J. Am. Chem. Soc. **1988**, *110*, 5702-5705

Electrochemical Behavior of Lithium Dialkylamides: The Effect of Aggregation

Philippe Renaud and Marye Anne Fox*

Contribution from the Department of Chemistry, University of Texas at Austin, Austin, Texas 78712.
Received December 10, 1987. Revised Manuscript Received March 28, 1988

Abstract: Electroanalytical methods can be successfully employed to characterize aggregation in lithium dialkylamides. The ability of a given $LiNR_2$ to act as an electron donor is highly dependent on its aggregation, the more highly associated species acting as the better donor. Observed shifts in cyclic voltammetric peak position are caused by delocalization of the oxidized radical center in the aggregated salts. The larger anodic shift of the oxidation peak of lithium hexamethyldisilazide (relative to monomeric lithium diisopropylamide) is caused partially by delocalization of charge from nitrogen to vacant d-orbitals on silicon.

Sterically hindered lithium dialkylamides are known to be very effective non-nucleophilic metalating agents and are thus of critical importance to synthetic organic and organometallic chemistry. Recently, it was demonstrated that lithium diisopropylamide may also be an efficient electron donor with suitable substrates as, for instance, alkyl halides,[1] polynuclear hydrocarbons,[1] and pyridine.[2] Because differential reactivity is often observed in free and aggregated bases, it is important to have convenient methods for establishing the extent of aggregation under a desired set of conditions.

Since studies of $LiNR_2$ aggregation in the solid state[3] and in solution[4] have been reported, the lithium dialkylamides appeared to us to be very attractive models for an investigation by electrochemical methods of the influence of the degree of aggregation on the electron donor character of anions. Modification of the solvating properties of the solvent (by adding, for instance, HMPA to a THF solution) is known to have a dramatic influence on the cyclic voltammograms of allyllithium,[5] *tert*-butylpropargyllithium,[5] and dilithiated thiophenoxyacetic acid.[6] However, in none of these cases could a clear correlation between the oxidation peak potentials and aggregation states be made since the latter were not known with sufficient certainty. We report here a cyclic voltammetric study of three of the most widely used lithium dialkylamides: lithium diisopropylamide (LDA), 2,2,6,6-(tetramethylpiperidinato)lithium (LiTMP), and lithium 1,1,1,3,3,3-hexamethyldisilazide (LiHMDS). We establish that electrochemical methods can be effectively employed to characterize the aggregation equilibria of lithium dialkylamides.

Results and Discussion

Lithium Diisopropylamide. Two distinct irreversible oxidation peaks ($E_p(1) = -0.52$ V SCE and $E_p(2) = -0.23$ V SCE) were observed in the cyclic voltammogram of LDA at -25 °C in THF (Figure 1). The relative size of the peaks is nearly independent of concentration over a range from 2 to 20 mM. Partial fouling of the electrode occurred after the first scan. When several scans were recorded with the same electrode, a relative decrease of the peak at -0.52 V [$E_p(1)$] was noticed. Upon adding increasing amounts of HMPA, disappearance of the peak at -0.52 V was observed. After addition of 5% vol HMPA, only one peak remained, corresponding to the peak (2) in THF (Figure 3). A cathodic shift was also observed during the addition of HMPA.

Table I. Oxidation Peak Potentials (E_p) and Half-Wave Oxidation Potentials ($E_{1/2}$) for LDA and LiHMDS

substance	T [°C]	HMPA content [vol %]	$E_p{}^a$ [V SCE]	$E_{1/2}$ [V SCE]
LDA	-12	10	-0.41	-0.39 - -0.34
	-25	10	-0.35	-0.33 - -0.28
	-78	10	-0.04	-0.02 - +0.03
LiHMDS	+33	0	+0.81	+0.83 - +0.88
	+1	0	+0.66	+0.68 - +0.73
	-25	0	+0.56	+0.58 - +0.63
	0	10	+0.69	+0.71 - +0.76

[a] Scan rate = 100 mV/s.

Cryoscopic study in THF[4b] has shown that LDA exists in solution in a monomer–dimer equilibrium and that the two oxidation peaks observed by cyclic voltammetry represent the dimer [peak (1)] and the monomer [peak (2)]. The relative intensities of the two peaks are governed not only by the equilibrium constant between the monomer and the dimer but also by the kinetic approach to this equilibrium. This was proven by examining LDA by cyclic voltammetry in THF containing 2% HMPA (low dimer concentration) at different temperatures. When LDA in THF was allowed to warm from -78 and -20 °C, the dimer/monomer peak ratio increased slowly from 1:10 to 1:4. The relative increase of the concentration of the more aggregated species upon raising temperature is a well-known phenomena caused by decoordination of solvent molecules upon increasing the self-association of the salt[7] (Figure 2). At higher temperature, a dramatic increase in intensity of the peak corresponding to the dimer was observed, becoming the main peak at -14 °C. This sudden rise is explained by the fact that the monomer–dimer conversion has become fast enough on our electrochemical time scale so that all the monomer is converted to the more easily oxidized dimer as it is electrooxidatively removed from the equilibrium. The peak area can then no longer relate to the concentration of the species in solution.

The electrochemical behavior of the monomer alone could be examined in THF containing 10% HMPA (Figure 3). At -78 °C, the peak is still totally irreversible at scan rates <1 V/s.[8] However, based on work of Breslow et al.,[6] it is possible to estimate the oxidation potential of LDA since no charge-transfer problem was detected (narrow peak, $E_p - E_{p/2} = 90$ mV). The half-wave oxidation potential ($E_{1/2}$) can be obtained from the oxidation peak

---

[1] Ashby, E. C.; Goel, A. B.; DePriest, R. N. *J. Org. Chem.* **1981**, *46*, 2429.

[2] Newkome, G. R.; Hager, D. C. *J. Org. Chem.* **1982**, *47*, 599.

[3] For the X-ray structure of LiHMDS, see: Power, P. P.; Xiaojie, X. *J. Chem. Soc., Chem. Commun.* **1984**, 358 and references cited therein. For LiTMP: Lappert, M. F.; Slade, M. J.; Sing, A. *J. Am. Chem. Soc.* **1983**, *105*, 302. For lithium dibenzylamide: Barr, D.; Clegg, W.; Mulvey, R. E.; Snaith, R. *J. Chem. Soc., Chem. Commun.* **1984**, 285.

[4] (a) LiHMDS: Kimura, B. Y.; Brown, T. L. *J. Organomet. Chem.* **1971**, *26*, 57. (b) LDA: Bauer, W.; Seebach, D. *Helv. Chim. Acta* **1984**, *67*, 1972. (c) Lithiated cyclohexanone phenylimine: Kallman, N.; Collum, D. *J. Am. Chem. Soc.* **1987**, *109*, 7466.

[5] Jaun, B.; Schwarz, J.; Breslow, R. *J. Am. Chem. Soc.* **1980**, *102*, 5741.

[6] Renaud, P.; Fox, M. A. *J. Org. Chem.* **1988**, in press.

[7] Seebach, D.; Hassig, R.; Gabriel, J. *Helv. Chim. Acta* **1983**, *66*, 308.

[8] This is an upper limit for obtaining a cyclic voltammogram undistorted by uncompensated resistance.

0002-7863/88/1510-5702$01.50/0

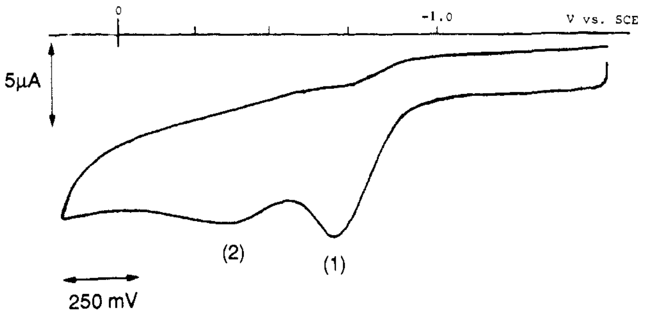


Figure 1. Cyclic voltammogram of LDA in THF at -25 °C (100 mV/s), $E_{peak(1)} = -0.52$ V versus SCE, $E_{peak(1)} = -0.23$ V versus SCE: (1) dimer and (2) monomer.

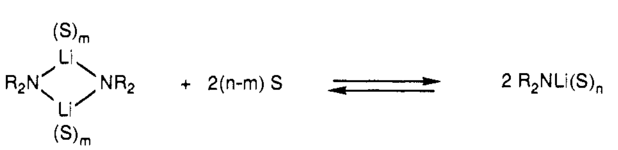


Figure 2. Influence of solvation on the equilibrium monomer–dimer, S = solvent molecule (THF or HMPA): LDA and LiHMDS, $n > m$; LiTMP; $n \sim m$.

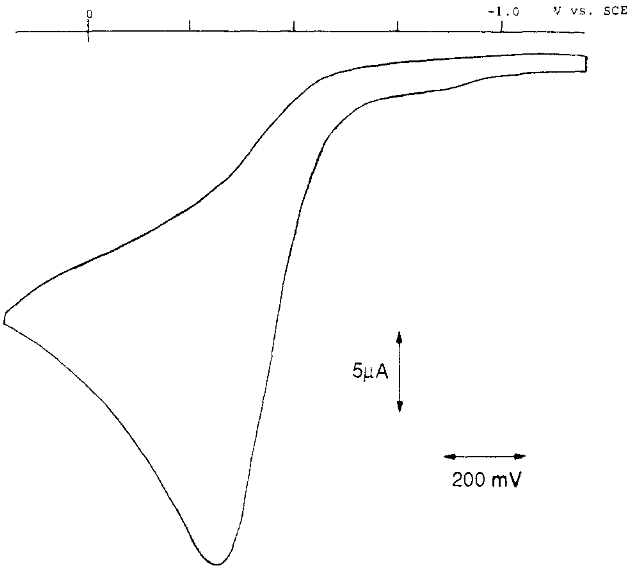


Figure 3. Cyclic voltammogram of LDA in 10% vol HMPA in THF at -25 °C (100 mV/s), $E_p = -0.35$ V SCE.

potential (E_p) by adding a correction factor of 0.02–0.07 V [$E_{1/2} = E_p + (0.02\text{–}0.07)$ V]. This term corrects for the effect of a rapid destruction of the oxidation products by dimerization of the radicals.[5,9] The peak potentials E_p and estimated $E_{1/2}$ at different temperatures are reported in Table I. The oxidation potential was shown to be temperature dependent, an anodic shift of approximately 6 mV/K having been observed on lowering the temperature. The oxidation potential was found to be nearly independent of the concentration of LDA.[10]

(2,2,6,6-Tetramethylpiperidinato)lithium. The cyclic voltammogram of LiTMP in THF (Figure 4) at -30 °C is very similar to that of LDA under the same conditions. Two peaks at -0.45 [peak (1)] and +0.15 V SCE [peak (2)] were observed. In contrast to the behavior observed with LDA, the peak (1) did not disappear immediately upon addition of HMPA (20% HMPA were added) at -40 °C, rather requiring about 15 min. The process was much faster at -10 °C; above this temperature, the decomposition of LiTMP occurred rapidly, giving a brown solution.

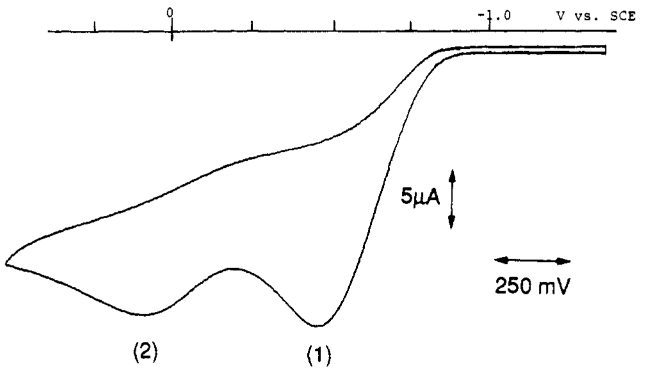


Figure 4. Cyclic voltammogram of LiTMP in THF at -30 °C (100 mV/s), $E_{peak(1)} = -0.45$ V SCE, $E_{peak(2)} = +0.15$ V SCE: (1) dimer and (2) monomer.

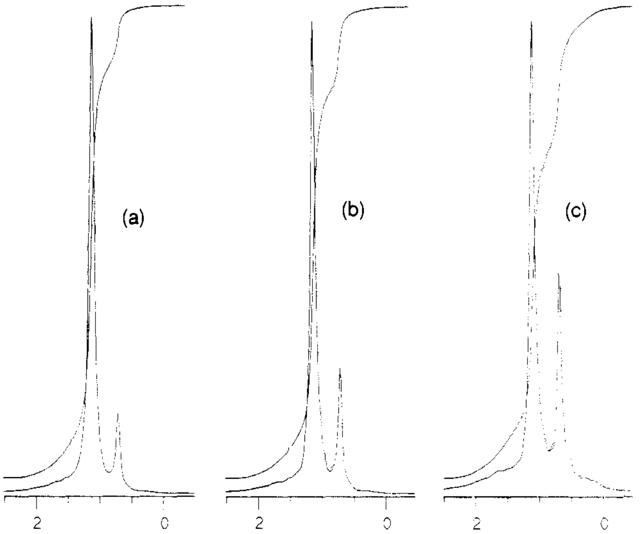


Figure 5. ^{7}Li NMR of LiTMP in THF at -50 °C at different concentrations: (a) 167, (b) 83, (c) 42 mM.

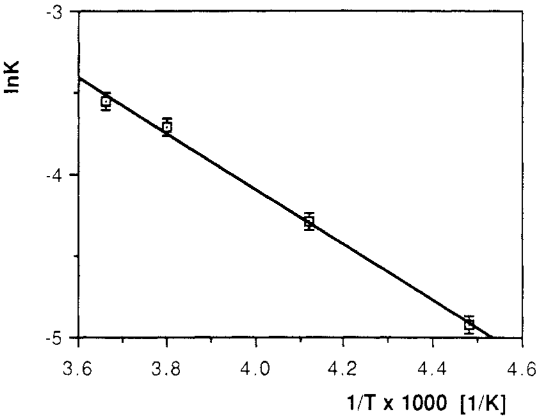


Figure 6. Plot of ln K_{eq} versus $1/T$ based on a dimer–monomer equilibrium for LiTMP in THF (temperature range: 0 °C to -50 °C, 42 mM solution).

By adding a relatively concentrated solution of LiTMP (0.3 M) to a -78 °C cooled THF solution containing HMPA, we could observe the presence of an intense peak (1) stable for more than 10 min. This peak was assigned by analogy to LDA[4b] to a dimeric species. LiTMP is present exclusively as dimer in our 0.3 M stock solution.

As nothing is reported in the literature about the degree of association of LiTMP in etheral solutions, we decided to investigate such solutions by proton and ^{7}Li NMR. Four major points deduced from our cyclic voltammetry experiment needed to be checked: (1) whether LiTMP exists in a monomer–dimer equilibrium; (2) whether the dimer is predominant at the con-

---

(9) Preparative electrolysis of lithium amides is reported to produce hydrazine derivatives by radical coupling: Bauer, R.; Wendt, H. *Angew Chem., Int. Ed. Engl.* **1978**, *17*, 202.

(10) Our study was limited to concentrations lower than 25 mM because of electrode fouling at higher concentrations.

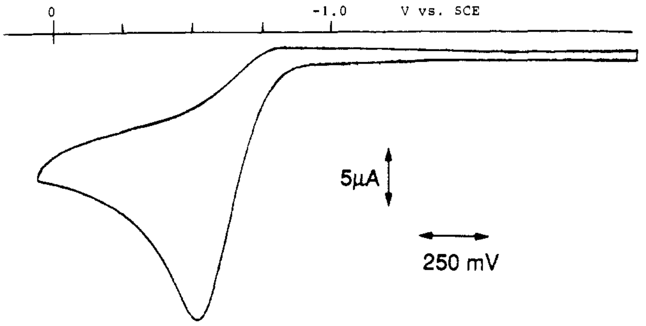


Figure 7. Cyclic voltammogram of LiHMDS in THF at -25 °C (100 mV/s), E_p = +0.56 V SCE.

centration of our stock solution; (3) whether the exchange rate between monomer and dimer is very slow; and (4) whether the presence of lithium perchlorate (supporting electrolyte) interferes with the equilibrium. At -50 °C, the ^{7}Li NMR spectrum of LiTMP in THF consists of two singlets at 0.7 and 1.3 ppm. The concentration dependence of the relative peak intensities (Figure 5) supports the involvement of a monomer (0.7 ppm)–dimer (1.3 ppm) equilibrium (K_{eq} = 6.5·10^{3} mol/L at -50 °C). This equilibrium constant establishes that LiTMP exists principally as dimer in our 0.3 M stock solution.

Thermodynamic parameters could be deduced from a study of the equilibrium at different temperatures. A plot of ln K_{eq} versus $1/T$ is shown in Figure 6 for data in the temperature range from 0 to -50 °C, establishing values for ΔH^0 = +5.4 kcal/mol and ΔS^0 = +3.4 cal/mol·K. The positive valves of ΔH^0 and ΔS^0 suggest that, unlike LiHMDS,[4a,11] the solvent does not solvate lithium in monomeric LiTMP much better than in the dimer (Figure 2). This reflects the greater steric demand of the 2,2,6,6-dimethylpiperidinato ligand compared to $N(SiMe_3)_2$.[12] Coalescence of the two peaks was observed only at room temperature (coalescence occurs already at 0 °C with LiHMDS), indicating that the dimer-to-monomer conversion rate is very slow at low temperature.

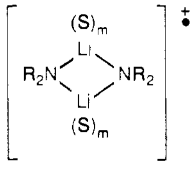
The ^{1}H NMR spectra confirms all the results obtained from the ^{7}Li NMR study. At -50 °C in THF, the methyl groups of the dimer formed a singlet at 1.18 ppm, while those of the monomer formed two singlets at 0.99 and 1.01 ppm. The monomer–dimer ratio is the same as that observed in the ^{7}Li NMR experiment. By measuring the spectrum in THF containing HMPA (20%), it could be established that the disappearance of the dimer was accompanied by a strong increase in the intensity of the monomer signal. The spectrum of a THF solution containing $LiClO_4$ (0.15 M) showed no change relative to that in pure THF, establishing that the supporting electrolyte does not perturb the monomer–dimer equilibrium at room temperature.

Lithium 1,1,1,3,3,3-Hexamethyldisilazide. NMR studies of LiHMDS have shown that it exists in THF solution in a monomer–dimer equilibrium.[4a] However, the cyclic voltammogram of LiHMDS in THF (Figure 7) revealed only a single irreversible oxidation peak at a surprisingly anodic potential (E_p = +0.56 V SCE, -25 °C). The narrow shape of the peak ($E_p - E_{p/2}$ = 110 mV) proves that no major charge-transfer problem occurs. The oxidation potential of LiTMP can be estimated from the E_p value in the same way as for LDA (see Table I for values at different temperatures). A cathodic shift of 4 mV/K was observed upon warming the solution (E_p = +0.56 V SCE, 33 °C). No additional peak(s) could be observed when cosolvents such as HMPA or 12-crown-4 were added to the solution. This suggests that the observed oxidation peak corresponds to the monomeric species. From the value for the monomer–dimer equilibrium constant,[4a] we calculate that the dimer concentration cannot exceed 0.13 mM at -20 °C for a 20 mM[13] total concentration of LiTMP. However, the absence of a dimer oxidation peak at temperatures above 0 °C (where the rate of monomer–dimer exchange is very fast from NMR coalescence studies) may only be explained by two hypotheses: either E_{ox} (dimer) ≥ E_{ox} (monomer) or the oxidation peak of the dimer is not detectable with our electrode system because of some barrier to heterogeneous charge transfer.[14]

Single Electron Transfer. Our observation that the facility of electron transfer in lithium dialkylamides depends on aggregation may be relevant to the current controversy on the ubiquity of single electron transfer (SET) in many organic reactions. For example, Ashby's claim that the reductive cyclization of haloalkenes upon treatment with lithium aluminum hydride proceeds via SET[15] diverges from the interpretation offered by Curran.[16] In addition, Newcomb and co-workers have reported several cases where apparent electron donation by lithium dialkylamides may proceed through a different mechanism.[17] Our work suggests that an important component of such studies is a clear definition of the degree of aggregation of the base or reducing agent under the experimental conditions used.

Conclusions

This work demonstrates that the ability of lithium dialkylamides to transfer electrons is highly dependent on their aggregation, the more associated species being also the best electron donor. Considerable differences between the oxidation peak potentials for the monomer and dimer, 0.29 and 0.60 V, were observed in the cyclic voltammograms of LDA and LiTMP, respectively. These shifts correspond to a stabilization by delocalization of the radical generated from the dimeric lithium amide (I) by comparison with that derived from the monomer (II). In LDA, both oxidation peaks are sufficiently narrow to allow an estimation of the stabilization energy. The observed shift of 0.29 V corresponds to a stabilization energy of 6.7 kcal/mol.



I

$R_2N^{\bullet} + Li^{+}(S)_p$

II

Generalization of this result to other organolithium compounds can be considered. Seebach et al., for instance, have observed from stereochemical considerations that the lithium derivative obtained from alanine diketopiperazine reacts by an ionic mechanism in the monomeric state and by electron transfer in the dimeric state.[18]

Another important observation is the very large anodic shift of the oxidation peak of LiHMDS relative to monomeric LDA (ΔE_p = 1.04 V at -25 °C in THF). This is caused partially by stabilization of the anion by delocalization of negative charge density from nitrogen into the empty d-orbitals of silicon. This stabilization effect has also been invoked to explain the higher acidity of hexamethyldisilazane (pK_a = 29.5) than diisopropylamine (pK_a = 35.7).[19,20] Other factors, such as increase of the

---

[11] An X-ray structure of monomeric [LiHMDS-12-crown-4] shows that the lithium atom is coordinated by four oxygen atoms.[3a] In the dimeric form, $[LiHMDS{\cdot}OEt_2]_2$, the lithium atom was surrounded by one molecule of Et_2O: Engelhardt, L. M.; May, A. S.; Raston, C. L.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1983**, 1671.

[12] This greater steric demand is also responsible for the tetrameric structure of crystalline LiTMP.[3b] (LiHMDS forms a trimer under the same conditions.)

[13] This value represents the upper limit of the concentration range we were able to study. At higher concentrations, extensive electrode fouling was observed.

[14] Failure to observe any oxidation peak is reported for some aggregated species as $Me_4Cu_2Li_2$: House, H. O. *Acc. Chem. Res.* **1976**, 959 and dilithiated alkanoic acids: ref 6.

[15] Ashby, E. C.; DePriest, R. N.; Wenderoth, B.; Pham, T. M. *J. Org. Chem.* **1984**, *49*, 3545.

[16] Curran, D. P.; Kim, D. *Tetrahedron Lett.* **1986**, *27*, 5821.

[17] Park, S. V.; Chung, S. K.; Newcomb, M. *J. Org. Chem.* **1987**, *52*, 3275.

[18] Seebach, D.; Imwinkelried, R.; Weber, T. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Springer Verlag: Berlin, 1986; pp 190–191.

[19] Fraser, R. R.; Mansour, T. S. *J. Org. Chem.* **1984**, *49*, 3443.

N–H bond dissociation energy, solvation of the lithium cation, and the degree of covalence of the Li–N bond also contribute to the shift of the oxidation potential. In consequence, the choice of the base used for metalations may be a determinant factor when competing reactions can occur by electron transfer. The use of LiHMDS instead of the more generally used lithium dialkylamides may permit such side reactions to be avoided.

Experimental Section

Materials. Diisopropylamine, 1,1,1,3,3,3-hexamethyldisilazane, and 2,2,6,6-tetramethylpiperidine (Aldrich) were distilled over CaH$_2$ and stored under argon. Tetrahydrofuran (THF) was distilled under Ar over potassium, and hexamethylphosphoramide (HMPA) was heated at 180 °C over CaH$_2$ for 2 h before distillation under reduced pressure. The lithium amide solutions (0.3 M) were freshly prepared by metalation of the corresponding amine in THF with *n*-butyllithium (Aldrich, 2.5 M in hexane). The solutions were stored at −50 °C under Ar. Solutions of LDA and LiTMP in THF/HMPA were not stable at temperatures higher than −10 °C for more than 5 min. LiHMDS was stable at room temperature, even in the presence of HMPA. Lithium perchlorate (Aldrich, anhydrous) was dried at 200 °C (0.05 mmHg) for 12 h in an electrolyte storage flask. The flask was then flushed with Ar, and THF was transferred from the distillation apparatus via a cannula to give a 0.2 M solution.

Cell and Apparatus. Cyclic voltammetry measurements were performed in a three compartment cell. The working electrode (glassy carbon, V25, Atomergic Chemetals Corp., polished with diamond paste (50 000 mesh)) was separated from the counterelectrode (platinum mesh) by a medium porosity fritted glass. A silver wire coated with AgCl, employed as the pseudo-reference electrode, was separated from the working electrode by a fine fritted glass. LiClO$_4$ (0.2 M) was used as the supporting electrolyte. Potentials were measured relative to an internal ferrocene standard ($E_{1/2}$ = +510 mV versus SCE). Cyclic voltammograms were recorded with a BAS-100 electrochemical analyzer or with a PAR 173 potentiostat driven by a PAR 175 universal programmer.

NMR Measurements. Solutions of LiTMP (187, 84, and 42 nM) in THF/THF-d_8 were prepared by adding the appropriate amounts of solvent to solid LiTMP (isolated by evaporation of the solvent after metalation as described above). NMR tubes were sealed with rubber stoppers. ^{7}Li NMR spectra were recorded on a General Electric GN-500 (194 MHz) spectrometer. Chemical shifts are reported relative to an external LiCl reference. ^{1}H NMR spectra were recorded on a Nicolet NT-200 (200 MHz), and chemical shifts are reported relative to TMS.

Acknowledgment. We are grateful to the National Science Foundation and to the Robert A. Welch Foundation for support of this work. We thank Dr. Ben Shoulders, J. Wallia, and S. Sorey for assistance with the NMR measurements.

---

(20) A review about the use of electrochemical methods to estimate the basicities of a variety of carbanions is given by Breslow (Breslow, R. *Pure Appl. Chem.* **1974**, *40*, 493) and Fox (Fox, M. A. In *Comprehensive Carbanion Chemistry, Part C*; Buncel, E.; Durst, T.; Eds.; Elsevier: Amsterdam, 1987; p 93).

An Electrochemical Characterization of Dianions: Dilithiated Carboxylic Acids

Philippe Renaud and Marye Anne Fox*

Contribution from the Department of Chemistry, University of Texas at Austin, Austin, Texas 78712.

Received December 15, 1987.
Revised Manuscript Received March 28, 1988

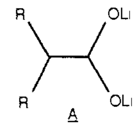
Abstract: The oxidation of dilithiated carboxylic acids has been studied by cyclic voltammetry. The pK_as for the second deprotonation of phenylacetic acid, diphenylacetic acid, and phenylthioacetic acid have been determined by an equilibration method. From the electrochemical results and the pK_a values, the bond dissociation energies were calculated, via a thermodynamic cycle, for the α C–H bonds of the corresponding carboxylate salts. The noncoplanarity of the two phenyl rings for the radical derived from diphenylacetic acid was deduced.

The use of electrochemical methods to obtain physical and chemical information about carbanions has been recently reviewed.[1] For instance, molecular orbital energies, conformation analysis, and the ability to react by electron transfer[2] have been studied. A correlation between the pK_a values of carbon acids and the oxidation potentials of their conjugated bases has been reported by Kern and Federlin.[3] On the basis of gas-phase bond dissociation energies and oxidation potentials of organolithium compounds, Breslow and co-workers have estimated the pK_as of such very weak carbon acids as toluene, propene, and 4,4-dimethyl-2-pentyne.[4] More recently, Bordwell and Bausch have used acidity-oxidation potential values as estimates of relative bond dissociation energies and radical stabilities in DMSO.[5]

Only few studies of dianionic systems, however, have been reported in the literature.[6] Because of their electron-rich character, they represent an interesting target for study by electrochemical methods.

Dianions have been shown to react in many cases by electron transfer. For example, attempts to methylate the dipotassium salt of *p*-xylene with an excess of methyl iodide produced exclusively a dibenzyl derivative, presumably via one electron oxidation and dimerization of the generated radical anion.[7] The dianion derived from diisopropylbenzene was shown to dimerize spontaneously.[8] Oxidative coupling of dicarbanions is also described in the literature.[9]

We have chosen to examine in this work dilithiated carboxylic acids (A). They are known for their high stability, ease of preparation, and great utility from a synthetic point of view.[10]



A

---

(1) Fox, M. A. In *Comprehensive Carbanion Chemistry, Part C*; Buncel, E., Durst, T., Eds.; Elsevier: Amsterdam, 1987; p 93.

(2) House, H. O. *Acc. Chem. Res.* **1976**, 959.

(3) Kern, J. M.; Federlin, P. *Tetrahedron* **1978**, 661.

(4) Jaun, B.; Schwarz, J.; Breslow, R. *J. Am. Chem. Soc.* **1980**, *102*, 5741.

(5) Bordwell, F. G.; Bausch, M. J. *J. Am. Chem. Soc.* **1986**, *108*, 1979.

(6) Some highly stabilized dianions have been studied: Aharon-Shalom, E.; Becker, J. Y.; Agranat, I. *Nouv. J. Chim.* **1979**, *3*, 643. Acton, N.; Hon, D.; Schwarz, J.; Katz, T. J. *J. Org. Chem.* **1982**, *47*, 1011.

(7) Bates, R. B.; Ogle, C. A. *J. Org. Chem.* **1982**, *47*, 3949.

(8) Willhelm, D.; Clark, T.; von Rague Schleyer, P. *J. Chem. Soc., Chem. Commun.* **1983**, 211.

(9) Fox, M. A.; Chen, C.-C. *J. Chem. Soc., Chem. Commun.* **1985**, 23.

(10) Petragnani, N.; Yonashiro, M. *Synthesis* **1982**, 521.

0002-7863/88/1510-5705$01.50/0