Is it possible that a Lewis acid has revolving acid strengths?

B. Kovács[1], É. Dorkó[2], B. Kótai[2], A. Domján[2], T. Soós[2]

[1] *NMR and Structure Analysis Research Group, Department of Organic and Macromolecular Chemistry, Ghent University*

[2] *Hungarian Academy of Sciences, Research Centre for Natural Sciences, Institute of Organic Chemistry, Budapest, Hungary*

Affiliation: Benjamin.Kovacs@UGent.be

Introduction

The idea of Frustrated Lewis pair (FLP) chemistry is based on the notion that the combinations of Lewis acids and bases which are sterically prevented from forming classical Lewis acid–base adducts (Fig. 1) have Lewis acidity and basicity available for interaction with a third molecule. This concept has been extended to provide homogeneous, metal-free catalysis including reactions like hydrogenation, hydroamination, and CO_2 reduction [1,2]. Moreover, a certain group of triaryl boranes substituted with F or Cl in each *orto* position (Fig. 2, the roman numbers refer to the total number of fluorines), showed to be somewhat water tolerant as well, thus applicable *e. g.* for reductive amination [3] in which water is a byproduct. Since these boranes have at least one assymetrically substituted ring, that means a multifarious environment for the accessing Lewis base what directly leads to the possibility for the complex to manifest multifarious conformation. (In our work piperidine was chosen as model amine). The steric and electronic relations always depend on the pathway of adduction. Accordingly, since the Gibbs free energies for complexation are different in each case we face a peculiar situation: multiple Lewis acid strengths can be derived for a single Lewis acid within the same reaction. Therefore, our main goal was to identify the conformers of the above mentioned triaryl borane – piperidine adducts. Besides the theoretical delicacy (what emerged from merely the definiton of Lewis acidity) the proof of the concept would bring us closer to influence the stereoselectivity of a reaction by designing the steric and electronic relations properly [4]. In addition, if these conformations are at dynamic equilibrium, the multiple acid strengths of the Lewis acid are even oscillating in time. That would indirectly reflect the ”frustrated” feature of the complex, thus may support the relative catalytic effectiveness of the triaryl boranes in question. Herein the results for the borane II – piperidine system will be presented in details, but a comparison with the adducts of boranes I and III will be given in the Conclusion.

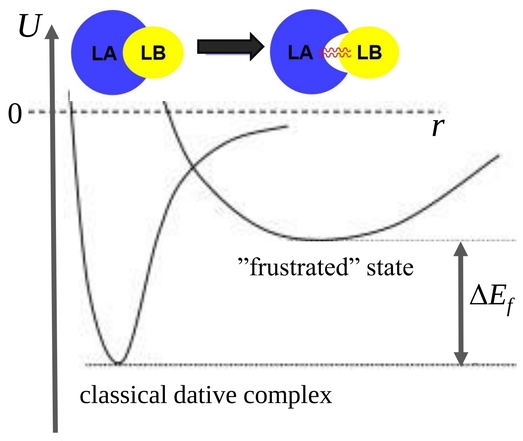


Figure 1: Schematic potential curves illustrate the difference between the classical bonding and the ” frustrated” state [2]

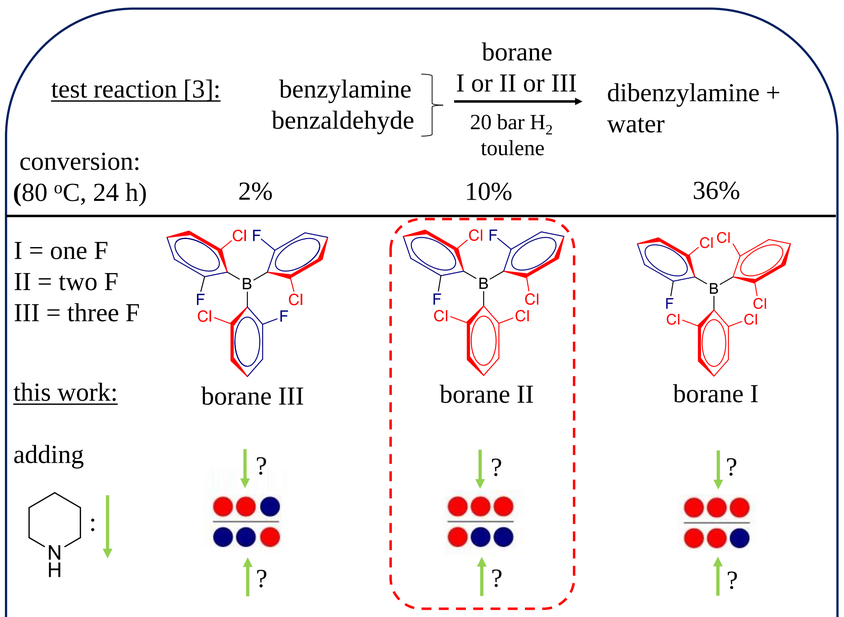


Figure 2: the asymmetrically substituted boranes catalysed reductive amination though their effectiveness differed (up). The piperidine experience multifariuos environment when it is accessing towards these Lewis acids. Only the most stable borane conformations are depicted (down).

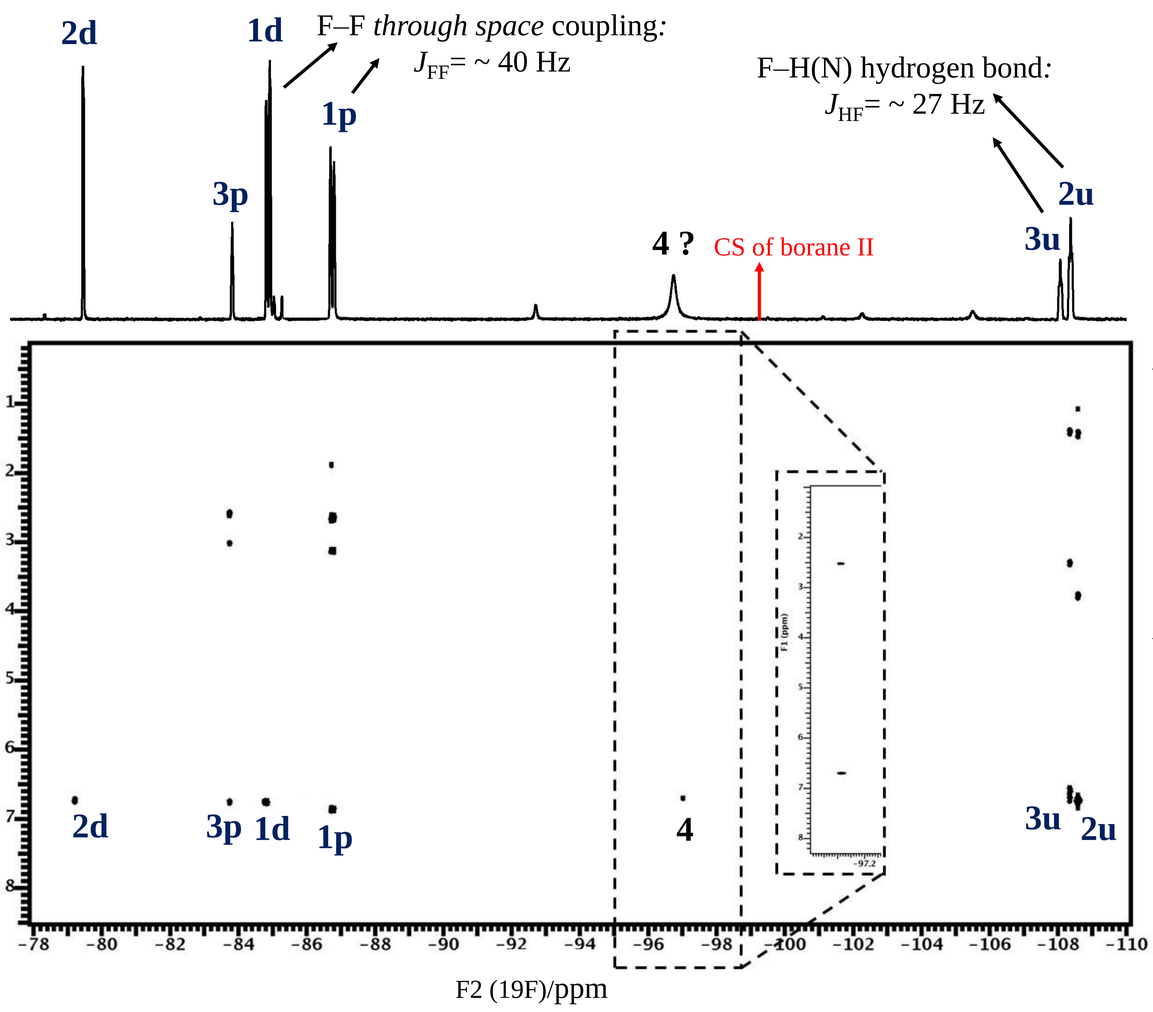
Methods

Theoretical: The experiments were preceded by Monte Carlo conformational search which was followed by *ab initio* (level of theory: B3LYP-D3/6-311G(d,p)) geometry optimization. The respective calculated Gibbs free energies of adduction (ΔG_a) characterized the stability of each complex conformation. Theoretical normalized Boltzmann factors could be derived from these values which – after their comparison with the observed ones – validated the assignment (Table 1). Another useful tool was the calculation of chemical shielding properties (level of theory: B3LYP-D3/6-311+G(2d,p)). *Experimental:* For the assignment 19F spectra were recorded, and 19F DOSY and 19F-1H HOESY experiments were also carried out, while 2D EXSY measurements provided information about dynamical exchange phenomena.

Results

We see that several peaks appeared in the 19F spectrum of the borane II – piperidine mixture, not only two. Each complex conformer (totally three, marked with arabic numbers) is represented by two peaks with matching intensities. The chemical shifts (and partly the hyperfine structures) reflect the orientation of the respective fluorinated ring. If the fluorine is pointing upwards (”u”) to the H(N) of the piperidine, so forms hydrogen bond with it, a lower 19F chemical shift is experienced. If the adjacent chlorine does so (then the fluorine is pointing downwards: ”d”), or if the ring is remoted (perpendicular-like position: ”p”) from the piperidine’s H(N), a higher chemical shift can be measured (check: figures in the red frame). The error of the calculated 19F chemical shifts showed to be ring orientation dependent, and were consistently ~11 ppm for the ”d”, ~14 ppm for the ”p” and ~18 ppm for the ”u” positions. (As that was the case for the borane I – piperidine and borane III – piperidine complex conformers as well.) There is a lone peak close to the position of the borane II’s (respective 19F spectrum recorded beforehand), which gives weak correlations with the aliphatic protons of piperidine in the 19F-1H HOESY spectrum. Per the results of the DOSY measurements ($D_4 < D_1 \sim D_2 \sim D_3 < D_{\text{borane II}}$) it likely represents the ”frustrated” state.

19F spectrum (273 K)

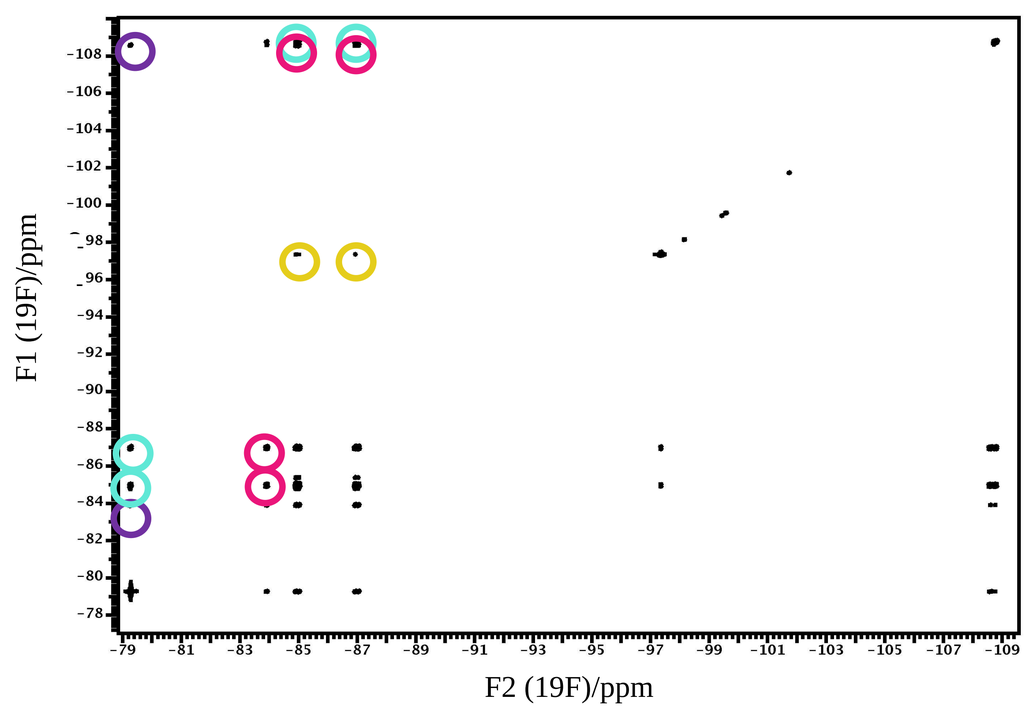


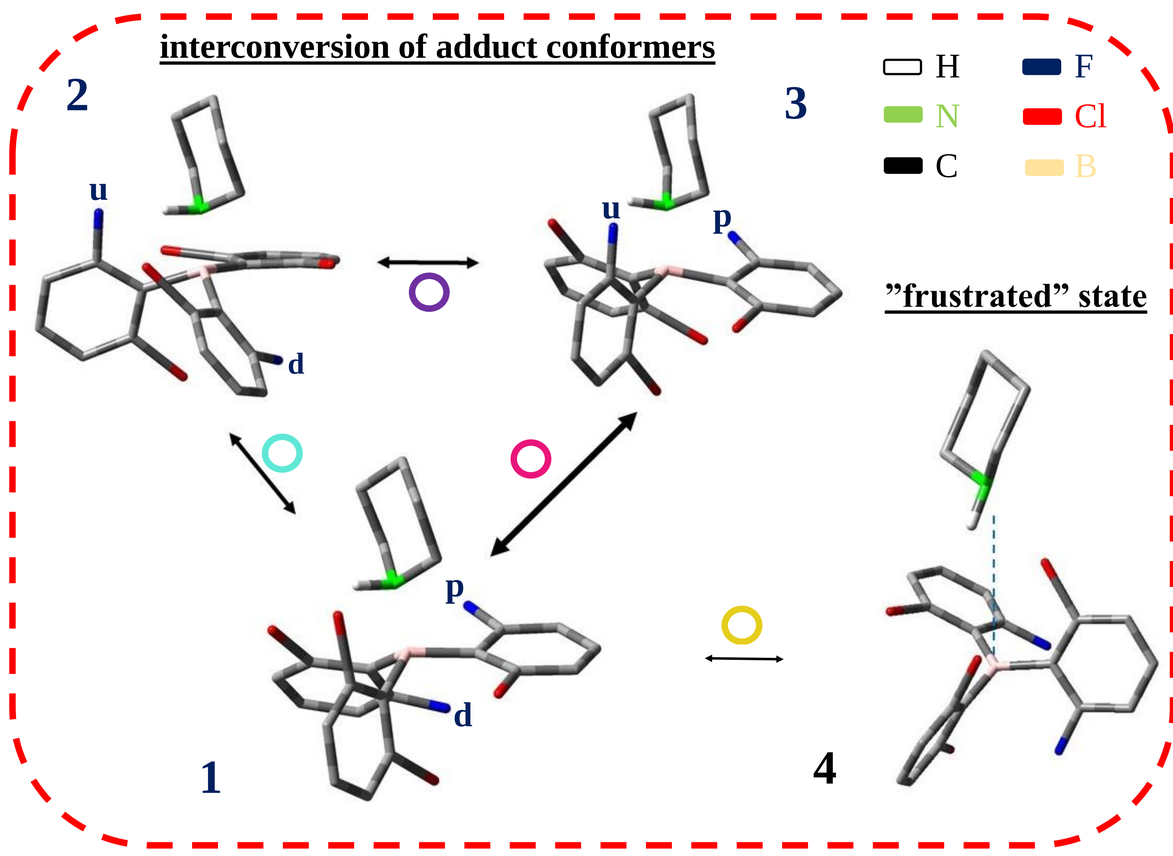
19F-1H HOESY (273 K, mixing time: 500 ms)

Results

After the assignment the 2D EXSY experiments disclosed exchange relations. In the summarizing scheme with the red frame the size of the black arrows between the identified structures qualitatively reflect the relative ratio of the exhange phenomena. The values were sort out by the stepwise raise of the mixing time. The cross peaks indicating the same exchange were marked with the same color.

2D 19F EXSY (303 K, mixing time: 800 ms)





Form	ΔG_a /kcal·mol^{-1}	X_t	X_o
1	2,5	0,54	0,53
2	2,8	0,32	0,30
3	3,3	0,14	0,17

Table 1: the comparison of the theoretical (X_t) and observed (X_o) normalized Boltzmann factors (298 K) confirmed the assignment

Conclusion

The revolving Lewis acidity of the chosen Lewis acid has been disclosed, since the theoretical prognostisations and experimental observations were in great agreement. The ratio of the three borane II – piperidine adduct conformations suggests that the preferred pathway for the adduction is when three chlorines point towards the piperidine (since 1 is the most stable). Moreover, the ”frustrated” feature of the system was not merely pointed out indirectly by the exchange of the Lewis pair conformers, but also in a direct fashion, what never had been successful before using NMR spectroscopy. The summarized investigations were performed with the borane III – piperidine and borane I – piperidine Lewis pairs as well. Those adducts manifested four and three conformations respectively, and the ”frustrated” state for the former was also identifiable directly. On the timescales of the EXSY measurements (up to 1000 ms) no exchange phenomena could be discovered between the borane III – piperidine complex conformers. On the other hand, the borane I – piperidine Lewis pair is so floppy, that above 273 K the forms were still in *fast* exchange, so only their average was detectable. By these results we can say that for these complexes the level of ”frustration” is decreasing with the number of the fluorines and that is perfectly reflected in their catalytic effectiveness (Fig. 2).

References:

[1] Stephan, D. W., *Acc. Chem. Res.*, 2015, *48*, 306–316; [2] T. A. Rokob *et al.*, *Angew. Chem., Int. Ed.* 2008, *47*, 2435–2438;

[3] É. Dorkó *et al.*, unpublished; [4] Stephan, D. W., *J. Am. Chem. Soc.*, 2015, *137*, 10018–10032