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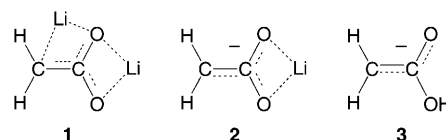140 PUBLICATIONS 2,340 CITATIONS

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Communications

Gas-Phase Synthesis and Reactivity of the Lithium Acetate Enolate Anion, $^-CH_2CO_2Li$**

Matthew M. Meyer, George N. Khairallah, Steven R. Kass,* and Richard A. J. O'Hair*

Dedicated to Professor Helmut Schwarz on the occasion of his 65th birthday

Dianions are versatile reagents that are widely used in organic synthesis.[1] They are typically prepared by two-fold deprotonation at carbon, nitrogen, oxygen, or sulfur centers. These reactive intermediates have a long history going back more than one hundred years to Grignard himself, who prepared the dianion of phenylacetic acid.[2] Ivanoff et al. subsequently exploited the dimagnesium salts of carboxylic acids possessing α hydrogen atoms and developed their reactivity with a variety of electrophiles.[3] Despite the widespread use of Ivanoff reagents and related dilithiated carboxylic acids in organic synthesis, surprisingly little is known about the fundamental properties of these salts.[4] Aggregation and solvation effects complicate studies of these species, and their sensitivity to moisture and oxygen has played a large role in the absence of X-ray crystal structures to date. Theoretical calculations by Schleyer and Kos[5a] and Streitwieser et al.,[5b] however, suggest that the monomeric structure of the dilithium salt of acetic acid (**1**) is non-symmetrical with 1,3- and 1,3′-lithium bridges.[6] We have shown that the decarboxylation of lithium and other metal complexes of mono- and dicarboxylic acids can produce a variety of organometallic ions.[7] Herein, the gas-phase preparation and reactivity of the lithium acetate enolate anion (**2**, $^-CH_2CO_2Li$), a species directly related to **1** and the prototypical lithium salt of an α-

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deprotonated carboxylate, is described. The results of high-level computations also are presented, as is a comparison of **2** with the acetic acid enolate anion (**3**).[8]

Electrospray ionization of a 3:1 (v/v) water/methanol solution containing malonic acid and lithium hydroxide readily provided the anionic lithium complex of doubly deprotonated malonic acid ($^-O_2CCH_2CO_2Li$, *m/z* 109; Figure 1). Collision-induced dissociation (CID) of this ion resulted in the loss of carbon dioxide to afford the lithium acetate enolate anion (*m/z* 65).[9] Its structure was explored by carrying out density functional calculations (B3LYP)[10] with the 6-311+G(2df,2pd) basis set. Two low-energy anion conformations were located, both of which bind the lithium in a bidentate fashion (Figure 2). These structures are directly related to the parent dilithium salt **1** by removal of either of the non-equivalent bridging lithium ions. The more
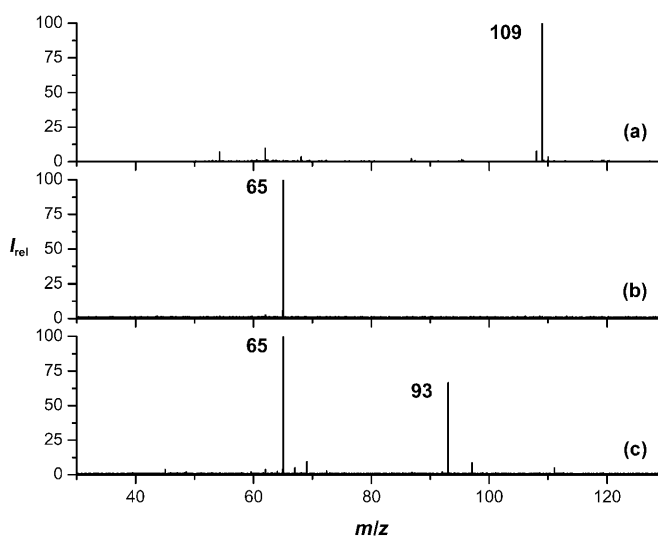

Figure 1. a) Electrospray ionization of malonic acid and lithium hydroxide from a 3:1 (v/v) MeOH/H2O solution. The *m/z* 109 ion corresponds to $LiO_2CCH_2CO_2^-$. b) Formation of $^-CH_2CO_2Li$ (*m/z* 65) by CID and its subsequent isolation. c) Reaction of $^-CH_2CO_2Li$ with EtOH (1.7×10^{-8} Torr) for 200 ms. The ion at *m/z* 93 (HC≡C−O$^-$···Li$^+$···$^-$OEt) is the only primary reaction product, but small amounts of secondary products at *m/z* 69 (HO$^-$···Li$^+$···$^-$OEt) and 97 (EtO$^-$···Li$^+$···$^-$OEt) also are observed.
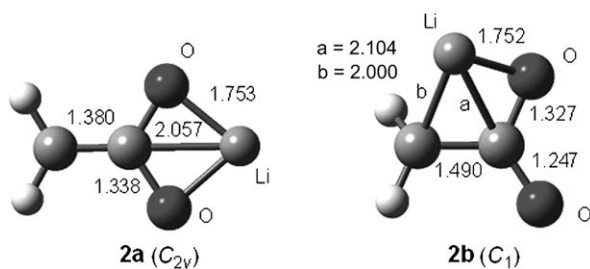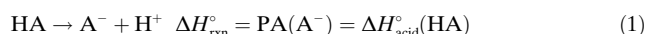
Figure 2. B3LYP/6-311 + G(2df,2pd) structures of the lithium acetate enolate anion. Bond lengths are in Å.

stable structure (**2a**) has C_{2v} symmetry, and both oxygen atoms of the carboxylate group interact with the lithium. In contrast, when the lithium ion coordinates to the α carbon and one oxygen atom, the resulting C_1 structure (**2b**) is predicted to be 25.6 kJ mol^{-1} less stable at 298 K. This energy difference is nearly the same when high-level G3 calculations are used (22.9 kJ mol^{-1}),[11] which strongly suggests that **2a** is the preferred structure for the lithium acetate enolate anion.

To further assess the structure of **2**, and as the replacement of hydrogen by lithium has been shown to dramatically increase the proton affinity (PA) of LiO$^-$ over HO$^-$ while simultaneously decreasing the electron affinity (EA) of LiO$^·$ relative to HO$^·$,[12] the PA of **2** and the EA of its corresponding radical were measured. This was accomplished by reacting **2** with acids of known strength or electron-transfer reagents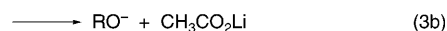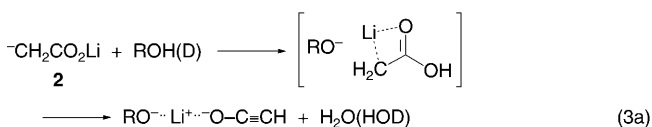 with known electron affinities [Eqs. (1) and (2)]. More specifically, **2** was found to readily react by proton transfer with acetone, toluene, and pyridazine ($\Delta H°_{acid}$ = 1543.1 ± 8.4, 1599.5 ± 5.0, and 1600.0 ± 10.5 kJ mol^{-1}, respectively),[13] but only sluggishly (i.e., the reaction efficiency was less than 5%) with fluorobenzene and furan ($\Delta H°_{acid}$ = 1619.6 ± 8.8[14] and 1636.4 ± 1.7 kJ mol^{-1}, respectively). Proton transfer was not observed with pyrazine or deuterium oxide ($\Delta H°_{acid}$ = 1642.6 ± 10.5 and 1642.6 ± 0.4 kJ mol^{-1}, respectively) but the former reagent led to an adduct–H$_2$ ion, and the latter induced two sequential hydrogen–deuterium (H/D) exchanges. These data suggest that the proton affinity of **2** is between that of the conjugate bases of pyridazine and fluorobenzene, so PA(**2**) = 1610.0 ± 12.1 kJ mol^{-1} was assigned. Calculations indicate that protonation of **2** at carbon is favored over protonation at oxygen by 141 kJ mol^{-1} at the B3LYP/6-311 + G(2df,2pd) level. The observed H/D exchange behavior of **2** with D$_2$O is consistent with this finding. Likewise, the predicted proton affinities of 1610.4 (B3LYP) and 1618.9 (G3) kJ mol^{-1} are in accord with the experimental results.
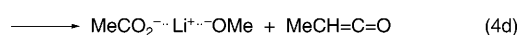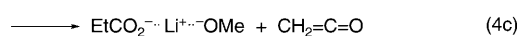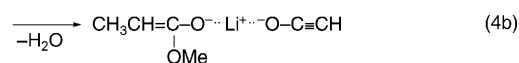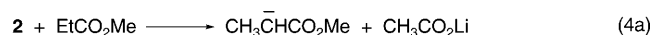
To determine the electron affinity of the radical corresponding to **2**, the anion was bracketed in a similar manner to the proton affinity measurements, but neutral reagents with known electron affinities were used. Electron transfer readily occurred with *p*-fluoronitrobenzene and *m*-fluoronitroben-

$$HA \rightarrow A^- + H^+ \quad \Delta H°_{rxn} = PA(A^-) = \Delta H°_{acid}(HA) \quad (1)$$

$$A^- \rightarrow A^· + e^- \quad \Delta H°_{rxn} = EA(A^·) \quad (2)$$

zene (EA = 1.101 ± 0.048 and 1.210 ± 0.048 eV, respectively),[13] but not with carbon disulfide or sulfur dioxide (EA = 0.58 ± 0.05 and 1.107 ± 0.008 eV, respectively). These results suggest that the electron affinity lies between the values for sulfur dioxide and *m*-fluoronitrobenzene; that is, EA($^·$CH$_2$CO$_2$Li) = 1.16 ± 0.06 eV. This quantity can be combined with the proton affinity of **3** to obtain the C−H bond dissociation energy (BDE) of CH$_3$CO$_2$Li (410.0 ± 13.4 kJ mol^{-1}) as BDE(HA) = $\Delta H°_{acid}$(HA)−IP(H$^·$) + EA(A$^·$), where IP(H$^·$) is the ionization potential of hydrogen and is known to be 1312.0 kJ mol^{-1}. Both of these values are in excellent accord with computations, which predict EA($^·$CH$_2$CO$_2$Li) = 1.07 and 1.06 eV (B3LYP and G3, respectively) and BDE(H−CH$_2$CO$_2$Li) = 407.5 and 415.9 kJ mol^{-1} (B3LYP and G3, respectively). These results also reveal that replacement of a hydrogen atom with lithium increases the proton affinity of **3** (PA = 1540.1 ± 13.0 kJ mol^{-1})[8b,13] by 70 ± 18 kJ mol^{-1} while decreasing the electron affinity of the corresponding radical (EA = 1.80 ± 0.17 eV)[8b,13] by 0.64 ± 0.18 eV or 62 ± 17 kJ mol^{-1}. Consequently, the C−H BDEs for CH$_3$CO$_2$H and CH$_3$CO$_2$Li are the same within 8 kJ mol^{-1}, which is well within the experimental uncertainty for this quantity.

To gain further insights into the behavior of **2**, its reactions with a variety of compounds were examined. Alcohols react via an addition–water elimination pathway [Eq. (3a), R = Me,

$$^-CH_2CO_2Li + ROH(D) \longrightarrow \left[RO^- \begin{array}{c} Li \cdots O \\ H_2C \end{array} \begin{array}{c} O \\ OH \end{array} \right]$$
2

$$\longrightarrow RO^{-}\cdots Li^{+}\cdots {}^-O{-}C{\equiv}CH + H_2O(HOD) \quad (3a)$$

$$\longrightarrow RO^- + CH_3CO_2Li \quad (3b)$$

Et and Figure 1c], and by proton transfer [Eq. (3b)] when more acidic reagents are used (R = C$_6$H$_5$CH$_2$ and CF$_3$CH$_2$). The former transformation presumably occurs by the protonation of an oxygen atom, which is facilitated by the presence of the newly formed alkoxide. In accord with this hypothesis, HOD was lost exclusively when deuterated alcohols were used. Several esters (RCO$_2$R′) and a ketone (acetone) also were examined, and up to four different products were observed, as illustrated for methyl propionate [Eq. (4)].[15] Both proton transfer [Eq. (4a)] and addition–water elimination products [Eq. (4b)] were observed, just as with the alcohols. Two new reaction channels, corresponding to an LiO$^-$ transfer [Eq. (4c)] and an E2-type elimination [Eq. (4d)], were also found. The former of these also occurred to afford LiOSO$_2^-$ and LiOCOS$^-$ upon the reaction of **2** with SO$_2$ and COS, respectively; $^-$CH$_2$COSLi was also produced in the reaction with COS. Lastly, nucleophilic aromatic substi-

$$\mathbf{2} + EtCO_2Me \longrightarrow CH_3\bar{C}HCO_2Me + CH_3CO_2Li \quad (4a)$$

$$\xrightarrow{-H_2O} CH_3CH{=}C{-}O\cdots Li^+\cdots {}^-O{-}C{\equiv}CH \quad (4b)$$
$$\qquad\qquad\qquad \underset{\textstyle OMe}{|}$$

$$\longrightarrow EtCO_2^{-}\cdots Li^{+}\cdots {}^-OMe + CH_2{=}C{=}O \quad (4c)$$

$$\longrightarrow MeCO_2^{-}\cdots Li^{+}\cdots {}^-OMe + MeCH{=}C{=}O \quad (4d)$$

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tution was found to take place with perfluorobenzene, and presumably the product is a pentafluorobenzyl anion [Eq. (5)].

(5)
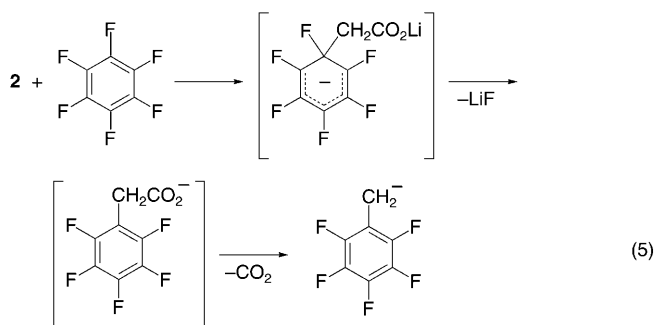
Decarboxylation of appropriate precursors has proven to be a versatile method for the gas-phase generation of textbook organometallic reagents.[7,9] The current work demonstrates that this strategy can be extended to the formation of other reactive intermediates and reagents involved in organic synthesis. Thus, we have shown that anions related to Ivanoff reagents can be prepared and studied in the absence of aggregation and solvent effects.

Experimental Section

Preliminary experiments were conducted using a modified Finnigan LCQ quadrupole ion-trap mass spectrometer equipped with a Finnigan electrospray ionization source.[9a] Electrospray solutions contained malonic acid and lithium hydroxide (both ca. 0.1 mg mL^{-1}) in a 3:1 (v/v) methanol/water mixture. Subsequent ion–molecule reactions were carried out in a Fourier transform ion-cyclotron mass spectrometer as previously described.[12] In both cases, the lithiated salt of malonate dianion was observed at m/z 109 upon ESI and subsequently carbon dioxide was expelled by CID to afford **2**.

Density functional theory (DFT) calculations were carried out at the B3LYP/6-311 + G(2df,2pd) level of theory using Gaussian 03[16] at the Minnesota Supercomputer Institute for Advanced Computational Research. Stationary points were characterized by computing vibrational frequencies, and the resulting unscaled values were used for obtaining the zero-point energies and the thermal corrections for the enthalpies to 298 K. Selected species also were computed using G3 theory as described in the literature,[11] and in all instances, the energetics reported herein are given as enthalpies at 298 K. The Cartesian coordinates and energies of the species mentioned in this work are provided in the Supporting Information.

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