li−O3			4.308	4.166	3.938	3.947	1.930
C1−C5	1.500	1.498	1.494	1.499	1.489	1.576	1.574
C1−C9			3.882	3.704	2.798	1.576	1.547
O1−Li−C1	111.7	112.0					
O2−Li−C1			102.4	102.7	79.3	43.0	34.6
O2−C9−O3			177.5	176.0	168.7	128.6	122.2
C1−S2	1.801	1.798	1.798	1.797	1.815	1.839	1.845
C1−S2	1.798	1.798	1.797	1.798	1.843	1.834	1.841
S2−C5	1.822	1.823	1.823	1.823	1.807	1.818	1.818
S1−C4	1.823	1.823	1.823	1.823	1.820	1.815	1.816

the complexed CO_2 swings the activated carbonyl carbon close enough to the lithiated carbanion for bond formation to take place at a C_1-C_9 distance of 2.8 Å (Table 3). Due to the complexity of this coupled vibrational/rotational process, it proved extremely difficult to cleanly locate the transition structure **3ts_a**. The product formed in the course of reaction (**4a**) closely resembles the transition structure **3ts_a**. A major difference between the two structures is to be found only in the C_1-C_9 bond length (2.8 Å in **3ts_a** and 1.6 Å in **4a**). The activation energy of the reaction relative to the complexes **2a** and **2b** (+11.9 and +10.1 kcal/mol, respectively) is quite high as compared to that reported for the unsolvated reaction of CO_2 with CH_3Li (6.8 kcal/mol at the HF/6-31G* and 0.9 kcal/mol at the MP2/6-31G*//HF/6-31G* level).[14] In accordance with the results reported by Schleyer et al.,[14] we calculated the unsolvated transition structure **3ts_b** to be 0.1 kcal/mol more instable at the B3LYP/6-31+G*//HF/6-31+G* level of theory than the encounter complex **2c**. In the absence of specific solvent effects (gas-phase scenario), the addition of CO_2 to organolithium compounds proceeds practically without a barrier. Introduction of specific solvation leads to a significant increase in the activation barrier. Indeed, one could say that the presence of a reaction barrier is due to specific solvent effects.

The solvent induced increase in the energy of activation is most probably due to a reduced electrostatic interaction between CO_2 and Li. The presence of the donor solvent TMEDA weakens the charge polarization calculated for **2a** as compared with **2c**, thus making the CO_2 less susceptible to intramolecular nucleophilic attack.

The Hartree−Fock calculations give an even higher activation barrier (18.8 kcal/mol relative to **2a**) as compared with the B3LYP/6-31+G*//HF/6-31+G* results (11.9 kcal/mol). It has been shown for the addition of CO_2 to CH_3Li that the introduction of electron correlation effects stabilizes the transition structure as compared to the HF results.[14] The density functional method B3LYP is known to underestimate activation barriers.[28] The DFT and HF results therefore present a lower and an upper bound for the activation energy.

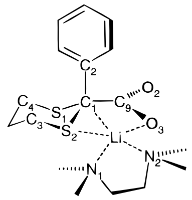

Figure 5. Transition structure **3ts_a**.

The transition structure **3ts_a** is quite interesting (Figure 5). When **3ts_a** is formed from either **2a** or **2b**, the lithium simply moves to one side of the complex and forms an electrostatic contact with one of the sulfur atoms. At the same time, a partial rotation about the C−Li bond takes place, thus positioning the bound CO_2 so that it can easily interact with the metalated carbon atom. As seen from the length of the carbon−carbon bond being formed in the transition structure (2.78 Å) and the fact that the carbon dioxide is only slightly bent (<OCO = 168.6°), the reaction proceeds via an early transition structure. This is in good agreement with the Hammond

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[28] Salahub, D. R.; Chrétien, S.; Milet, A.; Proynov, E. I. In *Transition State Catalysis in Computational Chemistry*; Truhlar, D. G., Morokuma, K., Eds.; submitted for publication.

Table 4. Selected Structural Parameters for 1a Calculated at the PM3 and the HF/6-31+G* Level of Theory as Compared with X-ray Structural Data

	X-ray[a]	HF/6-31+G*	PM3[b]
	Bond Lengths (Å)		
$\mathrm{Li-O}$	1.970	2.092	2.077
$\mathrm{Li-N_1}$	2.148	2.264	2.244
$\mathrm{Li-N_2}$	2.110	2.257	2.231
$\mathrm{Li-C_1}$	2.280	2.259	2.203
$\mathrm{C_1-C_2}$	1.468	1.499	1.471
$\mathrm{C_1-S_1}$	1.776	1.801	1.789
$\mathrm{C_1-S_2}$	1.769	1.798	1.788
	Bond Angles (deg)		
$\mathrm{O-Li-N_1}$	105.8	104.4	101.8
$\mathrm{O-Li-N_2}$	108.8	109.6	106.7
$\mathrm{O-Li-C_1}$	117.2	111.7	124.8
$\mathrm{C_1-Li-N_1}$	119.8	122.4	117.5
$\mathrm{C_1-Li-N_2}$	114.1	121.3	114.4
$\mathrm{N_1-Li-N_2}$	86.9	83.4	83.8
$\mathrm{C_2-C_1-Li}$	119.5	111.7	121.4

[a] Data were taken from refs 15 and 21. [b] Reference 21.

postulate, which states that exothermic reactions proceed preferentially via early transition structures.

Reaction to form **4a** is exothermic. Product **4a** is 12.8 kcal/mol more stable than the sum of the energies of the reactants (**1a** and CO_2). The reaction does not stop here, however. The initial carboxylate **4a** undergoes rearrangement to yield **5a** since a much stronger electrostatic contact is formed between lithium and oxygen than between lithium and sulfur. Due to the excessive amount of computational time and resources required for calculations of this size, we did not investigate the mechanism of this rearrangement in any great detail.

The NBO analysis shows that the $n_C \rightarrow \sigma^*_{S-C}$ hyperconjugative interactions in the transition structure **3ts_a** are smaller as compared to those in the precomplexes **2a/2b**. This can be easily understood since the electron pair is needed for the formation of the new C−C bond. Once the C−C bond is fully formed (the initial carboxylate **4a**), the hyperconjugative interactions become zero. The structural information in Table 3 correlates closely with the NBO analysis. As the reaction progresses, the negative hyperconjugation is weakened due to bond formation. This is accompanied by a lengthening of the C1−S bond. The C1−S bond increases continually from ca. 1.80 Å in **1a** and **2a** over 1.815 Å in **3ts_a**, 1.839 Å in **4a** to 1.845 in **5a**. At the same time, the diminishing negative hyperconjugative effect of the lone pair causes the adjacent S1−C4 and S2−C3 bonds to become slightly shorter (1.823 Å in **1** to 1.816 Å in **5a** for the S1−C4 bond).

PM3 Calculations. A comparison of HF/6-31+G* and PM3 *structural* parameters of **1a** with experimental values taken from an X-ray analysis[15] (Table 4) shows that the semiempirical results are, on average, directly comparable with experiment and slightly better than the ab initio values. Both computational methods give Li−N bond lengths that are somewhat too long as compared with experiment. PM3 yields a C−Li contact that is a little too short, a known deficiency of this method. The C−Li−N bond angles are too large at the HF/6-31+G* level, and the O−Li−C angle is too large for PM3.

The same qualitative reaction mechanism for the addition of CO_2 to **1a** is found for both computational methods. CO_2 replaces a molecule of THF in **1a** to generate the complexes **2a** and **2b**, which then react via **3ts_a** to form the carboxylate **4a**. Interestingly enough, **3ts_a** differs slightly for PM3 as compared to the structure obtained at the HF/6-31+G* level. The CO_2 molecule in the ab initio transition structure is oriented perpendicular to the plane of the benzene ring (Figure 5). The semiempirical results show the CO_2 axis as lying in the plane of the benzene ring. This is probably a computational artifact of the semiempirical method, as a corresponding transition structure could not be found at the HF level of theory.

Table 5. Relative Energies Calculated Using the Semiempirical Method PM3 for the Intermediates Involved in the Reaction of 1 with Various Heterocumulenes

	CX_2			
	CO_2[c]	COS[a]	COS[b]	CS_2
1a + CX_2	0.00 (0.00)	0.00	0.00	0.00
1b + CX_2	3.45 (−0.27)	3.45	3.45	3.45
2a + THF	−0.70 (+5.30)	−1.44	−3.17	−3.13
2b + THF	1.90 (+7.10)	1.29	−1.50	−0.64
3ts + THF	10.07 (17.21)	20.90	11.35	30.91
4 + THF	3.13 (−12.76)	12.70	4.45	6.37
5 + THF	0.88 (−18.79)	4.65	0.67	1.09

[a] The atom attached to Li is O. [b] The sulfur is coordinated to the lithium atom. [c] B3LYP/6-311+G*//HF/6-31+G* values for comparison are given in parentheses.

In direct contrast to the relatively good structural picture found for PM3, calculation of the activation energies for the reaction of **1a** with CO_2 is qualitative in nature (Table 5). The exchange of THF with CO_2 is endothermic (5.3 kcal/mol) at the B3LYP/6-311+G*//HF/6-31+G(d) level of theory, but slightly exothermic with PM3 (−0.70 kcal/mol). As a consequence of this, the energy required to reach the transition structure **3ts_a** appears much lower than in the case of the DFT results. However, the energy required to generate the transition state **3ts_a** from the precomplex **2a**, for example, is reproduced relatively well. A distinct disadvantage of the semiempirical method lies in the fact that the overall exothermicity of the reaction (−18.8 kcal/mol at the B3LYP/6-311+G*//HF/6-31+G* level vs +0.9 kcal/mol for PM3) is very poorly reproduced.

These errors could, however, be systematized by examining the heat of formations of the various species involved in more detail since a distinct advantage of the semiempirical methods is their tendency toward error cancellation, especially for larger molecules. The energy of small specific molecules is often connected with large computational errors at the semiempirical level. As an example, PM3 underestimates the stability of carbon dioxide by ca. 9 kcal/mol[19] and thus introduces a large error into the computational results. With careful calibration of the semiempirical results, it should be possible to obtain more accurate energetical results.

We expect the error in the energetics to be relatively constant for the reaction of **1a** with heterocumulenes such as CO_2, COS, and CS_2. Two pathways for the COS conversion are conceivable. The precoordination to the lithium (structures **2a** and **2b**) can proceed via sulfur or via oxygen. Substitution of oxygen by the less electronegative, more polarizable sulfur does not alter the general mechanism of addition. Nevertheless, a different energetic pattern is calculated. When COS is coordinated with the oxygen being bound on lithium, an increase in activation energy of 11 kcal/mol is observed as compared with CO_2. The presence of the sulfur results in a less activated cumulene. A smaller electrostatic interaction between C1 and C(OS) has to compete with an almost constant energy of deformation for the substrate which results in a higher activation energy. In contrast to this, the activation barrier for COS is only slightly higher than CO_2 when the sulfur is bound to the lithium. The highly polarizable sulfur binds strongly to the metal thus withdrawing electron density from the cumulene and resulting in a more electrophilic substrate. Comparing the activation barriers obtained for both pathways, we suspect that the reaction with COS will procced via sulfur coordination. The same reasoning can be applied to CS_2. Further deactivation of the central carbon due to the presence of two sulfur atoms leads to an activation barrier of 31 kcal/mol. Since the reaction pathway is similar for all three cumulenes, it should be possible to transform COS and CS_2 into the analogous products once the activation barrier has been overcome. Joint experimental and theoretical investigations on the mechanism of heterocumulene fixation and its synthetic possibilities are currently underway in ongoing studies.[29]

Conclusions

The quantum chemical calculations performed here reveal that the solvate complex **1a** with a mixed coordination (THF and TMEDA) is the most stable one. Since TMEDA is the better donor solvent, an electrophile (CO_2) will preferably replace the THF in the first solvate sphere of the lithiated dithiane. Precomplexation activates the CO_2, which then adds to the lithiated dithiane via the transition structure **3ts_a**. The overall reaction of solvated **1a** with CO_2 is considerably exothermic (−18.8 kcal/mol) but proceeds, however, with a relatively high activation barrier. This barrier (ca. 11.9 kcal/mol relative to the precomplex **2a**) is a lower estimation. The HF (17.7 kcal) results should, in contrast, provide an upper boundary.

The semiempirical method PM3 is capable of reproducing the general mechanism of addition found at the HF/6-31+G* level of theory; the relative energies thus obtained are, however, not as reliable. The exothermicity of the reaction, in particular, is very poorly reproduced. Substitution of CO_2 with COS and CS_2 at the PM3 level indicates that the general reaction mechanism is independent of the heteroatom (oxygen/sulfur) involved. However, the substitution of oxygen by sulfur requires a higher activation energy.

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