

Hans-Beat Bürgi in Strasbourg – the story of an encounter

Jean-Marie Lehn*

Institute for Advanced Study (USIAS), University of Strasbourg, BP 70028, 8 Allée Gaspard Monge, Strasbourg, Alsace 67083 Cedex, France. *Correspondence e-mail: lehn@unistra.fr

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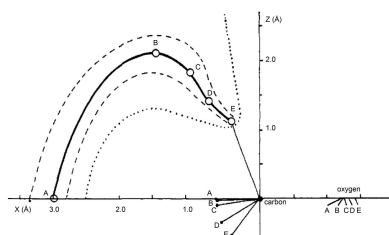
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It happened that the scientific path of Hans-Beat Bürgi crossed ours in Strasbourg. Here is the story.

From 1968 to 1980, we had been pursuing *ab initio* molecular quantum computational studies using the *ab initio* SCF-LCAO-MO (Hartree–Fock) program *IBMOL*. This program had been developed around the mid-1960s by Enrico Clementi at IBM with the collaboration of Alain Veillard, who subsequently joined our Chemistry Department at the University of Strasbourg and brought the program to Strasbourg (thus initiating quantum chemistry at our university). Thanks to the availability of the *IBMOL* program, a series of *ab initio* quantum chemical studies were pursued in my group, concerning especially nitrogen inversion barriers, electronic structures and stereo-electronic effects in organic molecules [for a review, see Lehn (1970)].

At the beginning of the 1970s, Hans-Beat Bürgi, then a PhD student in the laboratory of Jack Dunitz at the ETH in Zurich, Switzerland, was examining the working hypothesis that data obtained from static crystal structures may provide a picture of the changes that occur along the pathway of a chemical reaction. These ideas were applied to derive the minimum-energy pathways for two types of inorganic reaction, ligand addition (Bürgi, 1973) and ligand removal (Bürgi *et al.*, 1975), at non-carbon tetrahedral centres, as well as for nucleophilic addition/elimination reactions at carbonyl (Bürgi *et al.*, 1973). The results suggested that important features of the minimum-energy paths were largely independent of the nature of the central atom and of the ligands but were characteristic of the reaction type.

In 1973, Hans-Beat spent several months in my group in Strasbourg to perform quantum chemical computations using the *IBMOL* program, with the goal of providing theoretical support in favour of the conjecture that crystal structures could indeed provide information about the pathway of nucleophilic reaction at a carbonyl group. Stemming from data on the positioning of nitrogen sites with respect to carbonyl groups in various crystal structures, the trajectory of the first step, the approach of the two reagents, in the condensation of an amine with an aldehyde or a ketone could be pictured (Bürgi *et al.*, 1973). The crystal structures were taken as frozen snapshots on a dynamic evolution from the starting reactants to their products for at least a major part of the process. Of course, the conjecture would acquire a much broader significance if it could be extended to a whole set of different chemical reactions.



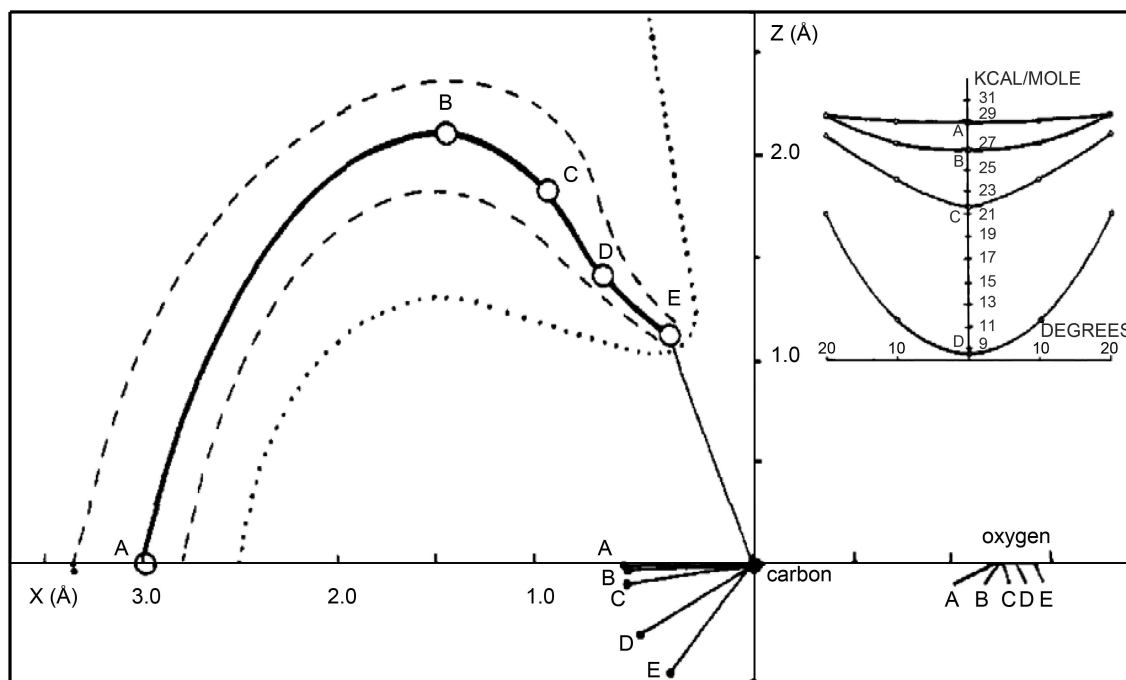


Figure 1

(Left) The minimum-energy path for the addition of a hydride ion to formaldehyde. The points A, B, C, D, E correspond to $\text{H}^- \cdots \text{C}$ distances of 3.0, 2.5, 2.0, 1.5 and 1.12 Å, respectively, for which the calculated binding energies (relative to infinitely separated $\text{H}^- + \text{CH}_2\text{O}$) are 19.4, 21.2, 26.7, 39.9 and 48.4 kcal mol⁻¹, respectively. The dashed and dotted curves show paths that are 0.6 and 6.0 kcal mol⁻¹ higher than the minimum-energy path. (Right) Energy profiles for lateral angular displacements out of the XZ plane. Reprinted with permission from Bürgi *et al.* (1974), copyright (1974) Elsevier.

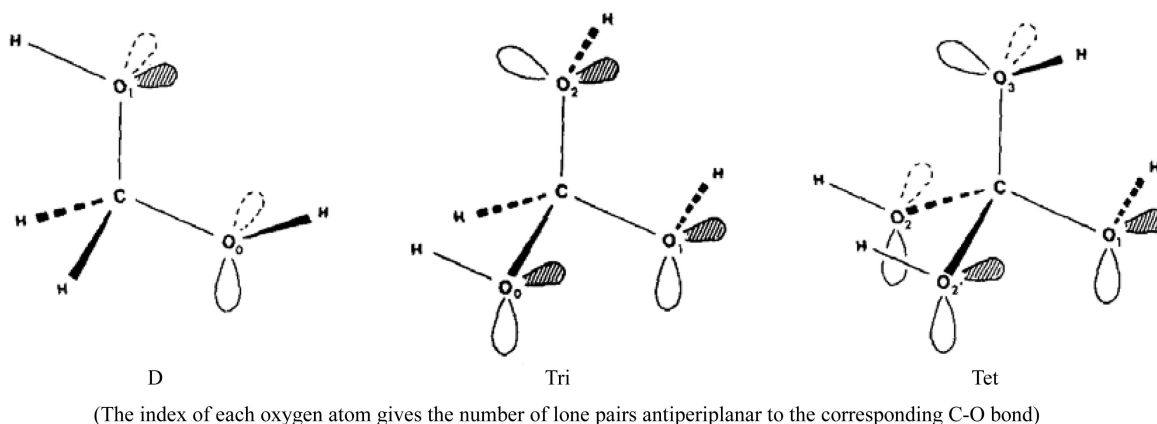


Figure 2

The study of stereoelectronic effects in hydroxymethanes. Reproduced with permission from Lehn *et al.* (1974), copyright (1974), John Wiley & Sons Inc.

The study performed by Hans-Beat together with Georges Wipff, then a graduate student in my group, concerned the ‘idealized’ case of the approach of a hydride ion H^- to the carbonyl group of formaldehyde. The then available computers made such drastic simplification compulsory for *ab initio* calculations with a reasonably extended basis set of atomic orbitals. The results are pictured in Fig. 1 and the analysis of the pathway led to the identification of three steps: (i) electrostatic guided approach along the direction of the carbonyl group in the plane of the molecule at a distance larger than 3 Å; (ii) contact with the H atoms of the formaldehyde molecule leading to the path curving out of the plane in the intermediate domain between 3 and 2.5 Å; (iii) finally, bond formation at an angle leading to a methoxide ion at short

distances below 2.5 Å. These results were reported in two papers [Bürgi *et al.* (1974) and Bürgi *et al.* (1974)].

The tetrahedral intermediate resulting from the addition of a nucleophile to a carbonyl group also has a major significance in the reactivity of imines, esters and, most importantly, amides in both organic chemistry and biochemistry. The stereoelectronic properties of the tetrahedral intermediates formed in ester and amide hydrolysis and their effect on reactivity, susceptible to operating on the intimate features of enzymatic reactions on ester and peptide bonds, were the subject of extensive theoretical studies by Georges Wipff in his PhD work, using as models the adduct of water with formic acid and formamide (Lehn *et al.*, 1974; Lehn & Wipff, 1974; 1980). In this context, Hans-Beat took part in studies on

hydroxymethanes, where methanetriol may be taken as a model of the tetrahedral intermediate in ester hydrolysis (Fig. 2) (Lehn *et al.*, 1974).

The amine–carbonyl condensation process, a pillar of organic reactions, and its electronic features have gained further significance as an emblematic reversible reaction in the subsequent development of dynamic covalent chemistry.

Thus was our very enjoyable common scientific story at the triple meeting point of chemical reactivity, crystal structures and quantum chemical computations. And so it is for me a great pleasure to wish Hans-Beat a very Happy 80th Birthday!

It happens that it has also become a fitting occasion to pay tribute to the great scientist and sharp mind, Jack Dunitz, who passed away on 12 September 2021.

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