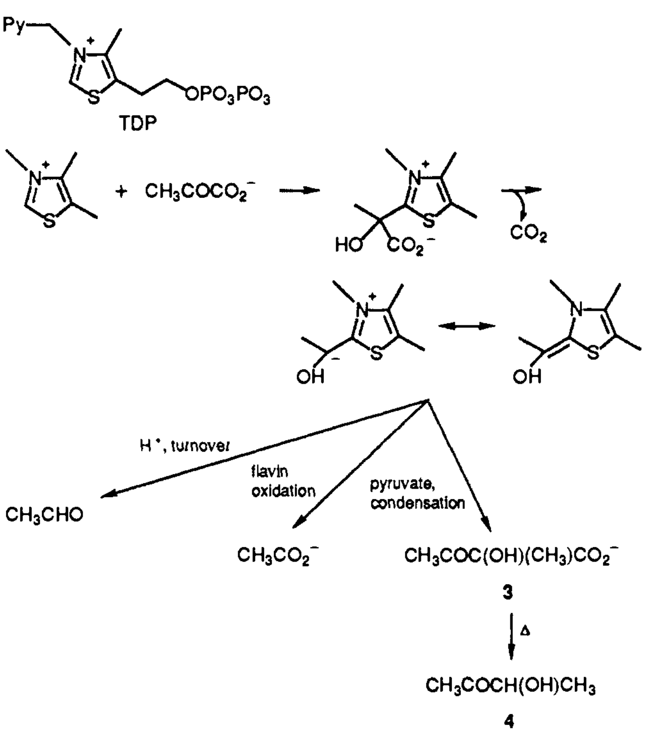
Scheme I[a]



[a] Py = 5-(4-amino-2-methylpyrimidinyl)

be four molecules of **1** per holo-PDC (M_r = 260 kDa) or one per subunit.

The isoalloxazine at the active center was chemically competent according to the following criteria; (1) under aerobic conditions, the A_{340} due to *N*-propyl-1,4-dihydronicotinamide or NADH was reduced by 8-AcI-PDC in a time-dependent reaction; (2) when a mixture of NADH and 8-AcI-PDC was deoxygenated in an anaerobic cell, there was no time-dependent decrease (the small amount of 8-AcI-PDC being used did not allow detection of a single turnover) in A_{340}; (3) in an anaerobic cell and in the presence of excess catalase and superoxide dismutase, pyruvate diminished the isoalloxazine absorbance at 450 nm; (4) under aerobic conditions, 8-AcI-PDC produced acetate[15] in a time-dependent fashion (Figure 2), not enhanced in rate or quantity by the presence of electron acceptors, such as 0.5 mM 3-(4,5-dimethylthiazol-2-yl)-2,4-diphenyltetrazolium bromide, 1 mM NAD$^+$, and 0.2 mM ubiquinone, and suggesting that dioxygen is responsible for the reoxidation of the reduced isoalloxazine; (5) interestingly, the 8-AcI-PDC also produced acetolactate, **3** (detected as acetoin, **4**).[16] Control reactions proved that all observations were due to the reactivity of the isoalloxazine covalently linked to PDC, not to model TDP reactions.[17] The ratio of acetate to acetoin produced at pH 6 is 300.

It has been shown that the enzyme acetolactate synthetase (ALS) is similar in sequence to pyruvate oxidase; it possesses FAD, which, however, has no redox function.[19] The two enzymes also bear considerable primary sequence homology to PDC isolated from yeast or *Zymomonas mobilis*.[20] The 8-AcI-PDC embodies functions attributed to both POX and ALS. The better inactivation achieved by the 8-bromoacetyl derivative compared to the 6-bromoacetyl analogue is probably due to steric factors, Steric factors probably also explain why the semisynthetic enzyme is more active as a POX model than as an ALS model since the latter would demand access of a second pyruvate to the enamine intermediate. The stoichiometry of bound 8-AcI confirms that there is a highly nucleophilic side chain near the active center of each subunit (probably Cys). The inactivity toward acetaldehyde release suggests that a group responsible for this release is no longer available (perhaps it is the Cys). Finally, the slow rate at which acetate is released may reflect slow nonenzymatic hydrolysis of the 2-acetyl-TDP, or hindered binding of pyruvate to the crowded active center, rather than an inefficient redox process. Resolution of this and other remaining questions will provide further significant details about the oxidative mechanisms involving thiamin-bound enamine intermediates, as envisioned in Scheme I,

Acknowledgment. This work was supported by the donors of the Petroleum Research Fund, administered by the American Chemical Society; the National Science Foundation (DMB 87-09758); the Rutgers University Busch Fund; and Hoffmann-La Roche, Nutley, NJ. We are grateful to Drs. Franz Scheidl and Wolfgang Benz of Hoffmann-La Roche, Nutley, NJ, for elemental and mass spectral analyses, respectively, and to the Anheuser-Busch Brewing Co., Newark, NJ, for their continued generosity in supplying the brewer's yeast.

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On the Behavior of Quantum Chemical Bond Order in the Vicinity of a Saddle Point on the Reaction Path

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Received August 1, 1989

We report that the computed profile of a generalized quantum chemical bond order index of the bond being broken or formed in a reaction may often reveal the existence of a point of inflection when viewed along the reaction path. It is conjectured that in many instances inflection point may be identified as the saddle point of the particular reaction. The relevance of this observation to bond energy–bond order (BEBO) methods is suggested.

The bond energy–bond order method (BEBO) was initially proposed by Johnston and Parr.[1,2] The method as such is capable of constructing narrow, curving, parabolic potential energy channels between the reactants and the products in a typical collinear-light atom-transfer reaction ($A + HX \rightarrow AH + X$). The predicted minimun energy path has many desirable properties and predicts saddle-point characteristics well.[3]

The key of the BEBO method lies in the use of the Pauling rule[4] relating bond order (n_{AB}) and bond length (R_{AB}) for a singly bonded system [$R_{AB} = R_{AB}^e - 0.26$ (Å) ln n_{AB}], the postulate of the conservation of total bond order of the bonds being formed and broken[1,2] ($n_{HX} + n_{AH}$ = constant), and an empirical relation

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Table I. Computed Structural Characteristics and Other Features of HNO and NOH in $^3A''$ State Along with the Corresponding Features for the Transition State Encountered in the Isomerization HNO → NOH in the $^3A''$ State

	geometrical parameters			bond orders			
species	r_{NH}, Å	r_{OH}, Å	HNO, deg	N–H	O–H	N–O	energy, au
H–N–O ($^3A''$)	1.072	1.927	115.4	0.869	0.007	1.444	−29.37970
N H O ($^3A''$)	1.188	1.138	55.5	0.483	0.405	1.141	−29.29537
N–O–H ($^3A''$)	1.818	1.42	33.5	0.006	0.886	1.229	−29.33878

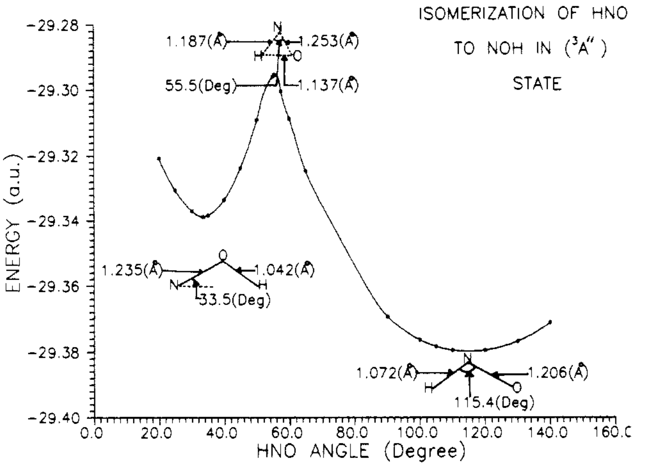

Figure 1. Energy profile along the pathway of the isomerization of H–N–O to N–O–H in the lowest $^3A''$ state. Remaining geometrical parameters have been completely optimized for each value of the HNO angle.

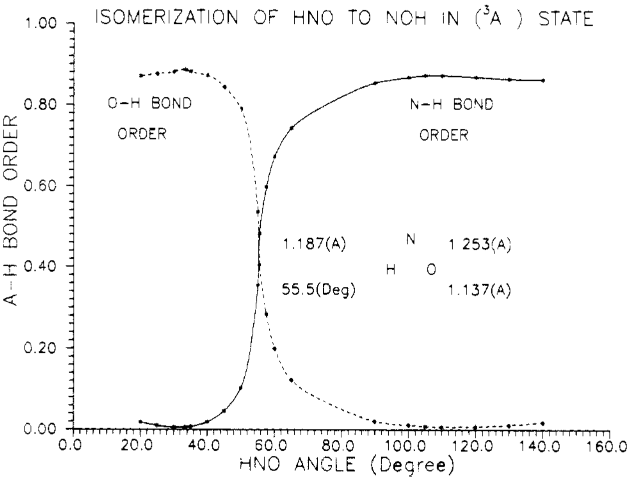

Figure 2. A–H bond-order profiles (A = N, O) along the pathway of the isomerization of H–N–O → N–O–H in the $^3A''$ state. Note the point of inflection.

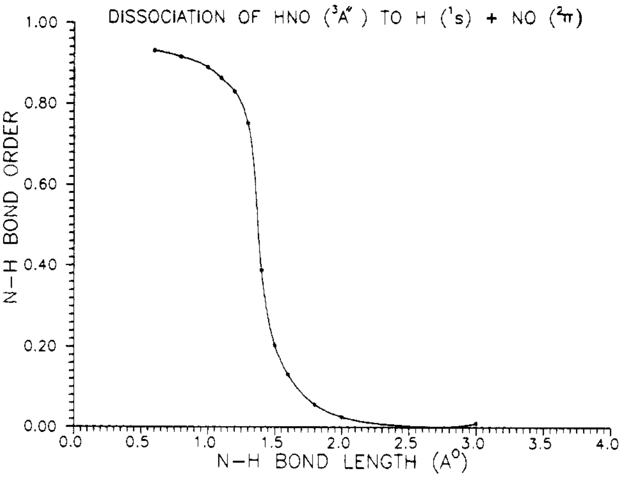

Figure 3. N–H bond-order profile along the path of photochemical decomposition of H–N–O ($^3A''$) ($h\nu$) → H (^1S) + NO ($^2\pi$).

between the bond order and bond energy ($D = D_S n_{AB}{}^p$).[1,2] Various generalizations and modifications of the original BEBO method can be found in the literature,[5-10] e.g., the reduced variable BEBO[5] method, the rotated Morse BEBO[6] method, and Agmon–Levine modified BEBO[7] method, etc. These methods undoubtedly hinge on judicious use of semiempiricism. But the success of BEBO formalism merits further attention. One wonders whether the quantum chemical bond order or some other property of the bond being broken or formed would generally reveal some "exalted" features when examined along the reaction path.[30] If the answer is in the affirmative, one can exploit this information for fixing the parameter p in $D = D_S n^p_{AB}$ so that D exhibits a maximum in its profile along the reaction coordinate. With this basic idea in mind, we have studied the photochemical decomposition and isomerization of the X–N–O (X = H, Li, F, etc.) type of molecules

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Table II. Variation in the Computed Hydrogen Free Valence Index (f_H) along the Photodissociation Path of HNO ($^3A''$)[a] → H + NO

r_{NH}, Å	f_H	r_{NH}, Å	f_H
0.6	0.033	1.6	0.866
0.8	0.058	2.0	0.974
1.0	0.090	4.0	0.999
1.2	0.154	8.0	1.000
1.4	0.606	10.0	1.000

[a] The dissociation in the $^1A''$ state also shows similar behavior.

in their lowest $^{1,3}A''$ states. The excited-state calculations have been carried out by applying a variant of the orthogonal gradient method of orbital optimization[11-16] in an INDO-MCSCF framework. The method has been shown to perform well in the calculation of molecular structure in excited states.[17,18] The quantum chemical valence parameters (bond order, free valence, etc,) have been calculated by adopting[23,24] definitions proposed by Mayer.[19-22]

Figure 1 shows the section of the potential energy surface along the reaction path for the isomerization of HNO to NOH in the lowest $^3A''$ state. The transition state has been located by optimizing the two bond lengths for different values of the HNO angle till the maximum is reached.

The left well corresponds to N-O-H and the right one to H-N-O in the lowest $^3A''$ state. The computed energies, bond order, and structural parameters of each are reported in Table I. The transition state corresponds to a triangular arrangement of the H, N, and O atoms. The barrier height from the reactant (HNO) side is 53 kcal/mol, From the product side, it is 50% less, Figure 2 displays the profiles of the computed N-H and O-H bond orders along the reaction path. In each case, the plot exhibits a point of inflection at $\theta = \theta_c$ (critical HNO angle), 55,5°. At this point, both the N-H and O-H bond orders are approximately 0,5, while beyond this point, N-H bond order rapidly falls to 0 and O-H bond order registers a sharp rise to the value 1. We conjecture that the points of inflection noted in the BO plots may be identified with the actual saddle point revealed in the energy profile (Figure 1). A close examination shows that the inflection points in Figure 2 and the saddle point in Figure 1 both occur at $\theta_c \sim 55.5$, The structural parameters and quantum chemical bond order indices of the transition state are recorded in Table I. It is heartening to note that an identical transition-state structure is predicted by the two methods, In the example just discussed, the process involves the breaking and simultaneous making of a single bond. However, even for a simple bond-breaking process, the BO profile may often reveal identical features. As an example, we consider the behavior of the N-H bond order as HNO photochemically dissociates into H + NO, in the lowest $^3A''$ state. Here also, the plot of B_{NH} against R_{NH} (Å) (HNO angle and N-O length have been optimized for each value of R_{NH}) shows the occurrence of a similar inflection point (Figure 3). We have observed that the corresponding energy profile (figure not shown here) is rather flat around the transition point, making it difficult to trace the bond-breaking point.[25] Similar features have been noted in an ab initio CI calculation[26] of the potential energy surfaces of H-N-O in $^{1,3}A''$ states, The BO method, on the other hand, locates the bond-breaking point rather sharply. As a further check on the wave function, we have reported the computed free valence index of the H atom for different points on the reaction path (Table II). For large values of N-H distance, the free valence index of the H atom smoothly becomes unity, as it should. Similar behavior has also been noted in the photoisomerization of X-N-O-type molecules into N-O-X in the lowest A states (singlet as well as triplet) and in the photochemical dissociation of X-N-O → X + NO. The details of these calculations will be published shortly.[27]

Very recently, Lendvay[28,29] has studied the behavior of BO and valence indices in some chemical reactions (thermal) involving metathesis. These studies tend to confirm the validity of the bond order conservation principle invoked in BEBO calculations. The BO plots, however, reveal lack of coincidence of the inflection point in the BO profile with the saddle point in the corresponding energy plot in some unsymmetrical atom-transfer reactions. We feel that one of the key factors that determines the extent of this coincidence is the similarity between the bond being broken and formed. The significance of Hammond's postulates is worth investigating in this connection. A closer analysis of these phenomena may lead to a better understanding and wider generalization of the basic tenets of the BEBO method.

Acknowledgment. We sincerely thank the CSIR, Government of India, New Delhi, for providing computational facilities [Grant No. 5(136)188-EMR-II] and awarding a fellowship to D.K.M. We acknowledge partial financial support received from the National Bureau of Standards, U.S,A. [Grant No. NBS(a-004)].

Cubyl Cation[1]

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Received October 23, 1989

Everything about cubyl cation seems unfavorable.

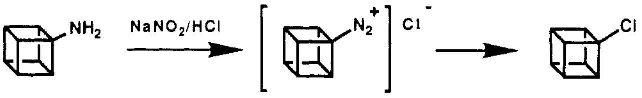
1. The geometry about the cation carbon is very far from the preferable planar arrangement. A planar cation has a pyramidalization angle of 0 °C; if the cubyl cation carbon had the same geometry as a carbon in the parent hydrocarbon its pyramidalization angle would be 35°.[2] Even the 1-norbornyl cation is "flatter"; its pyramidalization angle would be 24° if the geometry were the same as at the norbornane bridgehead.[3]

2. The exocyclic orbitals in cubane are s-rich, Forming a cation from a hybrid orbital is more difficult the greater the s character therein. The carbon orbital in the central CH bond of isobutane, that in the bridgehead CH bond of norbornane, and those in the CH bonds of cubane are estimated from $J_{^{13}C-H}$ to have about 25%, 28%, and 31% s character, respectively.[4,5]

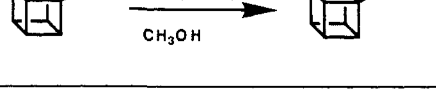
3. Although the vicinal CH bonds eclipse the empty orbital in cubyl cation, hyperconjugation would require high-energy, cubene-like structures.[6]

4. Ab initio calculations (6-31G*, but without electron correlation) place cubyl cation about 20 kcal/mol higher in energy than *tert*-butyl cation and about 5 kcal/mol above 1-norbornyl cation.[7]

Nevertheless, numerous reactions have been observed that might involve the intermediacy of cubyl cation: (1) decomposition of cubyl diazonium salts,[4a,8]



(2) photolytic solvolysis of iodocubanes,[9]



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[1] Dedicated to Prof. Christoph Rüchardt on the occasion of his 60th birthday.

[2] Defined as 90° − θ, where θ is any one of the three equal angles between the three bonds originating at the cation carbon and an axis chosen to pass through it (cf.: Radziszewski, J. G.; Downing, J. W.; Wentrup, C.; Kaszynski, P.; Jawdosiuk, M.; Kovacic, P.; Michl, J. *J. Am. Chem. Soc.* **1984**, *106*, 7996).

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