Chromatograms were recorded on a Hewlett-Packard Model 3393A recorder-integrator. Infrared spectra were recorded on a Beckman Microlab 620MX computing infrared spectrophotometer, and nuclear magnetic resonance (NMR) spectra were recorded with a JEOL FX 90Q Fourier transform NMR spectrometer using deuteriobenzene or deuterioacetone as solvents. Benzene ($C_6D_5H$) or acetone ($C_3D_5H$) was used as the internal standard.

**Synthesis. Method A.** In a typical procedure *O*-ethylxanthic acid, potassium salt (7.05 g, 44 mmol), and the amine (100 mmol) were dissolved in 100 mL of deionized water in a 500-mL Erlenmeyer flask. When an amine hydrochloride was used, the pH of the solution was first adjusted to >11 with 10 N NaOH. The flask was immersed in an ice bath, and potassium triiodide (103.6 mL of a 0.38 M solution (40 mmol) freshly standardized with sodium thiosulfate[6]) was added dropwise with magnetic stirring over 20–30 min. A yellow milky suspension was formed. Once the addition of potassium triiodide was completed, the mixture was stirred for another 30 min to complete the reaction. The yellow organic layer was then extracted with anhydrous ether three times. The ether layer was dried with anhydrous sodium sulfate, and the solution was concentrated on a rotary evaporator. The yellowish oil contained yellow crystals, which, by their solubility, melting point (112–114 °C), and ignition, appeared to be sulfur. The oil was removed and purified by a simple vacuum distillation. The purity of the compounds was generally greater than 98%. The identity of the products was confirmed by their melting points, boiling points (where possible), elemental analysis (percent compositions of C, H, N, and S were within 0.3% of theoretical values), and NMR and IR spectral data. All compounds showed C=S stretching vibrations between 1520 and 1552 $cm^{-1}$.

**Method B.** Thiocarbamates were also prepared by reacting the chloroamine with potassium ethyl xanthate. The chloroamine was prepared by the dropwise addition of a standardized solution of sodium hypochlorite (40 mmol) to 100 mL of an aqueous solution of the amine (100 mmol). The resulting oily suspension was added to 100 mL of an aqueous solution containing 44 mmol of potassium ethyl xanthate.

**Method C.** Thiocarbamates were prepared by the dropwise addition of a standardized solution of sodium hypochlorite (40 mmol) to 100 mL of an aqueous solution containing amine (100 mL) and potassium ethyl xanthate (44 mmol).

**Methylcarbamothioic acid *O*-ethyl ester**: bp 60–62 °C (1.4 mmHg) [lit.[7] bp 93 °C (10 mmHg)]; $^1H$ NMR ($C_6D_6$) $\delta$ 7.5–5.5 (2 broad m, 1 H, NH), 4.37 (q, 2 H, $CH_2$), 2.44 (d of d, 3 H, $NCH_3$), 1.02 (t, 3 H, $CH_3$); IR (film) 3280, 2985, 1537, 1365, 1221, 1056 $cm^{-1}$. Anal. Calcd for $C_4H_9NOS$: C, 40.30; H, 7.63; N, 11.75; S, 26.90. Found: C, 40.43; H, 7.69; N, 11.69; S, 26.75.

**Dimethylcarbamothioic acid *O*-ethyl ester**: bp 88–89 °C (12 mmHg) [lit.[8] bp 81–82 °C (10 mmHg)]; $^1H$ NMR ($C_6D_6$) $\delta$ 4.40 (q, 2 H, $OCH_2$), 3.0 (s, 3 H, $NCH_3$) 2.55 (s, 3 H, $NCH_3$) 1.03 (t, 3 H, $CH_3$); IR (film) 1525, 1398, 1292, 1195, 1038 $cm^{-1}$. Anal. Calcd for $C_5H_{11}NOS$: C, 45.08; H, 8.32; N, 10.52; S, 24.07. Found: C, 44.79; H, 8.25; N, 10.38; S, 23.83.

**Isobutylcarbamothioic acid *O*-ethyl ester**: bp 78–80 °C (1.4 mmHg); $^1H$ NMR ($C_6D_6$) $\delta$ 7.79 (broad s, 0.4 H, NH), 6.22 (broad s, 0.6 H, NH), 4.40 (d of q, 2 H, $OCH_2$) 3.21 (t, 1.2 H, $NCH_2$) 2.80 (t, 0.8 H, $NCH_2$) 1.65 (m, 1 H), 1.05 (d of t, 3 H), 0.67 (d, 6 H); IR (film) 3250, 2960, 1525, 1200 $cm^{-1}$. Anal. Calcd for $C_7H_{15}NOS$: C, 52.13; H, 9.38; N, 8.69; S, 19.88. Found: C, 52.02; H, 9.41; N, 8.65; S, 19.79.

**Phenylcarbamothioic acid *O*-ethyl ester**: recrystallized from ethanol; mp 66.5–67.5 °C (lit.[9] mp 68–70 °C); $^1H$ NMR ($C_6D_6$) $\delta$ 8.4 (broad s, 1 H, NH), 6.7–7.2 (m, 5 H, aromatic), 4.33 (q, 2 H, $CH_2O$), 0.96 (t, 3 H, $CH_3$); IR (KBr) 3223, 1600, 1552, 1499, 1409, 1377, 1335, 1200, 1040 $cm^{-1}$.

**1-Pyrrolidinecarbothioic acid *O*-ethyl ester**: bp 91–92 °C (1.5 mmHg) [lit.[10] bp 141 °C (17.5 mmHg)]; $^1H$ NMR ($C_6D_6$) $\delta$ 4.5 (q, 2 H, $CH_2O$), 3.57 (broad t, 2 H, ring), 3.07 (broad t, 2 H, ring), 1.4–0.93 (m, 7 H); IR (film) 1495, 1474, 1455, 1260, 1223, 1046 $cm^{-1}$. Anal. Calcd for $C_7H_{13}NOS$: C, 52.79; H, 8.23; N, 8.80; S, 20.13. Found: C, 52.56; H, 8.26; N, 8.72; S, 20.03.

**1-Piperidinecarbothioic acid *O*-ethyl ester**: bp 91–92 °C (1.4 mmHg) [lit.[10] bp 147.9 °C (25 mmHg)]; $^1H$ NMR ($C_6D_6$) $\delta$ 4.47 (q, 2 H, $OCH_2$), 3.86 (m, 2 H, ring), 3.27 (m, 2 H, ring), 2.24 (m, 6 H), 1.15 (t, 3 H, $CH_3$); IR (film) 1492, 1443, 1292, 1268, 1243, 1190 $cm^{-1}$. Anal. Calcd for $C_8H_{15}NOS$: C, 55.45; H, 8.73; N, 8.08; S, 18.50. Found: C, 55.37; H, 8.77; N, 8.06; S, 18.42.

**Allylcarbamothioic acid *O*-ethyl ester**: bp 71–73 °C (1.0 mmHg) [lit.[11] bp 64–65 °C (0.3 mmHg)]; $^1H$ NMR ($C_6D_6$) $\delta$ 7.7 (broad m, $^1/_3$ NH), 6.7 (broad m, $^2/_3$ NH), 5.6 (m, 1 H, vinylic), 4.95 (d of d, 2 H, vinylic), 4.32 (q, 2 H, $OCH_2$), 3.95 (broad s, 1.3 H, allylic), 3.55 (broad s, 0.7 H, allylic), 1.06 (t, 3 H, $CH_3$); IR (film) 3250, 1520, 1393, 1324, 1270, 1193 $cm^{-1}$.

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**Registry No.** *O*-Ethylxanthic acid, potassium salt, 140-89-6; methylcarbamothioic acid *O*-ethyl ester, 817-73-2; dimethylcarbamothioic acid *O*-ethyl ester, 17996-38-2; isobutylcarbamothioic acid *O*-ethyl ester, 82360-11-0; phenylcarbamothioic acid *O*-ethyl ester, 3111-89-5; 1-pyrrolidinecarbothioic acid *O*-ethyl ester, 56525-82-7; 1-piperidinecarbothioic acid *O*-ethyl ester, 56525-81-6; allylcarbamothioic acid *O*-ethyl ester, 817-97-0; aniline, 62-53-3; methylamine, 74-89-5; *N*-chloro-*N*-methylamine, 6154-14-9; dimethylamine, 124-40-3; isobutylamine, 78-81-9; pyrrolidine, 123-75-1; piperidine, 110-89-4; *N*-chloropiperidine, 2156-71-0; allylamine, 107-11-9.

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## On the Relative Energies of ab Initio Structures of *N*-Methylformamide Anions and Their Lithium Derivatives. An Estimate of the Magnitude of Chelate Stabilization

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The term "dipole-stabilized anion" was coined by Beak to describe the situation that results when a carbanion is stabilized by an adjacent dipole.[1] Such a situation arises when, for example, an amide is deprotonated $\alpha$ to nitrogen.[2] The simplest model for such a system is *N*-methylformamide anion: $HCONHCH_2^-$. In 1981, a collaborative effort from Houk, Beak, and Schleyer compared the relative energies of several dipole-stabilized anions with non-dipole-stabilized analogues.[3] For *N*-methylformamide anion, the effect of dipole stabilization was demonstrated by comparing the proton affinities of $HCONHCH_2^-$ and $NH_2CH_2^-$. Single-point calculations using the 4-31+G basis set on STO-3G optimized geometries showed that formylating the nitrogen of $NH_2CH_2^-$ provided 28 kcal/mol stabilization.

(1) Beak, P.; Reitz, D. B. *Chem. Rev.* **1978**, *78*, 275–316.
(2) Beak, P.; Zajdel, W. J.; Reitz, D. B. *Chem. Rev.* **1984**, *84*, 471–573.
(3) Rondan, N. G.; Houk, K. N.; Beak, P.; Zajdel, W. J.; Chandrasekhar, J.; Schleyer, P. v. R. *J. Org. Chem.* **1981**, *46*, 4108–4110.

0022-3263/89/1954-2980$01.50/0 

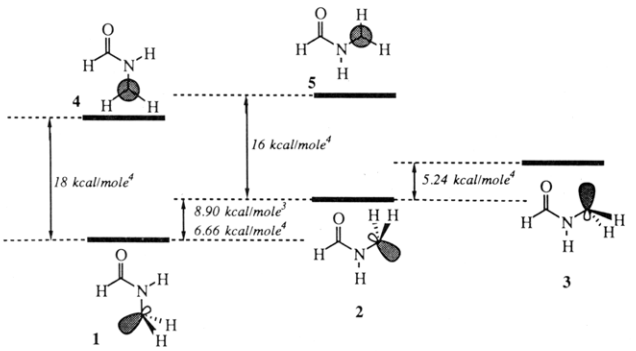
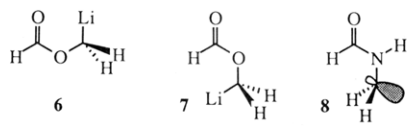



**Figure 1.** Relative energies of various *N*-methylformamide anion geometries. Rondan et al. (ref 3), optimized the geometries with the minimal STO-3G basis set and estimated the energies with single-point calculations using the 4-31G basis set. Bach et al. (ref 4) optimized all geometries with the 4-31G basis set.

In a subsequent study,[4] Bach refined and extended the previous calculations and explained the experimental preference for equatorial alkylation of conformationally locked systems[3,5] using stereoelectronic arguments. Both of the previous theoretical studies showed pyramidal carbanion geometries for *N*-methylformamide anion (**1**-**3**, Figure 1), and Bach also calculated the energy of the two isomers in which the carbanion electrons are in conjugation with the amide $\pi$-system (**4** and **5**, Figure 1). The latter are 16–18 kcal/mol higher in energy than the rotamers (**1** and **2**, Figure 1), which place the carbanion lone pair in the nodal plane of the amide $\pi$-system.

The chemistry of dipole-stabilized anions is explained by the intermediacy of species most closely resembling **3** (Figure 1), *the least stable* of the three "low-energy" geometries, an effect usually attributed to the lithium cation. The lithiated species might benefit from chelation by the carbonyl oxygen (a thermodynamic effect), while a preference for deprotonation syn to the carbonyl oxygen (a kinetic effect) would result from prior complexation of an alkyllithium base with the carbonyl oxygen, an experimentally verified phenomenon.[6] Confirming the greater stability of a syn-lithiated species, calculations using the 4-31G basis set on the lithiated methyl formate anion show a 13 kcal/mol stabilization of **6** over **7**,[3] but no calculations have been reported for the synthetically more important lithiated amides.




Our interest in the chemistry of chiral dipole-stabilized anions[7] led us to wonder about two points: (1) If the carbanion is indeed stabilized by a dipole, why isn't a low-energy geometry one in which the dipoles are most nearly opposite (i.e. **8**)? (2) What is the magnitude of stabilization by internal chelation of the lithium ion by the carbonyl oxygen? We now report the results of a theoretical investigation which reveal that **8** is indeed a low-energy geometry, that the barrier to "in plane" inversion of the carbanions (**1** $\rightleftarrows$ **8** and **2** $\rightleftarrows$ **3**) is about 10 kcal/mol, and that the magnitude of chelate stabilization in a lithiated amide is substantially higher than for the analogous esters (**6** and **7**).

**Table I. Calculated Energies (*E*, hartrees) and Relative Energies (kcal/mol)**

| structure | 6-31G* | $E_{rel}$ |
|---|---|---|
| **1** | −207.2856 | 0 |
| **2** | −207.2728 | +8.03 |
| **3** | −207.2661 | +12.2 |
| **8** | −207.2820 | +2.26 |
| **9** | −207.2654 | +12.7 |
| **10** | −207.2494 | +22.7 |
| **1**-Li | −214.7886 | +28.2 |
| **2**-Li | −214.7825 | +32.1 |
| **3**-Li | −214.8336 | 0 |
| **8**-Li | −214.7854 | +30.2 |

## Results

The refined energies for structures **1**–**3** and **8** are presented in Table I, and the relative energies are shown schematically in Figure 2.[8] Also presented are the calculated energies and relative energies of the syn and anti anions constrained such that the $C^1$–N–$C^2$–H torsional angles are +90 and −90°. The calculated energies of **8**-Li, **1**-Li, **2**-Li, and **3**-Li are listed in Table I, and the relative energies are shown in Figure 3. Details of the geometry for all calculated structures are given in Table 2, which is included as supplementary material.

## Discussion

As expected, a new minimum energy geometry, **8**, was found. However, the calculated energy differences between **8** and **1** are so small that a conclusion regarding relative stabilities of the two species is not justified.[9]

There are two possible modes for the interconversions **1** $\rightleftarrows$ **8** and **2** $\rightleftarrows$ **3**: rotation around the N–$CH_2$ bond and "in-plane" inversion. The transition state for the former is represented by **4** and **5** (Figure 1), and for the latter by **9** and **10** (Figure 2). The rotational barrier, calculated using the 4-31G basis set, is substantial: 16–18 kcal/mol.[4] This high rotational barrier has been rationalized as being the result of a four electron "HOMO–HOMO" interaction. In the amide anion, $\psi_3$ is elevated by 44.6 kcal/mol above the isolated p orbital whereas $\psi_2$ is only 27.4 kcal/mol below the amide HOMO, resulting in a 17 kcal/mol increase in relative energy for the two frontier orbitals.[4]

The "in-plane" inversion barrier is less, about 10 kcal/mol, when calculated with the 6-31G* basis set. This barrier is higher than the calculated inversion barrier for free $CH_3^-$ (1–2 kcal/mol), but is within the range of measured values for a number of carbanion inversions.[10]

The chemistry of conformationally rigid piperidine amides is characterized by deprotonation syn to the carbonyl oxygen and by equatorial alkylation.[3,5] The latter phe-

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(8) All geometries were optimized with the 6-31G* basis set, using the Gaussian 86 series of programs: Frisch, M. J.; Binkley, J. S.; Schlegel, H. B.; Raghavachari, K.; Melius, C. F.; Marten, R. L.; Stewart, J. J. P.; Bobrowicz, F. W.; Rohlfing, C. M.; Kahn, L. R.; Defrees, D. J.; Seeger, R.; Whiteside, R. A.; Fox, D. J.; Fleuder, E. M.; Pople, J. A. *Carnegie Mellon Quantum Chemistry Publishing Unit*; Pittsburgh, PA, 1984.

(9) Optimum geometries for structures **1** and **8** were also calculated with the 6-31+G basis set, with little difference in geometry, but the relative energy difference decreased to 1.60 kcal/mol.

(10) See: Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 2nd ed; Harper and Row: New York, 1987; p 529, and references cited therein.

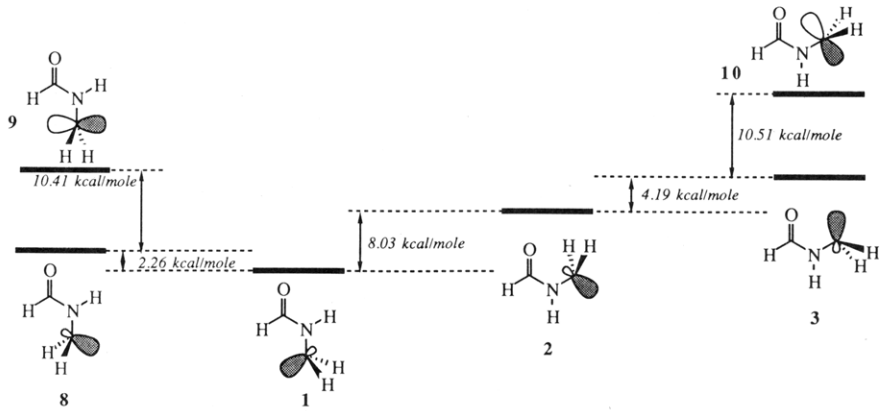


**Figure 2.** Relative energies of *N*-methylformamide anion geometries (fully optimized using 6-31G* basis set).

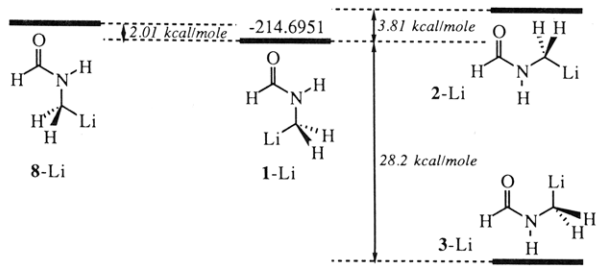


**Figure 3.** Relative energies of *N*-methylformamide lithium (fully optimized using 6-31G* basis set).

nomenon is readily accounted for by the relative energies and stereoelectronic arguments presented by Bach.[4] The former effect has been postulated to result from the chelation of the lithium by the amide carbonyl. If chelation is important, the energy gained would have to be substantial in order to explain the chemistry, since **3** is 10–12 kcal/mol less stable than **1**, and the calculated difference for the corresponding esters **6** and **7** (13 kcal/mol)[3] is probably not enough.

The total energy difference between **1**, **8**, and **2** (6-31G* level) is about 8 kcal/mol but decreases to less than 4 kcal/mol when a lithium cation is added. The lowering of energy of **3**-Li, relative to the other lithiated species, is dramatic: the difference between the anti and syn isomers (**1**-Li and **3**-Li) is 28 kcal/mol. Considering that for the free anions **3** is 12 kcal/mol less stable than **1**, the 28 kcal/mol difference between **3**-Li and **1**-Li is remarkable. The energy difference is considerably larger than the calculated difference for the two ester anions **6** and **7**.[3] It is likely that the major reason for the larger effect in the amide anions is the larger dipole and hence greater charge on oxygen created by delocalization of the amide nitrogen lone pair.

The geometries of the lithiated species (Table 2, supplementary material) are quite similar, with the exception of **3**-Li, for which the N–$C^2$–Li bond angle is compressed to 93°. The fact that the oxygen is responsible for this bond angle compression is seen from the Li–O bond distance of 1.86 Å.[11] Note, however, that the effect of chelation has little effect on the C=O and $C^1$–N bond lengths: the C=O bond is 1.20 Å for **1**-Li, **2**-Li, and **8**-Li, and 1.23 Å for **3**-Li; the $C^1$–N bond lengths are 1.33 Å for **1**-Li, 1.34 Å for **2**-Li and 8-Li, and 1.31 Å for **3**-Li. Otherwise, the stereoelectronic effects that dictate anion geometry[4] appear to be fully operative here.[12]

(11) In an effort to discount "overchelation" by the lithium in **3**-Li, attempts were made to calculate the relative energies of **3**-Li and **1**-Li, each solvated by three water molecules. No conclusions could be drawn due to lack of convergence in these attempts.


## Summary

A new low-energy geometry for *N*-methylformamide anion has been calculated, and the barrier to in-plane inversion is estimated to be 10 kcal/mol for both the syn and anti amide geometries. The presence of a lithium cation drastically changes the relative energy of one of the four isomeric *N*-methylformamide anion structures. Specifically: the isomer **3**, which models chemically important species such as piperidine amide anions, is 12 kcal/mol higher in energy than its isomer **1**, when calculated with the 6-31G* basis set. In the presence of a lithium ion, **3**-Li is 28 kcal/mol more stable than **1**-Li. We attribute this relative energy change to chelation of the lithium by the carbonyl oxygen. It therefore seems most appropriate to call these species "dipole-stabilized organometallics."



**Acknowledgment.** We thank the National Institutes of Health, Grant No. GM-37985, for financial support.

**Registry No.** **3**-Li, 120446-29-9; $HCONHCH_2^-$, 78715-78-3.


**Supplementary Material Available:** Table 2, containing the geometries of all the calculated structures (1 page). Ordering information is given on any current masthead page.

(12) Semiempirical (MNDO) calculations on lithiated aminooxazolines also show a preference for maintaining a relatively flat chelated metallocycle: see ref 7. For an X-ray crystal structure of a pivaloylisoquinoline Grignard with a flat metallocyclic ring, see: Seebach, D.; Hansen, J.; Seiler, P.; Gromek, J. M. *J. Organomet. Chem.* **1985**, *285*, 1–13.

## Nucleophilic Reaction of Azulene Derivatives with Some Ketone Enolates


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While general nucleophilic aromatic substitution occurs by addition–elimination mechanisms,[1] photoinduced $S_{RN}1$ reaction of haloarenes is known to proceed by an electron transfer from the nucleophile, and hence no extra acti-

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