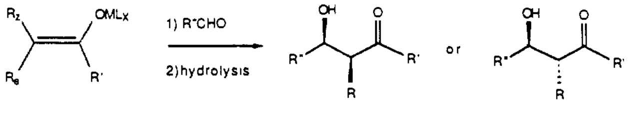
Transition Structures of Aldol Reactions

Yi Li,[1a] Michael N. Paddon-Row,[1b] and K. N. Houk*[,1c]

Department of Chemistry, University of Pittsburgh
Pittsburgh, Pennsylvania 15260
Department of Chemistry and Biochemistry
University of California, Los Angeles
Los Angeles, California 90024-1569

Received September 18, 1987

The aldol reaction[1] is a useful reaction for which diverse stereochemical observations and theoretical considerations have led to a variety of transition state models.[2-11,13] We have located the first *ab initio* transition structures for aldol reactions, and report here the information that these calculations reveal about models of stereoselectivity.

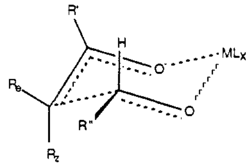


1 (Z) (R_z= alkyl, R_e = H)
(E) (R_z = H, R_e = alkyl)

2 *(syn)*

3 *(anti)*

The Zimmerman–Traxler chairlike transition state model,[2,3] **4** (M = metal, L = ligands), has been proposed to explain why some metal (Li, BR_2, Mg, Zn) *Z* enolates (R_z = alkyl, R_e = H) react with aldehydes to give the syn products, while the *E* enolates (R_e = alkyl, R_z = H) give the anti.[3] As shown in **4**, the aldehyde substituent, R″, prefers to be equatorial in both cases. Because *Z* enolates react with higher stereoselectivity than the *E* enolates, it has been proposed by both Dubois and Heathcock that the transition structures are skewed away from the idealized 60° torsional angle about the forming CC bond, ϕ, toward a 90° torsional angle.[4] TAS enolates always give syn products, and it has been suggested that these are formed from the acyclic nonchelated transition structure with $\phi \approx 180°$.[5] In such cases, R″ always prefers the position remote from the enolate substituent, and the *syn* product is formed. Some other metals (e.g., Sn, Zr, Ti, $B(OR)_2$) give the same product from both the *Z* or *E* enolate.[3,6-9] Evans proposed that a boat conformation ($\phi \cong 0°$) occurs when there are significant steric interactions between large groups on the forming bond.[7] Boat transition structures for *E* enolates are often invoked when both *Z* and *E* enolates give syn products. Hoffmann proposed that a twist-boat transition structure occurs with (*E*)-enol borates.[8] MNDO model calculations by Gennari et al. support this idea.[9]



4

Anh and Thanh proposed a different model which has the enolate and carbonyl moieties in parallel planes and ϕ about 30°.[10] Previously, Mulzer had proposed that secondary orbital interactions for lithium salts of acid dianions cause syn stereoselectivity by favoring the close approach of oxygens on each molecule.[11] The Dunitz–Bürgi trajectory of attack[12] of nucleophiles on carbonyl compounds has been cited as a determinant of stereoselectivity, most notably in Seebach and Golinski's topological rule.[13]

We have located transition structures for the reactions of acetaldehyde enolate and the lithium and several boron salts with formaldehyde with the 3-21G basis set.[14] All variables were optimized, and each transition structure has one negative force constant corresponding to motion along the reaction coordinate. The transition structures for the reactions of the boron enolate of acetaldehyde with acetaldehyde and of the (*Z*) and (*E*) enol borinates of propionaldehyde with formaldehyde were also located.

In the gas phase, the aldol mechanism involves formation of a complex, either the ion–dipole type for the free enolate or a Lewis acid–base adduct of the metal center with the carbonyl oxygen for Li^+ or BH_2. The energetics of the aldol processes described here are summarized in Table I, along with salient geometrical features relevant to the various models proposed in the literature. Conversion of the complexes to products requires little energy, and the transition structures are close in energy to the complexes. There is a remarkable similarity of the forming CC distance in all examples. Figure 1 shows the transition structures found for the reactions of free, lithium, and boron enolates of acetaldehyde with formaldehyde. The reaction of the metal-free acetaldehyde enolate with formaldehyde occurs by three distinct transition structures. The anti structure **5** and the gauche **6** are the same in energy. The other gauche isomer **7** is much higher in energy. This last structure has the two oxygens obviously avoiding each other, in accord with the electrostatic repulsion between them; there is no evidence for attractive secondary orbital interactions of the type proposed earlier.[10,11] The two best transition structures for the free anion reaction resemble those postulated for TAS enolate reactions by Noyori.[5]

There is only one lithium enolate transition state **8**, and it is a half-chair, with ϕ reduced to 48° and with the Li^+ approximately in the plane of the adjacent four atoms. Since the Li–O interactions are mainly electrostatic in nature, this general shape could also be present in the aggregates involved in reactions in solution.[15]

For the simplest enol borinate reaction, both chair **9** and twist-boat **10** transition states were found. The preferred structures of both the free boron enolate and the corresponding complex have torsional angle CCOB = 0°. Free boron enolate prefers s-trans. In **9** and **10** these angles are 84° and 25°, respectively. This twist-boat **10** is preferred because CCOB is closer to the ideal 0°,[8] and this structure also reduces the repulsion between the lone pairs on the two oxygens. Replacement of the hydrogens on B by alkyl groups should destabilize the twist-boat. When the axial BH in **9** and **10** was replaced by a methyl and calculations of the new transition structures were performed, the chair and the twist-boat transition structures were found to have the same energy. Larger alkyls should favor the chair even more.

Transition structures were also located for eight methyl-substituted cases. As shown in Table I, the relative energies of chair

---

[1] (a) Pittsburgh and U.C.L.A. (b) Pittsburgh; permanent address: University of New South Wales, Australia. (c) Pittsburgh and U.C.L.A., address correspondence to U.C.L.A.

[2] Zimmerman, H. E.; Traxler, M. D. *J. Am. Chem. Soc.* **1957**, *79*, 1920.

[3] (a) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, *13*, 1. (b) Heathcock, C. H., In *Asymmetric Synthesis*; Morrison, J. D., Eds.; Academic Press: New York, 1983; Vol. 3, Chapter 2, pp 154-161.

[4] Dubois, J. E.; Fellmann, P. *Tetrahedron Lett.* **1975**, 1225. Heathcock, C. E. in ref 3b.

[5] Noyori, R.; Nishida, I.; Sakata, J. *J. Am. Chem. Soc.* **1983**, *105*, 1598.

[6] Tin: Harada, T.; Mukaiyama, T. *Chem. Lett.* **1982**, 467. Yamamoto, Y.; Yatagai, H.; Maruyama, K. *Tetrahedron Lett.* **1980**, 4607. Titanium: Nakamura, E.; Kuwajima, I. *Acc. Chem. Res.* **1985**, *18*, 181 and references cited therein.

[7] Evans, D. A.; McGee, C. R. *Tetrahedron Lett.* **1980**, 3975.

[8] Hoffmann, R. W.; Ditrich, K.; Froech, S.; Cremer, D. *Tetrahedron* **1985**, *41*, 5517.

[9] Gennari, C.; Todeschini, R.; Beretta, M. G.; Favini, G.; Scolastico, C. *J. Org. Chem.* **1986**, *51*, 612.

[10] Anh, N. T.; Thanh, B. T. *Nouv. J. Chim.* **1986**, *10*, 681.

[11] Mulzer, J.; Brüntrup, G.; Finke, J.; Zippel, M. *J. Am. Chem. Soc.* **1979**, *101*, 7723.

[12] Bürgi, H.-B.; Shefter, E.; Dunitz, J. D. *Tetrahedron* **1975**, *31*, 3089. Bürgi, H.-B.; Dunitz, J. D. *Acc. Chem. Res.* **1983**, *16*, 153 and references cited therein.

[13] Seebach, D.; Golinski, J. *Helv. Chim. Acta.* **1981**, *64*, 1413. See, also: Brook, M. A.; Seebach, D. *Can. J. Chem.* **1987**, *65*, 836 and references therein.

[14] Calculations were performed with GAUSSIAN 82: Binkley, J. S.; Frisch, M. J.; DeFrees, D. J.; Raghavachari, K.; Whiteside, R. A.; Schlegel, H. B.; Fluder, E. W.; Pople, J. A. Carnegie-Mellon University, Pittsburgh, PA.

[15] (a) Bauer, W.; Seebach, D. *Helv. Chim. Acta.* **1984**, *67*, 1972. (b) Seebach, D.; Amstutz, R.; Dunitz, J. D. *Ibid.* **1981**, *64*, 2622.

0002-7863/88/1510-3684$01.50/0 © 1988 American Chemical Society

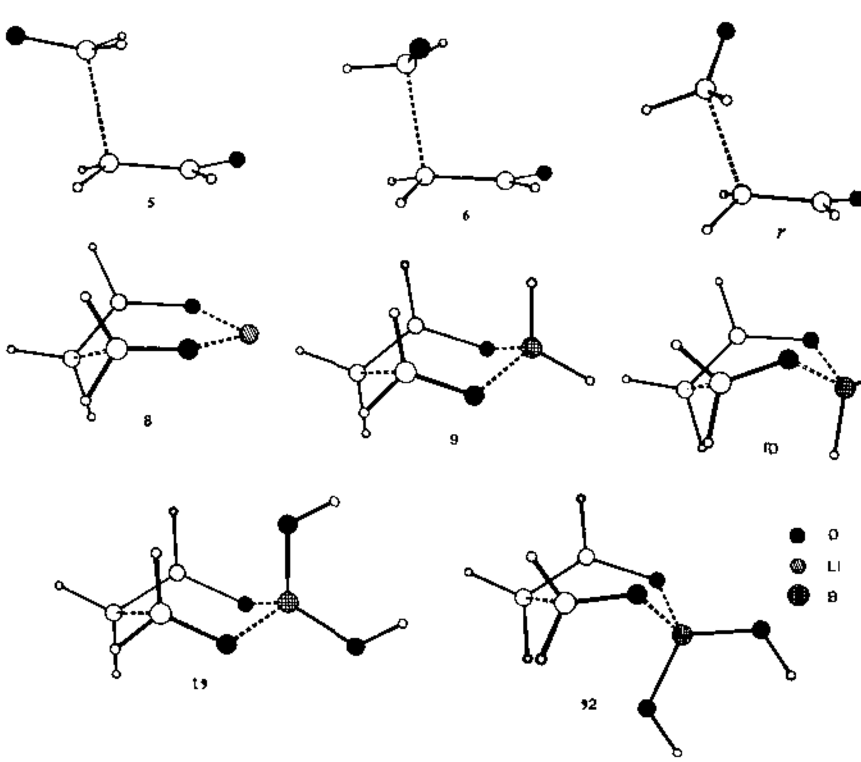
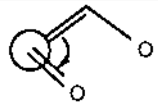
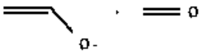
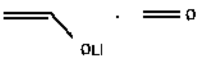
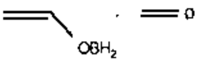
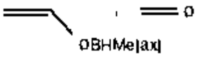
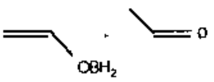
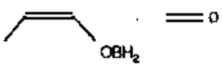
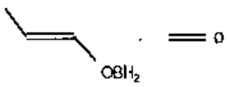
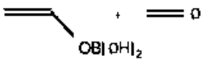


Figure 1. Transition structures for the aldol reactions of acetaldehyde enolate with formaldehyde (**5**–**7**), lithium acetaldehyde enolate with formaldehyde (**8**), the chair (**9**) and twist-boat (**10**) transition structures for the reaction of acetaldehyde enol borinate with formaldehyde, and the chair (**11**) and twist-boat (**12**) transition structures for the reaction of acetaldehyde enol borate with formaldehyde.

Table I. Activation Energies and Geometrical Features of Aldol Transition Structures

reaction	E_{rel}(complex)		E_{rel}(TS)	r_{C---C}	 (deg)	 (deg)	 (deg)
	−17.2	anti (**5**)	$-5.4^{a,b}$	2.022	105	113	**177**
		gauche (**6**)	-5.4^{a}	2.059	104	116	**−78**
		gauche (**7**)	-2.1^{a}	2.063	109	118	69
		product	−11.8				
	−28.0	**8**	−26.0	2.368	92	107	**48**
		product	−40.2				
	−10.2	chair (**9**)	+1.8	2.203	86	103	**57**
		twist-boat (**10**)	+0.4	2.323	91	103	**25**
		product	−32.0				
		chair	$+0.1^{c}$	2.222	87	103	**57**
		twist-boat	0.0	2.332	91	104	**23**
		chair-eq	+2.4	2.146	90	102	**57**
		chair-ax	$+4.2^{d}$	2.180	**89**	102	**55**
		twist-boat-eq^{e}	+1.6	2.283	93	101	**30**
		twist-boat-ax^{e}	0.0	2.234	94	103	**26**
		chair	0.0	2.225	82	104	**59**
		twist-boat	+4.0	2.316	85	108	**21**
		chair	+0.1	2.213	**84**	105	56
		twist-boat	0.0	2.330	89	105	**27**
		chair (**11**)^{f}	+2.5	2.171	87	103	**57**
		twist-boat (**12**)^{f}	0.0	2.279	91	104	**24**

[a] Calculations are 6-31G*//3-21G. These gave lower energies but similar relative energies to 6-31+G//3-21G calculations. [b] Energies are relative to isolated reactants. [c] This and subsequent energies are relative to the best transition structure. [d] This is not an authentic transition structure; it collapses to the axial-twist-boat upon optimization. [e] Eq and ax refer to the position of Me in the corresponding chair conformation. [f] HOBO dihedral angles were constrained to 0°.

and boat transition structures can be altered by substituents. (*Z*)-enol borinates with large alkyl substituents strongly prefer the chair transition structure. The *E* enolates prefer the chair less and consequently give lower stereoselectivity.

We have also carried out calculations on reactions of acetaldehyde enol borate. The chair transition structure **11** closely resembles the corresponding chair borinate 9. The 2.5 kcal/mol preference for the twist-boat will be overcome by the *Z* enolate 4.0 kcal/mol preference for the chair transition structure. However, the *E* enolate will still prefer the twist-boat. This is the origin of the (*Z*) → (chair) → syn and (*E*) → (twist-boat) → *syn* stereochemistry for borates.[8,9] The larger preference for the twist-boat transition structure by the borate is related both to the small size of the alkoxy substituent and to the greater preference for planarity of the enol borate than the enol borinate (3.0 kcal/mol versus 2.0 kcal/mol, respectively, to rotate to a 90° conformation at the 3-21G level). This conclusion is probably applicable to other cases, such as titanium and zirconium enolates, where the chair is favored for *Z* enolates, but the twist-boat is favored for *E* enolates.

Finally, as shown in Table I, Dunitz–Bürgi attack angles of 101–108° are observed in both Li and BH_2 reactions, similar to what is found for other nucleophilic additions to carbonyls.[16]

Acknowledgment. We are grateful to the National Institutes of Health for financial support of this research, the Harris Corporation for a computer grant, and the National Science Foundation and San Diego Supercomputer Center for some of the computer time used for this research, and Professors R. W. Hoffmann and C. Gennari for helpful comments.

---

(16) Wu, Y.-D.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 908.

---

cis-Diaquabis(2,2′-bipyridyl-4,4′-dicarboxylate)ruthenium(II) Sensitizes Wide Band Gap Oxide Semiconductors Very Efficiently over a Broad Spectral Range in the Visible

Paul Liska, Nick Vlachopoulos, Mohammad K. Nazeeruddin, Pascal Comte, and Michael Grätzel*

Institut de Chimie Physique
Ecole Polytechnique Fédérale
CH-1015 Lausanne, Switzerland

Received December 31, 1987

Trisbipyridylruthenium(II) and its homologues are extensively employed as redox sensitizers.[1] By contrast, very little is known about the excited-state electron-transfer properties of bis(bipyridyl)ruthenium(II) complexes. Apart from $Ru(bipy)_2(CN)_2$, for which the emission lifetime in methanol is ca. 100 ns,[2] the excited state of this class of compounds is too short-lived[3] to allow for the occurrence of bimolecular solution reactions. In addition, photoinduced ligand loss and cis–trans isomerization[4] constitute frequently the preferred pathway of electronic deactivation. We report here on the surprisingly effective, broad band sensitization of TiO_2 to visible light by *cis*-$Ru^{II}L_2(H_2O)_2^{2-}$ (L = 2,2′-bipyridyl-4,4′-dicarboxylate).

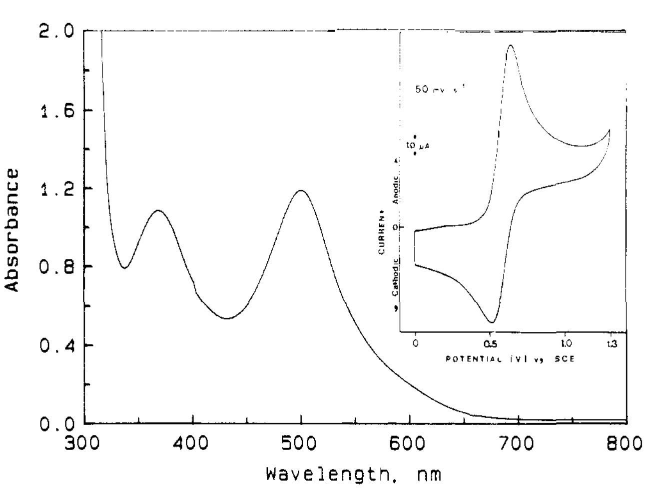


Figure 1. UV–vis absorption spectrum of 10^{-3} M *cis*-$Ru^{II}L_2(H_2O)_2^{2-}$ in water at pH 4.85. Optical pathlength 0.1 cm. Inset: cyclic voltammogram of the same solution; working electrode: In-doped SnO_2.

cis-$Ru^{II}L_2Cl_2 \cdot 2H_2O$ was obtained by refluxing under Ar 60 mg (0.229 mmol) of $RuCl_3 \cdot 3H_2O$ (Fluka, 38–40% Ru) and 113 mg (0.463 mmol) of ligand (Aldrich) in 20 mL of DMF for 8 h. After cooling, traces of RuL_3 were filtered. Most of the DMF solvent was evaporated under vacuum, and *cis*-$Ru^{II}L_2Cl_2$ was precipitated with acetone. The crystals were filtered off and dried in vacuum. Elemental analysis corresponded to $C_{24}H_{16}N_4O_8Cl_2Ru \cdot 2H_2O$.

cis-$Ru^{II}L_2(H_2O)_2$ was prepared by hydrolysis of the dichloro complex at pH 4.5 and precipitation at its isoelectric point (pH 2.8) with 0.1 M CF_3SO_3H (Fluka, further purified by vacuum distillation) for acidification. Crystallization in the dark for 24 h at 4 °C gave shining crystals dried in vacuum (yield 70%). In air, this compound adds three lattice water molecules. This procedure was repeated twice for purification. Elemental analysis for $C_{24}H_{18}N_4O_{10}Ru \cdot 3H_2O$ gave (calculated values in parentheses) C, 42.79 (42.55); H, 2.95 (2.68); N, 8.40 (8.27); Ru, 14.84 (14.91). Chloride was undetectable.

Figure 1 shows the absorption of *cis*-$Ru^{II}L_2(H_2O)_2^{2-}$ in water at pH 4.85. There are three bands with maxima at 500 nm (ϵ = 11 900 M^{-1} cm^{-1}), 370 nm (ϵ = 10 900 M^{-1} cm^{-1}), and 306 nm (ϵ = 49 200 M^{-1} cm^{-1}). This differs markedly from the spectrum of *cis*-diaquabis(2,2′-bipyridyl-5,5′-dicarboxylate)ruthenium(II) which has maxima at 550, 365, and 300 nm.[5]

The inset shows a cyclic voltammogram of *cis*-$Ru^{II}L_2(H_2O)_2^{2-}$ at pH 4.85. Oxidative and reductive peaks at 0.64 and 0.52 (SCE), respectively, are obtained indicating quasi-reversible behavior. The midpoint potential is at 0.58 V. In 0.5 M H_2SO_4 reversible one-electron oxidation occurs at 0.83 V. The unsubstituted analogue, $[cis\text{-}Ru(bpy)_2(H_2O)_2]^{3+/2+}$, exhibits a formal potential of 0.53 V (versus SCE) at pH 4 which increases to $E°$ = 0.65 V in 1 M $HClO_4$.[6] The pH dependence was attributed to the deprotonation of one aqua ligand of the complex.[7]

cis-$Ru^{II}L_2(H_2O)_2^{2-}$ in acidic aqueous solution is strongly adsorbed to the surface of TiO_2. When TiO_2 powder is introduced into $3 \leq pH \leq 5$ solutions of *cis*-$Ru^{II}L_2(H_2O)_2^{2-}$, an intense violet color develops onto the particles, while the supernatant spectrum shows simply the disappearance of the dye. The ability of the surface-bound *cis*-$Ru^{II}L_2(H_2O)_2^{2-}$ to sensitize electron injection

---

(1) (a) Gafney, H. D.; Adamson, A. W. *J. Am. Chem. Soc.* **1972**, *94*, 8238. (b) Whitten, D. G. *Acc. Chem. Res.* **1980**, *13*, 83. (c) Rubinstein, I.; Bard, A. J. *J. Am. Chem. Soc.* **1981**, *103*, 512. (d) Sutin, L. *Acc. Chem. Res.* **1982**, *15*, 275. (e) Kalyanasundaram, K. *Coord. Chem. Rev.* **1982**, *46*, 159. (f) Balzani, V.; Scandola, F. In *Energy Resources through Photochemistry and Catalysis*; Grätzel, M., Ed.; Academic Press: New York, 1983; p 1. (g) Adamson, A. W. *J. Chem. Ed.* **1983**, *60*, 803. (h) Meyer, T. G. *Prog. Inorg. Chem.* **1983**, *30*, 389. (i) Aken, G. H.; White, R. P.; Rillema, D. P.; Meyer, T. J. *J. Am. Chem. Soc.* **1984**, *106*, 2613. (j) Fuchs, Y.; Lofters, S.; Dieter, T.; Shi, W.; Morgan, R.; Strekas, T. C.; Gafney, H. D.; Baker, A. D. *J. Am. Chem. Soc.* **1987**, *109*, 2681. (k) Juris, A.; Barigelletti, F.; Campagna, S.; Balzani, V.; Belzer, P.; von Zelewsky, A. *Coord. Chem. Rev.*, in press and references cited therein.

(2) Balzani, V.; Juris, A.; Barigelletti, F.; Belzer, P.; von Zelewsky, A. *Sci. Papers I.P.C.R.* **1984**, *78*, 78.

(3) (a) Klassen, D. M.; Crosby, G. A. *J. Chem. Phys.* **1968**, *48*, 1853. (b) Demas, J. N.; Crosby, G. A. *J. Am. Chem. Soc.* **1971**, *93*, 2841. (c) Krause, R. A.; Ballnausen, C. J. *Acta Chem. Scand. Ser. A* **1977**, *31*, 535.

(4) Durham, B.; Wilson, S. R.; Hodgson, D. J.; Meyer, T. J. *J. Am. Chem. Soc.* **1980**, *102*, 600.

(5) Rotzinger, F. P.; Munavalli, S.; Comte, P.; Hurst, J. K.; Grätzel, M.; Pern, F. J.; Frank, A. J. *J. Am. Chem. Soc.* **1987**, *109*, 6619.

(6) Takenuchi, K. J.; Samuels, G. J.; Gersten, S. W.; Gilbert, J. A.; Meyer, T. J. *Inorg. Chem.* **1983**, *22*, 1407.

(7) In formulating $Ru^{II}L_2(H_2O)_2^{2-}$ as a dianion, it is assumed that at pH 4–5 the carboxylic acid groups of the ligands are fully deprotonated, while the H_2O ligands in the Ru^{II} state are not dissociated. Acid–base titration shows the isoelectric point of the Ru(II) complex to be at 2.8. Hence, above this pH the molecule is anionic. Combined acid–base titration and spectral analysis indicate the first H_2O ligand to deprotonate above pH 9. This is in agreement with literature data for the unsubstituted complex $Ru^{II}(bipy)_2(H_2O)_2^{2+}$ and $Ru^{II}(bipy)_2(py)(H_2O)^{2+}$ for which the first pK_a values are 11[11] and 10.3,[12] respectively. The cis configuration of the complex was ascertained by precipitation as sulfato complex and subsequent IR analysis.[5]