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Theoretical Model of Solvated Lithium Dienediolates of Methyl Substituted 2-Butenoic Acids

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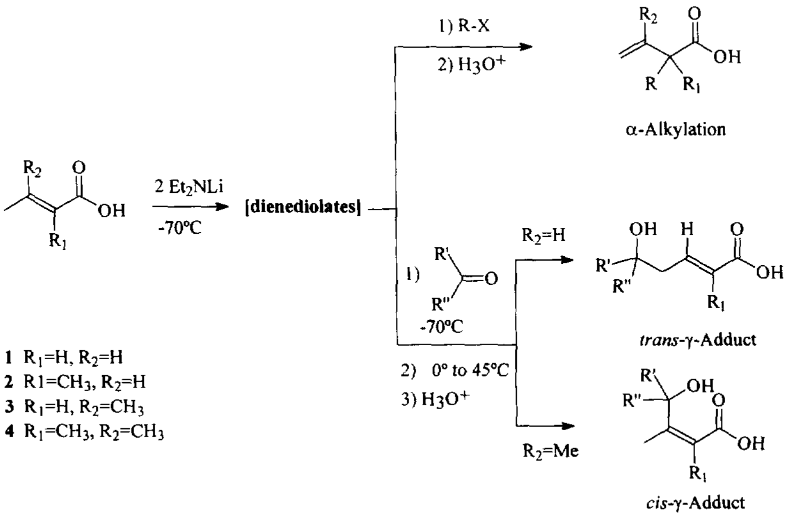
***Abstract*:** The structures of lithium dienediolates of methyl substituted 2-butenoic acids in ether solution have been studied at PM3 semiempirical level by means of two approaches: the continuum model and the implicit solvation. This study reveals the importance of including three ether molecules for each lithium atom to obtain structures for these species that are in good agreement with the chemical reactivity and ^{13}C NMR spectral data. Copyright © 1996 Elsevier Science Ltd

Introduction

Unsaturated carboxylic acids are synthetically useful building blocks. On deprotonation by two equivalents of lithium dialkylamides they afford dianions that react as ambident nucleophiles through their α or γ carbon, and lead to single, or clearly predominant compounds when allowed to react with electrophiles under adequate conditions.[1-3] Regioselectivity trends depend on the electrophile as well as on reaction conditions. Thus, α attack predominates in the irreversible reaction with alkyl halides and hydronium ion,[4,5] and in the additions to aldehydes and ketones under kinetic conditions, whereas γ-adducts are obtained when the last are carried out under thermodynamic conditions (Scheme 1).[6-10] In agreement with the kinetic



Scheme 1

Table 1. Averaged ^{13}C NMR shifts of the butenoic acid dianions and electron densities based on ^{13}C NMR shifts of butadiene.*

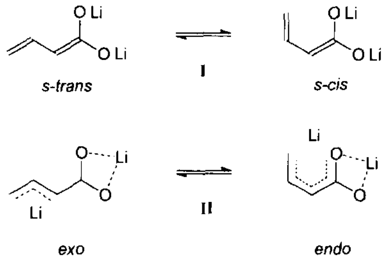
	C-1		C-2		C-3		C-4	
	δ	q_C	δ	q_C	δ	q_C	δ	q_C
1	173.9	0.36	73.4	-0.40	139.0	0.01	86.8	-0.19
2	172.0	0.37	76.8	-0.41	139.8	-0.01	88.1	-0.18
3	174.9	0.37	79.4	-0.38	142.2	-0.01	93.3	-0.15
4	171.3	0.36	76.3	-0.42	150.3	0.04	93.4	-0.12

(*) Charges obtained by equation $(\delta - \delta_n)/160 = q_C$

α-regioselectivity trend, the ^{13}C NMR chemical shifts of the dianions of the different 2-butenoic acids reveal higher π electron density charges at the C2 than at the C4 atoms (Table 1).[11]

The stereoselectivity for γ-attack is usually very high for acids **1** to **3**, and most frequently one single *trans*- or *cis*-compound is obtained, but the trend is determined by the substituents at C3. Thus, 2-butenoic acid **1** and 2-methyl-2-butenoic acid **2**, without methyl group at C3, afford *trans*-isomers, whereas 3-methyl-2-butenoic acid **3**, which has one methyl group at C3, leads to *cis*-isomers. However, poor cis-selectivity is usually found for 2,3-dimethyl-2-butenoic acid **4**.

The structures of dianions of unsaturated carboxylic acids can be simply formulated here as lithium dienolates **I** or as lithiumoxycarbonyl substituted allyl anions **II** (Scheme 2). In any case these formulations provide an oversimplified view of the structures of these dianions, which are expected to form ion pairs and aggregates in weakly polar solvents as diethylether or THF.[12]



Scheme 2

A good number of studies have been published on the structures of lithium and other metal enolates. The structure of the dienediolates of unsaturated carboxylic acids has been studied for 3-methyl-2-butenoic acid **3** by Bongini,[13] who found that the ^{13}C NMR spectrum of the dianion of this acid was consistent with a delocalized π system. An *endo* allyl anion structure was assumed by this author at STO-3G basis set level, which led to an optimized structure with the lithium atom placed above the molecular plane and coordinated to one of the oxygen atoms and to C2 and C4 atoms. The same calculations showed that the coordination of each lithium atom with two water molecules, as a model of ethereal solvent, do not modify substantially the *endo* structure. However, Bongini's model is not in agreement with the assignment of signals in the ^{13}C NMR spectrum and the almost exclusive protonation or alkylation of the dianion at the C2 centre, as STO-3G calculations for these models give a higher negative charge at the C4 than at the C2 centre. Kateni and Schleyer[14] had previously studied the lithium dianion of the acetic acid through 3-21G calculations and found an "*ate*" structure with a lithium atom placed above the molecular plane and coordinated to one of the oxygen atoms and to the C2 centre. Again lithium solvation with water did not lead to any important structural change. All these structures show a higher negative charge at the carbon atom coordinated to the lithium atom.

Quantum chemistry calculations are frequently carried out in gas phase, but these calculations are not adequate for the study of charged species. There are several computational approaches to the theoretical treatment of these species in solution. One consists in carrying out the *ab initio* calculations with the inclusion of a discrete number of solvent molecules coordinated to the charged centers of these species. Another approach based on the continuum model where the solute is embedded in a cavity while the solvent, treated as a continuous medium having the same dielectric constant as the bulk liquid, is incorporated in the solute Hamiltonian as a perturbation. In this structural approach, the bulk medium is polarized by the molecules of the solute. The electronic distribution of the solute polarizes the continuum, which generates an electric field inside the cavity, which in turn affects the solute's geometry and its electronic structure.

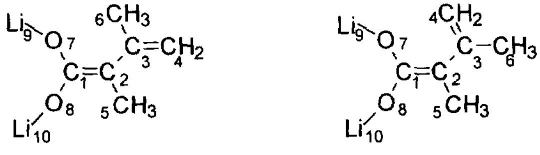
Recently, we reported a study of the solvated lithium dienediolate of 2-butenoic acid.[15] This study revealed the importance of including a discrete number of ether solvating molecules in the calculations of these charged species in solution, and also showed that these ether molecules cannot be substituted by water in the calculations when a conformational equilibrium is possible. MNDO and PM3 semiempirical procedures, and *ab initio* method at STO-3G and 3-21G basis set levels, showed that this model with implicit solvation is in good agreement with both its chemical reactivity and ^{13}C NMR spectral data. It showed as well that PM3 semiempirical calculations do not differ significantly from those obtained by the HF/3-21G calculations. Thus, PM3 calculations afford reliable results for these large systems, formed by the lithium dienediolates and ether solvent molecules.

In the present paper we report a study of the conformational analysis of lithium dienediolates of methyl substituted 2-butenoic acids in solution using the two approaches previously described. We were interested to find out whether similar results were obtained by both theoretical approaches.

Computing Methods and Models.

Geometry optimization for the stationary structures on potential energy surface for solvated lithium dienediolates of methyl substituted 2-butenoic acids was carried out using the PM3 semiempirical Hamiltonian,[16,17] included in the MOPAC93 package program.[18] The different conformations were optimized by means of the EF[19] procedure until the stationary points were obtained. The study of *s-trans* and *s-cis* conformations using the model of implicit solvation was achieved coordinating each lithium atom with three methyl ether molecules.

Geometry optimization using the continuum model was carried out at PM3 semiempirical level using the Conductor-like Screening Model (COSMO) option[20] including in the MOPAC93. This COSMO model, proposed by Klamt and Schuurmann,[20] calculates the electrostatic solvation energy by representing the solute charge distribution as a set of point charges and dipoles in the neglect differential diatomic overlap formalism. In this procedure the solvent is assimilated to a continuous medium characterized by the dielectric constant (ε) which surrounds a molecular-shaped cavity in which the solute is placed. We have used the dielectric constant at 298 K, ε=5.02, for the methyl ether.



s-trans *s-cis*

Scheme 3. Numbering of the atoms for the *s-trans* and *s-cis* structures.

Table 2. PM3 heats of formation (kcal/mol) and C1-C2-C3-C4 dihedral angles (degrees) of lithium dienediolates of methyl substituted 2-butenoic acids in ether obtained with COSMO option.

	Conformation	ΔH_f	dihedral angle
2-butenoic acid **1**	*s-trans*	-96.18	179.9
	s-cis	-99.14	28.7
2-methyl-2-butenoic acid **2**	*s-trans*	-105.89	179.5
	s-cis	-109.34	29.8
3-methyl-2-butenoic acid **3**	*s-trans*	-99.26	176.1
	s-cis	-106.34	23.3
2,3-dimethyl-2-butenoic acid **4**	*s-trans*	-111.76	175.9
	s-cis	-111.27	35.9

Results and Discussions

a) Continuum model calculations.

Table 2 shows the heats of formation and the C1-C2-C3-C4 dihedral angles of the lithium dienediolates, obtained by means of PM3 calculations with the COSMO model option, while Table 3 shows the charge distribution for their *s-trans* and *s-cis* structures obtained by the same approach.

Table 2 indicates that the inclusion of solvent effect by continuum model allows the establishment of the *s-trans* structures as stationary points, a feature which is not obtained in gas phase calculations. Interestingly, the calculations show that the s-*cis* structures have less energy than the *s-trans* structures (range 0.5-7.0 kcal/mol).

The *s-trans* structures present a C1-C2-C3-C4 dihedral angle in the range 176-180° (Table 2), showing a planar carbon skeleton for these conformers. On the other hand, the *s-cis* structures present a C1-C2-C3-C4 dihedral angle in the range 25-26°, similar to that obtained in gas phase calculations. These arrangements are due to a strong coordination of one of the lithium atoms with an oxygen atom and the C4 atom. This effect is in agreement with the charge analysis for these *s-cis* conformations with similar results to that found in gas phase. However this charge analysis is not in agreement with ^{13}C MNR data (Table 1 and 3).

Since the geometrical results and the charge analysis obtained for these dienediolates of 2-butenoic acids are not in agreement with the experimental data, we have discarded the continuum model for the study of these species in solution.

Table 3. PM3 charge distribution of lithium dienediolates of methyl substituted of 2-butenoic acids in ether obtained with COSMO option.

	1		**2**		**3**		**4**	
	s-trans	*s-cis*	*s-trans*	*s-cis*	*s-trans*	*s-cis*	*s-trans*	*s-cis*
C1	0.518	0.535	0.522	0.536	0.516	0.530	0.519	0.523
C2	-0.665	-0.644	-0.619	-0.615	-0.642	-0.627	-0.596	-0.579
C3	0.106	0.139	0.103	0.135	0.117	0.168	0.113	0.169
C4	-0.507	-0.441	-0.509	-0.425	-5.523	-0.446	-0.512	-0.422

Table 4. PM3 heats of formation and relative energies ΔE (kcal/mol) of lithium dienediolates of methyl substituted 2-butenoic acids solvated with ether molecules.

	Conformation	ΔH_f	ΔE
2-butenoic acid **1**	*s-trans*	-391.07	0.00
	s-cis	-387.92	3.15
2-methyl-2-butenoic acid **2**	*s-trans*	-401.29	0.00
	s-cis	-398.47	2.82
3-methyl-2-butenoic acid **3**	*s-trans*	-398.06	0.00
	s-cis	-399.10	-1.04
2,3-dimethyl-2-butenoic acid **4**	*s-trans*	-403.71	0.00
	s-cis	-405.41	-1.70

b) Implicit solvent effect calculations.

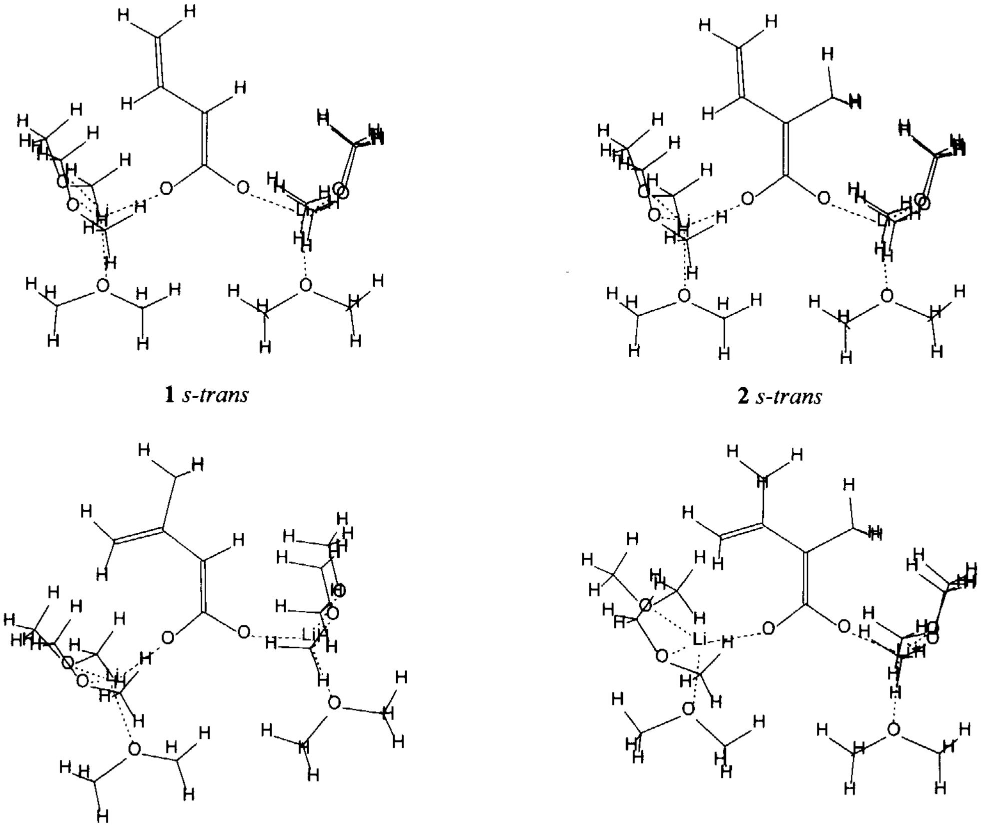
Table 4 shows the PM3 heats of formation and relative energies of the *s-trans* and *s-cis* conformations of the lithium dienediolates of methyl substituted 2-butenoic acids **1** to **4**, where each lithium atom is coordinated to three ether molecules. Table 5 shows the selected geometrical parameters and Table 6 presents the charge analyses of these species. Figure 1 displays a schematic representation of minima energy conformations of these solvated dienediolates.

These solvated dienediolates have a quasi planar carbon skeleton (Figure 1) with C1-C2-C3-C4 dihedral angles in the range 162-180° for *s-trans* structures and 2-34° for *s-cis* structures (Table 5). The loss of planar arrangement is related with the methyl substitution on the butadiene skeleton. The charge analyses for these solvated species are very similar (Table 6) and show a higher π-electron density charge at the C2 than at the C4 centre in agreement with the α-regioselectivity observed for the addition under kinetic conditions and with the ^{13}C MNR data.

The heats of formation for these *s-trans* and *s-cis* conformations shown in Table 4 are also in good agreement with the stereoselectivity observed for the addition to these dienediolates under thermodynamic control. Thus the dienediolates of the acids **1** and **2** give *γ-trans* products in accordance with *s-trans* structures in solution, while the dienediolates of the acids **3** and **4** give *γ-cis* products in accordance with *s-cis* structures.

Table 5. Selected geometrical parameters for lithium dienediolates of methyl substituted 2-butenoic acids solvated with ether molecules.

	1		**2**		**3**		**4**	
	s-trans	*s-cis*	*s-trans*	*s-cis*	*s-trans*	*s-cis*	*s-trans*	*s-cis*
C1-C2	1.406	1.407	1.413	1.416	1.403	1.406	1.411	1.418
C2-C3	1.417	1.413	1.426	1.421	1.427	1.421	1.439	1.432
C2-C4	1.344	1.345	1.344	1.346	1.352	1.349	1.350	1.354
C2-C5	-	-	1.480	1.485	-	-	1.486	1.4817
C6-C3	-	-	-	-	1.491	1.500	1.494	1.499
C1-C2-C3	123.9	128.6	121.2	125.9	129.9	129.0	125.8	122.6
C2-C3-C4	124.2	129.2	125.5	129.5	120.8	127.4	122.9	124.9
C1-C2-C5	-	-	119.6	118.3	-	-	116.9	118.3
C2-C3-C6	-	-	-	-	120.7	114.3	116.8	117.3
C1-C2-C3-C4	177.6	5.2	180.4	14.7	175.3	2.3	162.0	34.6



1 *s-trans*

2 *s-trans*

3 *s-cis*

4 *s-cis*

Figure 1. Conformations of minima energy for lithium dienediolates of methyl substituted 2-butenoic acids solvated with ether molecules.

The preferred conformation for these dianions can be explained by the arrangement of the methyl groups on the carbon skeleton of the butadiene system. For the 2-butenoic acid **1**, without methyl groups, the PM3 calculations afford two planar structures. The *s-trans* conformation presents a C1-C2-C3-C4 dihedral angle of 5.2°, while 3-21G calculations present a dihedral angle of only 0.5°.[15] The *s-trans* conformation has less energy than the s-cis (ΔE=3.2 kcal/mol), with a similar arrangement to that of *s-trans* butadiene.

The dienediolate of 2-methyl-2-butenoic acid **2** also has a *s-trans* preferred to the *s-cis* conformation (ΔE=2.8 kcal/mol). This *s-trans* conformation is very planar (C1-C2-C3-C4 dihedral angle of 179.5°), while the *s-cis* conformation presents a dihedral angle of 14.7°. This torsional angle can be attributed to the repulsive interactions between the hydrogen atom of the methyl group located in the molecular plane and the hydrogen atom at C3. On the other hand, calculations for the dienediolate of 3-methyl-2-butenoic acid **3** lead to two planar conformations; the *s-cis* with less energy than *s-trans* conformation (ΔE=1.0 kcal/mol), in agreement with stereoselectivity observed for this acid. Finally, the dienediolate of 2,3-dimethyl-2-butenoic acid **4**, shows also a *s-cis* conformation with less energy than the *s-trans* (ΔE=1.7 kcal/mol). The methyl group at C3 in the *s-trans* structure, is responsible of the higher energy of this conformation, as found as well in 3-methyl-2-butenoic acid **3**. The non planar arrangement of the *s-cis* conformation (C1-C2-C3-C3 dihedral angle of 34.6°) found for the dienediolate of acid **4** can be attributed to steric repulsions between the methyl groups at C2 and C3 in the planar conformation, which has more energy than the twisted conformation (ΔE=2.2 kcal/mol) and may justify the poor *cis*-selectivity experimentally found for γ-additions of this dienediolate.

Since the geometrical results and the charge analysis obtained for these dienediolates of 2-butenoic acids using the implicit solvation of the lithium atoms with three ether molecules are in agreement with the experimental data, we can conclude that this approach is the most adequate for the study of these species in solution.

Table 6. PM3 charge distribution of lithium dienediolates of methyl substituted 2-butenoic acids solvated with ether molecules.

	1		**2**		**3**		**4**	
	s-cis	*s-trans*	*s-cis*	*s-trans*	*s-cis*	*s-trans*	*s-cis*	*s-trans*
C1	0.52	0.51	0.53	0.52	0.54	0.53	0.53	0.52
C2	-0.58	-0.57	-0.57	-0.57	-0.62	-0.62	-0.63	-0.61
C3	0.14	0.12	0.13	0.12	0.16	0.12	0.14	0.13
C4	-0.35	-0.32	-0.33	-0.32	-0.34	-0.31	-0.35	-0.29

Conclusions

The structure of the lithium dienediolates of methyl substituted 2-butenoic acids in ether solution has been studied by means of two computational models: the continuum model and the implicit solvation with ether molecules. This study points out that the continuum model is not adequate for species with high density charges such as lithium dienediolates, thus necessitating the use of implicit solvation in these cases. On the other hand, the different conformations found for these solvated lithium dienediolates can be explained by means of two different effects: a) the preferred *s-trans* disposition of the butadiene system, and b) the different disposition of the methyl groups as substituents, with the presence of the methyl group at C3 determining that the *s-cis* structure has less energy.

Acknowledgments

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