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Registry No. Methyl 4-oxo-5-tetradecynoate, 77889-02-2; 1-decyne, 764-93-2; methyl 4-chloro-4-oxobutanoate, 1490-25-1; (*R*)-(−)-5-tetradecyn-4-olide, 72151-69-0; (*R*)-(−)-*Z*-5-tetradecen-4-olide, 64726-91-6; methyl 4-hydroxy-5-tetradecynoate cyclohexylamine salt, 78685-95-7; *B*-3-pinanyl-9-BBN, 64106-79-2.

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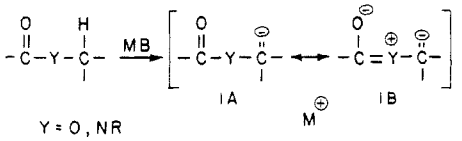
Dipole Stabilization of α-Heteroatom Carbanions: Theory and Experiment

Summary: The results of ab initio SCF calculations verify dipole stabilization in the carbanions formed by loss of a proton from the methyl groups of methyl formate and *N*-methylformamide, but differences between theory for the free anions and experiment is attributed to the effect of lithium ion complexation.

Sir: Carbanions **1** adjacent to the oxygen of an ester (Y = O) or to the nitrogen of an amide (Y = NR) are easily prepared and provide synthetically useful reagents.[1] Such



anions have been termed "dipole stabilized".[1a] While it is intuitively reasonable that carbanionic centers will be favorably influenced by adjacent dipoles, ab initio SCF calculations[2,3] now establish this stabilization to be of substantial magnitude. We also report parallel experimental work which tests the predictions from theory.

A number of conformations of neutral species **2**–**6** and the derived anions **2A**–**6A** were studied theoretically. Energies are summarized in Tables I and II. The preferred geometries are represented in Figure 1; those for **2A** and **4A** have already been discussed.[4] The anionic centers in

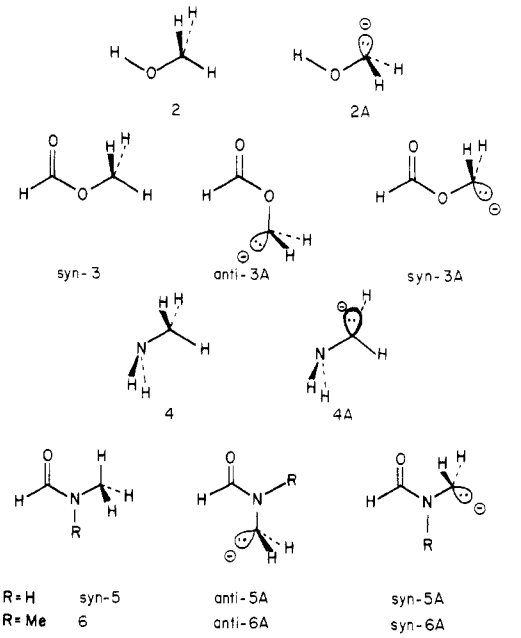
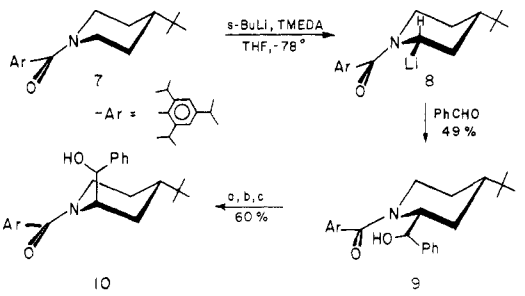


Figure 1. Preferred geometries of species studied theoretically. The anti isomers of **3A**, **5A**, and **6A** are favored over the syn isomers by ~9 kcal/mol (4-31G//STO-3G).

Scheme I. Reagents: a, pyridinium chlorochromate; b, NaOMe; c, $LiAlH_4$



3A, **5A**, and **6A** are distinctly pyramidal with the lone pair in the plane of the molecule oriented as shown.[5] That is, rotations around the O–CH_2 bond in *anti*-**3A** or *syn*-**3A** are unfavorable: 90° rotation of *anti*-**3A** requires 6.6 kcal/mol at the 4-31G//STO-3G level. Furthermore, **3A**, **5A**, and **6A** prefer the anti over the syn geometry by about 9 kcal/mol[6] even though the parent ester **3** and amide **5** favor the syn stereochemistry (by 7.6 and 1.4 kcal/mol, respectively).[7,8] Rotations around the CO–O or CO–N

(1) (a) For a review, see Beak, P.; Reitz, D. B. *Chem. Rev.* **1978**, *78*, 725. (b) For recent related cases, see Lubosch, W.; Seebach, D. *Helv. Chim. Acta* **1980**, *63*, 102. MacDonald, J. L. *J. Org. Chem.* **1980**, *45*, 193.

(2) The Gaussian 70 and Gaussian 76 series of programs were employed: Hehre, W. J.; Lathan, W. A.; Ditchfield, R.; Newton, M. D.; Pople, J. A. *QCPE*, 236 (1973). Binkley, J. S.; Whiteside, R. A.; Hariharan, P. C.; Seeger, R.; Pople, J. A.; Hehre, W. J.; Newton, M. D. *Ibid.* 368 (1978). Geometries, optimized with the minimal STO-3G basis set, were used in single point calculations, employing the split-valence 4-31G basis. Since diffuse basis functions are essential for a reliable estimation of anion proton affinities (PA), additional calculations on the preferred conformations were carried out with the 4-31+G basis set (the 4-31G basis set augmented by a set of diffuse s and p functions on all nonhydrogen atoms).[3] The use of only the STO-3G optimized geometries should not entail any serious error; geometry optimization at the 4-31+G level for a few cases leads only to insignificant changes in the calculated relative PA's (Table I).

(3) Chandrasekhar, J.; Andrade, J. G.; Schleyer, P. v. R. *J. Am. Chem. Soc.*, manuscript submitted for publication. The PA's and stabilization energies relative to CH_3^- are calculated to be lower at the 4-31+G level compared to calculations without diffuse functions.

(4) Clark, T.; Körner, H.; Schleyer, P. v. R. *Tetrahedron Lett.* **1980**, 743. See also, Hinde, A. L.; Pross, A.; Radom, L. *J. Comput. Chem.*, **1980**, *1*, 118. Lehn, J. M.; Wipff, G. *J. Am. Chem. Soc.* **1976**, *98*, 7498.

(5) In the anions, ∠HCH = 100–101° and ∠XCH = 99–102°. The energy to planarize *anti*-**3A** is 19.8 kcal/mol, whereas planarization of CH_3^- (∠HCH = 100°) requires +7.6 kcal/mol at the 4-31G//STO-3G level.

(6) Gund, P.; Veber, D. F. *J. Am. Chem. Soc.* **1979**, *101*, 1885, reported that anti DMF anion is favored by 6.7 kcal/mol by CNDO/2. These authors also report that N-methylation enhances the acidity of *N*-methylformamide by 3.6 kcal/mol (*syn*-Me) or 3.1 kcal/mol (*anti*-Me). Our calculations suggest this to be a CNDO/2 artifact; N-methylation has less than a 1 kcal/mol effect on the deprotonation energy of *N*-methylformamide.

(7) Experimental work. Methyl formate: Bock, C. *Can. J. Chem.* **1967**, *45*, 2761. O'Gorman, J. M.; Shank, W.; Shamiker, V. *J. Am. Chem. Soc.* **1950**, *72*, 4222. Wilmshurst, J. K. *J. Mol. Spectrosc.* **1957**, *1*, 201. Curl, R. F., Jr. *J. Chem. Phys.*, **1959**, 30, 1759. *N*-Methylformamide: LaPlanche, L. A.; Rogers, M. T. *J. Am. Chem. Soc.* **1964**, *86*, 337; Drakenberg, T.; Forsén, S. *Chem. Commun.* **1971**, 1404; Allmer, F.; Kriz, J.; Doskocilová, D. *Collect. Czech. Chem. Commun.* **1973**, *38*, 3252.

(8) Theoretical studies. Methylformate: Wennerstrom, H.; Forsén, S.; Roos, B. *J. Phys. Chem.* **1972**, *76*, 2530. John, I. G.; Radom, L. *J. Mol. Struct.* **1977**, *36*, 133. Larson, J. R.; Epiotis, N. D.; Bernardi, F. *J. Am. Chem. Soc.* **1978**, *100*, 5713. *N*-Methylformamide: Tonelli, A. E. *J. Am. Chem. Soc.* **1971**, *93*, 7153.

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Table I. Calculated Energies (E, hartrees) and Proton Affinities (PA, kcal/mol) of Anions

anion	4-31G//STO-3G		4-31+G//STO-3G		4-31+G//4-31+G	
	E	PA[a]	E	PA[a]	E	PA[a]
CH_3^-	−39.40042	463.9 (0.0)	−39.44105	439.1 (0.0)	−39.45004	433.5 (0.0)
$HOCH_2^-$	−114.15354	447.8 (−16.1)	−114.18376	433.5 (−5.6)	−114.20212	425.8 (−7.7)
$CH_3OCH_2^-$	−153.12187[b]	444.8 (−19.1)	−153.15281[b]	432.4 (−6.7)		
$CH_3CH_2OCH_2^-$	−192.10630[c]	443.9 (−20.0)				
CH_2=$CHOCH_2^-$	−190.94255[d]	431.1 (−32.8)				
$HCOOCH_2^-$						
anti-**3A**	−226.76626	420.9 (−43.0)	−226.79988	405.9 (−33.2)		
syn-**3A**	−226.75229	429.7 (−34.2)				
$H_2NCH_2^-$	−94.33441	458.4 (−5.5)	−94.37042	439.6 (0.5)	−94.38474	435.4 (1.9)
$HCONHCH_2^-$						
anti-**5A**	−206.96624	427.4 (−36.5)	−207.00213	411.5 (−27.6)		
syn-**5A**	−206.95206	436.3 (−27.6)				
$HCON(CH_3)CH_2^-$						
anti-**6A**	*e,f*					
syn-**6A**	−245.92193[e,f]	436.4 (−27.5)				

[a] Relative proton affinities in parentheses. [b] The optimized geometry of $HOCH_2^-$ was used with a standard methyl group replacing the hydrogen bound to the oxygen. [c] See *b*; a standard ethyl was used here. [d] The anti geometry like that of **3A** was assumed, but all geometrical parameters were fully optimized. Using standard geometries as described in *b* gives 33.1 kcal/mol stabilization by the vinyl group. [e] These geometries were not optimized, but were constructed by replacing the H(N) in **5A** with the corresponding methyl group from **5**. [f] Due to lack of convergence, the 4-31G//STO-3G energy was not obtained. The STO-3G PAs of *anti*-**6A** and *syn*-**6A** are 41.9 and 35.1 kcal/mol less than that of the methyl anion.

bonds lead to even higher energy structures.

How can these geometrical preferences be explained? Electrostatic repulsions are minimized in the preferred geometries of the neutral species, **3** and **5**.[9] In the anions, the internal dipoles are oriented for maximum stabilization. The energetic consequences are large. The formyl groups in *anti*-**3A** and in *anti*-**5A** provide 28 kcal/mol stabilization (4-31+G//STO-3G) when compared with **2A** and **4A**. This is not merely the result of the increased size of **3A** and **5A**, since much less stabilization is found in $CH_3OCH_2^-$ or $C_2H_5OCH_2^-$ (Table I). The less favorable syn forms, **3A** and **5A**, also benefit from considerable stabilization due to the attractive interaction between the partially positive carbonyl carbon (total charge +0.6 to +0.7) and the carbanionic carbon (total charge −0.3 to −0.4).[10]

The anion formed from *anti*-methyl vinyl ether is stabilized by 13 kcal/mol more than that from methyl ethyl ether, but this is also due to the significant polarization of the vinyl carbons by π-donation from oxygen.[11] The α-carbon has a positive charge of +0.30 and β-carbon a charge of −0.48, as compared to charges of +0.67 and −0.70 for C and O in *anti*-**3A**.

Both the geometries and stabilization energies are consistent with the "dipole-stabilization" mechanism proposed earlier.[1a] There is little or no enhancement of resonance structure, **1B**, however, as assessed by the only minor CO bond length alterations upon anion formation, or by the insignificant stabilization accompanying this geometrical relaxation.

To determine whether the anion stereochemistry which is predicted by ab initio calculations is related to that of the organometallic species in solution, the stereochemistry of lithiations of 2,4,6-triisopropylbenzamides[12,13] have been analyzed. Metalation of **7**, followed by reaction with benzaldehyde, gave syn equatorial **9**, as shown in Scheme I.[14] Equatorial substitution of **9** is confirmed by a sequence of oxidation, equilibration, and reduction to the more stable axial isomer, **10**.[15,16] A similar syn equatorial substitution of *N*-(2,4,6-triisopropylbenzoyl)-4-phenyl-

Table II. Calculated Energies of Neutral Species (in hartrees)

molecule	4-31G// STO-3G	4-31+G// STO-3G	4-31+G// 4-31+G
CH_4	−40.13976	−40.14087	−40.14087
CH_3OH	−114.86718	−114.87457	−114.87977
CH_3OCH_3	−153.83074[a]	−153.84200[a]	
$CH_3CH_2OCH_3$	−192.81377[b]		
CH_2=$CHOCH_3$	−191.62950[c]		
$HCOOCH_3$			
syn-**3**	−227.43706	−227.44669	
anti-**3**	−227.42528		
CH_3NH_2	−95.06500	−95.07102	−95.07855
$HCONHCH_3$			
syn-**5**	−207.64729	−207.65785	
anti-**5**	−207.64519[d]		
$HCON(CH_3)_2$			
6	−246.61735[e]		

[a] The geometry of CH_3OH was used with a standard methyl group replacing the H bound to O. [b] As in *a*; but a standard ethyl was used here. [c] The anti geometry was assumed but all other geometrical parameters were optimized. [d] The anti-N-Me prefers a conformation with one CH bond eclipsed with the N-CO bond. [e] This geometry was not fully optimized. A standard methyl was substituted for H(N) of *syn*-**5**, and the two CNC angles were reoptimized.

(9) Strozier, R. W.; Rondan, N. G.; Houk, K. N.; Fraser, R. R.; Chuauqui-Offermanns, N. *J. Am. Chem. Soc.* **1980**, *102*, 1426.

(10) A Coulomb's law estimate of the anion–carbonyl interaction, using 4-31G charges, indicates that *anti*-**5A** should be stabilized 6 kcal/mol more than *syn*-**5A**.

(11) Libit, L.; Hoffmann, R. *J. Am. Chem. Soc.* **1974**, *96*, 1370.

(12) Beak, P.; McKinnie, B. G.; Reitz, D. B. *Tetrahedron Lett.* **1977**, 1839.

(13) Schlecker, R.; Seebach, D.; Lubosch, W. *Helv. Chim. Acta* **1978**, *61*, 512.

(14) Staab, H. A.; Lauer, D. (*Chem. Ber.* **1968**, *101*, 864) have shown that C–N bond rotation in 2,6-disubstituted benzamides can be sufficiently slow to allow separation of syn and anti geometrical isomers. Their ^{1}H NMR assignments, the anti alkyl resonance is upfield from the syn, were used here.

(15) The ^{1}H NMR spectrum of **9** shows the remaining syn axial proton at δ 4.62, whereas the syn equatorial proton in **10** absorbs at δ 5.45. This allows assignments of the **2** syn protons in **7** of axial at δ 3.11 and equatorial at δ 4.38.[14] All new materials were fully characterized by analytical and spectral methods.

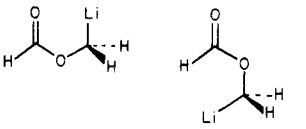
(16) In *N*-acylpiperidines A^{1,3} strain makes 2-equatorial substituents less stable than axial isomers: Johnson, F. *Chem. Rev.* **1968**, *68*, 375. Paulsen, H.; Todt, K. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 899; Scott, J. W.; Durham, L. J.; DeJongh, H. A. P.; Burckhardt, V.; Johnson, W. S. *Tetrahedron Lett.* **1967**, 2381. Chow, Y. L.; Colon, C. J.; Tam, J. N. S. *Can. J. Chem.* **1968**, *46*, 2821. Fraser, R. R.; Grindley, T. B. *Tetrahedron Lett.* **1974**, 4169; Quick, J.; Mondello, C.; Humora, M.; Brennan, T. *J. Org. Chem.* **1978**, *43*, 2705.

piperidine was reported by Seebach et al. based on ^1H NMR assignments.[17]

The syn metalation and substitution of amides appears to be general. We have shown that syn lithiations occur in an *N*-methyl lactam.[18] Seebach et al. have assigned syn geometry to the products of metalation and substitution of *N,N*-dimethyl-2,4,6-triisopropylbenzamide.[13] We have trapped the carbanions of *N,N*-dimethyl, *N,N*-diethyl, piperidyl, and 4-*tert*-butyl piperidyl-2,4,6-triisopropylbenzamides with a wide variety of electrophiles, including methanol-*d*, carbon dioxide, alkyl halides, trialkyl chlorosilanes, aldehydes, and ketones and obtained analytically pure products in 50–90% yield. The ^1H NMR spectra of all products have absorptions for the protons on the unsubstituted carbon upfield from 3.00 ppm, while the signals for the protons on the substituted carbon appear downfield from 3.00 ppm, consistent with designation of syn substitution.[14]

Since organolithiums appear to be configurationally stable at −78 °C and to react with retention of configuration with carbonyl compounds, the metalated intermediates can be assigned the syn stereochemistry.[19,20] For the reactions shown in Scheme I, the intermediate may be assigned the syn equatorial stereochemistry as shown for 8. Theory and experiment agree with respect to the pyramidal, in plane (rather than perpendicular) nature of amide carbanions but differ in that theory predicts a larger stabilization of the anti geometry, while only syn substitution is observed experimentally.

This discrepancy may reasonably be attributed to the effect of the lithium ion. If the reaction proceeds via initial complexation of the carbonyl oxygen with the lithium of the lithiating reagent, intracomplex transfer of a proton and loss of butane would lead to 8 (a kinetic effect). Alternatively, intramolecular complexation of the carbonyl oxygen with lithium could stabilize the chelated syn species, overcoming the normal anti preference. Model 4-31G calculations indicate that 11 is 13.2 kcal/mol more



11 12

stable than 12. MNDO optimizations provide similar results.[21] The role of lithium as a strongly complexing ion which directs a reaction is a recurrent theme in organolithium chemistry,[1,12,13,22] and one which will be the subject of future reports from these laboratories.

Acknowledgment. We are grateful to the National Institutes of Health and the Fonds der Chemischen Industrie for financial support of this work.

Registry No. *3*, 107-31-3; *3*$^-$, 78715-77-2; *5*, 123-39-7; *5*$^-$, 78715-78-3; *6*, 68-12-2; *6*$^-$, 78715-79-4; CH_3^-, 15194-58-8; $HOCH_2^-$, 3315-60-4; $CH_3OCH_2^-$, 61192-30-1; $CH_3CH_2OCH_2^-$, 78715-80-7; $CH_2{=}CHOCH_2^-$, 78715-81-8; $H_2NCH_2^-$, 74215-21-7; CH_4, 74-82-8; CH_3OH, 67-56-1; CH_3OCH_3, 115-10-6; $CH_3CH_2OCH_3$, 540-67-0; $CH_2{=}CHOCH_3$, 107-25-5; CH_3NH_2, 74-89-5.

(17) Seebach, D.; Wykypiel, W.; Lubosch, W.; Kalinowski, H. O. *Helv. Chim. Acta* **1978**, *61*, 3100.

(18) Beak, P.; Brubaker, G. R.; Farney, R. *J. Am. Chem. Soc.* **1976**, *98*, 3621.

(19) Curtin, D. Y.; Okehl, W. J. *J. Am. Chem. Soc.* **1962**, 84, 1967. Witanowski, M.; Roberts, J. D. *Ibid.* **1966**, *88*, 737. Applequist, D. E.; Chmurny, G. N. *Ibid.* **1967**, *89*, 875. Frankel, G.; Dix, D. T.; Carlson, M. *Tetrahedron Lett.* **1968**, 579. Still, W. C.; Sreekumar, C. *J. Am. Chem. Soc.* **1980**, *102*, 1201.

(20) An alternative explanation, that there is rapid equilibration of regioisomeric organolithiums and the substitution is controlled by the transition-state energies seems inconsistent with the high barriers to rotation in the amides,[14] the configurational stability of other systems,[19] and the probability that the transition state for equatorial substitution of 8 is more sterically crowded and of higher energy than that for an axial pathway.[16]

(21) Kos, A.; Schleyer, P. v. R., unpublished results.

(22) For reviews, see Wakefield, B. J. "The Chemistry of Organolithium Compounds"; Pergamon Press: New York, 1974; Kaiser, E. M. *J. Organomet. Chem.* **1978**, *158*, 1. Gschwend, H. W.; Rodriguez, H. R. *Org. React.* **1979**, *26*, 1.

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