J. Am. Chem. Soc. **1989**, *111*, 7671–7672

Crystal Structure of a Unique Aggregate Containing Lithium and Potassium Cations, Ketone Enolate, and *tert*-Butoxide

Paul G. Williard* and Gloria J. MacEwan

Department of Chemistry, Brown University
Providence, Rhode Island 02912

Received March 31, 1989

Cocrystallization of either lithium or potassium *tert*-butoxide with a preformed potassium or lithium metal enolate derived from 3,3-dimethyl-2-butanone in the presence of tetrahydrofuran yields a novel and unique aggregate composed of four enolate residues, four *tert*-butoxides, four lithiums, four potassiums, a potassium hydroxide residue, and five tetrahydrofuran molecules, i.e., $[(C_6H_{11}O^-)_4{\cdot}(C_4H_9O^-)_4{\cdot}Li^+_4{\cdot}K^+_4{\cdot}KOH{\cdot}(C_4H_8O)_5]$. We have determined the structure of this aggregate by X-ray diffraction analysis. This is the first example of a mixed alkali metal, ketone enolate/alkoxide aggregate.

Considerable effort is currently devoted to structural investigations of ketone enolate anions both in solution[1] and in the solid state.[2] Justification for these investigations stems from the central importance of enolate anions as ambident carbon/oxygen nucleophiles in preparative, synthetic organic chemistry. As an initial step in understanding the function of these aggregates it is necessary for us to understand and eventually to predict the metal-induced substrate organization.[3] In general, similarities exist between the structures of solid-state enolates and the aggregation states of alkali metal enolates in solution.[1c] Thus there is an emerging trend to associate aggregation state with enolate reactivity and reaction mechanism.[4] A recent example is the role of tetrameric aggregates in the aldol reaction.[5] At present, X-ray diffraction analysis provides a most efficient means for obtaining structural information about enolate aggregates. Hence we now report the first structural information obtained from X-ray diffraction analysis for a mixed alkali metal, enolate/alkoxide aggregate prepared according to either of the reactions in Scheme I.[6]

In reaction (a), we generated a solution of the lithium enolate in heptane at approximately 1 M concentration from a suspension of freshly prepared lithium diisopropylamide and the ketone.[2d] To this solution we added a stoichiometric amount of ~1.7 M solution of freshly sublimed potassium *tert*-butoxide in dry, distilled tetrahydrofuran. Cooling this homogeneous reaction mixture to −25 °C overnight effected the growth of transparent, single crystals suitable for X-ray diffraction analysis. Alternatively, in reaction (b), we first generated a suspension of the potassium enolate of pinacolone by reaction of the ketone with potassium hexamethyldisilazide in heptane.[2d] To this enolate suspension we added a stoichiometric amount of freshly prepared lithium *tert*-butoxide[7] in tetrahydrofuran/heptane solution so that the final concentration of the enolate was ~0.9 M, and the solvent was approximately 2:1 heptane/THF. This reaction also became homogeneous after stirring at room temperature and yielded crystals upon cooling.

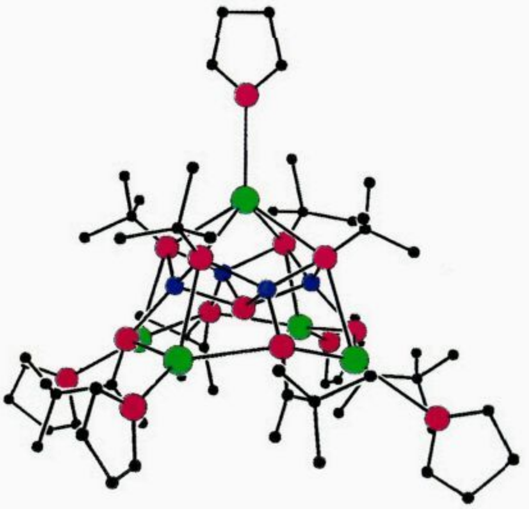
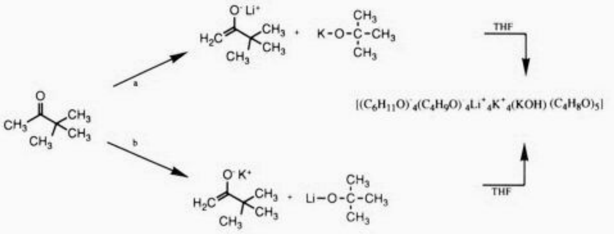


Figure 1. A computer-generated plot of the enolate/alkoxide aggregate. The color scheme is as follows: black = carbon, green = potassium, blue = lithium, and red = oxygen. All hydrogen atoms are not shown but were located by Fourier difference synthesis except the central hydroxide hydrogen that is required to balance charge. The average of all K–O bond lengths is 2.76 Å, and the average of all Li–O bond lengths is 1.94 Å except the central Li–OH distances which average 2.09 Å. A crystallographic diad axis passes vertically through the center of this aggregate; thus the central oxygen, the uppermost potassium, and the uppermost THF oxygen atom lie on this axis.

Scheme I[a]



[a] (a) Lithium diisopropylamide and (b) potassium hexamethyldisilazide.

Crystals from either reaction (a) or (b) exhibited identical unit cell parameters in the X-ray diffraction experiment. Hence we conclude that an identical substance was produced in both reactions. We determined the exact composition of the crystals as $[(C_6H_{11}O^-)_4{\cdot}(C_4H_9O^-)_4{\cdot}Li^+_4{\cdot}K^+_4{\cdot}KOH{\cdot}(C_4H_8O)_5]$ only during analysis of the X-ray diffraction data. Since the final agreement factors for our model structure depicted in Figure 1 with the diffraction data are $R = 0.097$ and $R_w = 0.076$, we are quite confident about the accuracy of this formula.[8]

---

[1] (a) Jackman, L. M.; Lange, B. C. *Tetrahedron* **1977**, *33*, 2737. (b) Wanat, R. A.; Collum, D. B.; van Duyne, G.; Clardy, J.; DePue, R. T. *J. Am. Chem. Soc.* **1986**, *108*, 3415. (c) Arnett, E. M.; Fisher, F. J.; Nichols, M. A.; Ribeiro, A. A. *J. Am. Chem. Soc.* **1989**, *111*, 748.

[2] (a) Amstutz, R.; Schweizer, W. B.; Seebach, D.; Dunitz, J. D. *Helv. Chim. Acta* **1981**, *64*, 2617. (b) Williard, P. G.; Carpenter, G. B. *J. Am. Chem. Soc.* **1985**, *107*, 3345. (c) Jastrzebski, J. T. B. H.; van Koten, G.; Christophersen, M. J. N.; Stam, C. H. *J. Organomet. Chem.* **1985**, *292*, 319. (d) Williard, P. G.; Carpenter, G. B. *J. Am. Chem. Soc.* **1986**, *108*, 462. (e) Williard, P. G.; Salvino, J. M. *J. Chem. Soc., Chem. Commun.* **1986**, 153. (f) Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1989**, *27*, 1624.

[3] Related phenomena such as "molecular preorganization" and "complex induced proximity effects" have recently been reviewed, see: Cram, D. J. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1039. Beak, P.; Meyers, A. I. *Acc. Chem. Res.* **1986**, *19*, 356.

[4] (a) Jackman, L. M.; Lange, B. C. *J. Org. Chem.* **1983**, *48*, 4789. (b) Jackman, L. M.; Lange, B. C. *J. Am. Chem. Soc.* **1981**, *103*, 4494. (c) House, H. O.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1971**, *36*, 2361.

[5] SeeBach, D.; Amstutz, R.; Dunitz, J. D. *Helv. Chim. Acta* **1981**, *64*, 2622.

[6] See: Cambillau, C.; Bram, G.; Corset, J.; Riche, C. *Nouv. J. Chem.* **1979**, *9*, for the structure of a 2,2,2-crypt, Li^+, K^+, ethylacetoacetate enolate.

[7] Lochmann, L.; Coupek, J.; Lim, D. *Coll. Czech. Chem. Commun.* **1970**, *35*, 733.

[8] Crystals of the mixed aggregate depicted in Figure 1 are monoclinic, space group *C*2/*c*, $a = 22.017$ (7) Å, $b = 19.801$ (5), $c = 17.808$ (4) Å, $\beta = 91.25$ (8)°, $Z = 4$ $[(C_6H_{11}O^-)_4{\cdot}(C_4H_9O^-)_4{\cdot}Li^+_4{\cdot}K^+_4{\cdot}KOH{\cdot}(C_4H_8O_5)]$ units, $D_c = 0.99$ g/cm³. The final agreement factors are $R = 0.097$ and $R_w = 0.076$ for 3153 unique, observed $[F_o \geq 3\sigma(F_o)]$ reflections and 377 independent variables. The atomic coordinates and anisotropic thermal parameters for this structure have been submitted as Supplementary Material and are also available on request from the Director of the Cambridge Crystallographic Data Center, University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

0002-7863/89/1511-7671$01.50/0

The aggregate depicted in Figure 1 is altogether novel. It is crown shaped with enolate residues and potassium atoms at the open end. A layer of lithium atoms and *tert*-butoxide residues connect the open end with a potassium atom at the peak. Each of the five potassium atoms is coordinated to a THF molecule. Each enolate oxygen is tricoordinate and is attached to two potassium atoms and one lithium atom. Currently we do not have an explanation for the origin of the encapsulated hydroxide at the center of the aggregate! This hydroxide could originate from accidental introduction of moisture into our enolate reactions from impure reagents or as a byproduct of a small amount of aldol condensation/dehydration of the pinacolone enolate with unenolized ketone.[9] We did not take unusual precautions to exclude moisture from our reactions, although we followed the routine protocol of generating enolate anions from amide bases under a nitrogen atmosphere in oven-dried glassware with freshly purified solvents and reagents utilizing syringe transfer of reagents. It is noteworthy that oxide encapsulation has previously been noted in the aggregates of some magnesium and lithium salts.[10]

The exchange of heavier alkali metal cations for lighter ones in solution has been established in several different contexts and has demonstrated utility for preparative reactions.[11] For example, this exchange phenomena is employed in the reaction of alkoxides with lithium amide bases to generate amide bases with enhanced reactivity.[12] Exchange of alkali metal cations is also useful in preparing alkyl sodium and potassium reagents from the corresponding alkyllithium reagents.[13] Evidence has previously been presented to indicate the interaction of alkoxides with enolates in solution.[14] Our results reported herein begin to provide structural information for the nature of this latter interaction. Structural results such as these may have important implications for the asymmetric synthesis of organic compounds since alkoxides are logical chiral auxiliaries in enolate reactions. Halide anions are also known to affect the reactivity of various enolate anions and amide bases.[2f,15] We suggest that halide anions may form complex aggregates with enolates and amide bases such as that characterized in Figure 1 with a halide anion in place of the hydroxide. We will continue to determine the structures of mixed alkali metal cation, alkoxide/enolate aggregates. These results will be reported in due course.

In summary, the first structure of a mixed lithium/potassium aggregate consisting of four pinacolone enolates, four *tert*-butoxides, and one potassium hydroxide has been determined and is reported herein.

Acknowledgment. This work was supported by the National Institutes of Health through Grant GM-35982 and a Research Career Development Award (CA-01330) to P.G.W. The X-ray equipment was purchased with assistance from an instrument grant from the NSF (CHE-8206423).

Supplementary Material Available: Crystallographic data, a computer-generated, atom-labeled structure, and tables of atomic coordinates, bond lengths and angles, and anisotropic thermal parameters (8 pages). Ordering information is given on any current masthead page.

---

(9) The aldol condensation reaction of pinacolone with itself during enolate crystallization has been observed previously, see: Amstutz, R.; Dunitz, J. D.; Laube, T.; Schweizer, W. B.; Seebach, D. *Chem. Ber.* **1986**, *119*, 434.

(10) (a) Stucky, G.; Rundle, R. E. *J. Am. Chem. Soc.* **1964**, *86*, 4821. (b) Gais, H.-J.; Vollhardt, J.; Günther, H.; Moskau, D.; Lindner, H. J.; Braun, S. *J. Am. Chem. Soc.* **1988**, *110*, 978.

(11) Lochmann, L.; Trekoval, J. *Coll. Czech. Chem. Commun.* **1988**, *53*, 76 and references therein.

(12) (a) Lochmann, L.; Trekoval, J. *J. Organomet. Chem.* **1979**, *179*, 123. (b) Margot, C.; Schlosser, M. *Tetrahedron Lett.* **1985**, 1035. (c) Hoffmann, H. M. R.; Paulloth, D. *Justus Liebigs Ann. Chem.* **1985**, 396.

(13) (a) Lochmann, L.; Pospisil, J.; Lim, D. *Tetrahedron Lett.* **1966**, 257. (b) Schlosser, M. *J. Organomet. Chem.* **1967**, *8*, 9. (c) Lochmann, L.; Lim, D. *J. Organomet. Chem.* **1971**, *28*, 153. (d) Weiss, E.; Koster, H. *Chem. Ber.* **1977**, *110*, 717. (e) Schlosser, M.; Strunk, S. *Tetrahedron Lett.* **1984**, 741 and references therein. (f) Schade, C.; Bauer, W.; Schleyer, P. v. R. *J. Organomet. Chem.* **1985**, *295*, C25.

(14) (a) Lochmann, L.; De, R. L.; Trekoval, J. *J. Organomet. Chem.* **1978**, *156*, 307. (b) Lochmann, L.; Trekoval, J. *J. Organomet. Chem.* **1975**, *99*, 329.

(15) (a) DePue, J. S.; Collum, D. B. *J. Am. Chem. Soc.* **1988**, *110*, 5524. (b) Jackman, L. M.; Szeverenyi *J. Am. Chem. Soc.* **1977**, *99*, 4954.